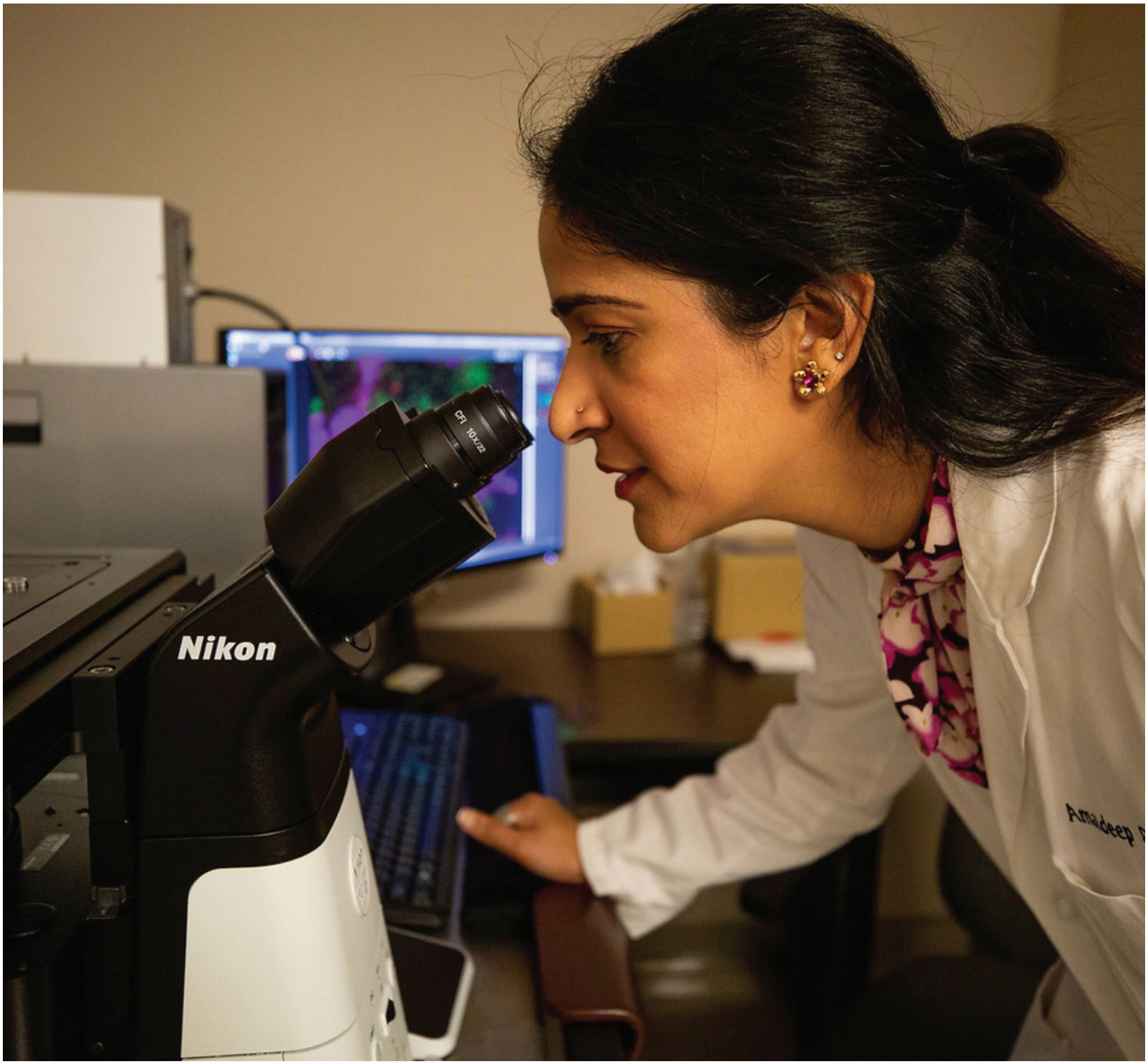
THE UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER

RESEARCH

Institutional Research Core Facilities

FY22 Core Activity and Analysis Reports



THE UNIVERSITY OF TENNESSEE
HEALTH SCIENCE CENTER

Research Core Facilities Activities and Analysis Reports

Seventh Analysis, FY22 (July 2021-June 2022)

Published February 2023

Prepared by:

Dr. Tiffany N. Seagroves
Associate VC for Research—Core Labs

Jacqueline Toney
Director of Finance and Administration, Office of Research

Natalie Smith, MS
Assistant Director, Finance and Administration
Business Manager, FCCS, RHC, mBIO, MedChem, MRC, AIC, RHC and RBL cores

Detric Stigall
Business Manager, LACU

Lee Ferguson
Director,Communications and Marketing, Office of Research

Table of Contents

Introduction

The purpose of the annual Institutional Core Facilities activities and analysis reports is to cultivate the research enterprise at The University of Tennessee Health Science Center by reporting on core financial stability, key core accomplishments and the tangible and intangible return on investment in institutional core facilities by the state of Tennessee and the institution. The ultimate goal of reporting core activities and summarizing the financial overview of each core is to optimize operations of the institutional core facilities.

The procedure for performing this analysis for fiscal year 2022 (FY22) [July 2021-June 2022] was as follows:

- The core directors and business managers submitted initial drafts of the annual core activity and core analysis reports in early October 2022 (after closeout of FY22 ledgers).
- During October-December 2022, the Associate VC for Research—Core Labs reviewed the reports with core directors and business managers and requested updates or corrections.
- The financial tables in the Executive Summary were approved by the Assistant Director and Director of Finance and Administration for the Office of Research (Natalie Smith and Jacqueline Toney) on January 27, 2023.
- In February 2023, Dr. Seagroves created the final versions of the reports.
- The final report drafts were presented to the VC for Research serving during FY22 (Steve Goodman, PhD) and to the current Interim VC for Research (Wesley Byerly, PharmD) on February 15, 2023.
- After revisions based on comments received, the Director of Communications and Marketing for the Office of Research (Lee Ferguson) collated the final copies of the reports for publication in March of 2023.

As noted in the body of the reports, there were several operational and financial achievements accomplished in FY22. Highlights are as follows:

- All cores were recommended to continue as Institutional Cores. However, it was recommended that the MPMS unit of the PMC be re-classified as a COM-administered core.
- During the continuation of the COVID-19 pandemic throughout FY22, all Institutional Cores remained operational as the cores were broadly considered to be essential services to support research.
- The total operational budget for the cores in FY22 was increased by $913,000 over FY21 levels; these state appropriation funds were divided among the cores based on the size of each core's operating budget.
- Five institutional cores, the Molecular Resource Center (MRC), the Lab Animal Care Unit (LACU), the Regional Biocontainment Lab (RBL), the Molecular Bioinformatics (mBIO) Core and the Proteomics and Untargeted Metabolomics Unit of the Proteomics and Metabolomics Core (PMC) ended FY22 with net income after accounting for subsidies from the Tennessee Higher Education Commission (THEC; MRC) and the institution, respectively. Five cores/units ended in a net deficit: Flow Cytometry and Cell Sorting (FCCS), Research Histology Core (RHC), Medicinal Chemistry (MedChem) Core, the Metabolic Phenotyping Mass Spectrometry Unit (MPMS) of the PMC, and the Advanced Imaging Core (AIC).

- Overall, the year-end net subsidy required to operate the institutional cores, excluding MRC THEC funds, which rollover to the MRC THEC budget each year, decreased from a deficit $172,357 in FY21 to a surplus of $179,679 in FY22 (Table 1). The primary drivers of the surplus were unfilled personnel positions in the LACU and RBL, and the increased revenues for animal per diem charges in the LACU.
- Three cores were allocated a smaller budget in FY22 than in FY21, the MedChem, AIC and FCCS cores. In FY21, the large deficit for the AIC was due to purchase of the Zeiss Elyra 7 instrument; however, in FY22, the AIC was allocated only $2,418 in operational funds. Similarly, the operational budgets for MedChem and FCCS cores were decreased in FY22 relative to FY21, resulting in larger deficits in FY22 than in FY21. The budgets for these three cores should be revised to reflect their actual operating costs.
- The Regional Biocontainment Lab (RBL) continued to respond to the COVID-19 pandemic by supporting new research projects on behalf of a variety of organizations, including several commercial entities and external academic users. The RBL generated $567,520 in revenues in FY22 while decreasing operating expenses by >$300,000, leading to a net income of $197,718.
- The LACU generated a record $3,245,108 in total revenues, $180,686 more than in FY21.
- The FCCS core director re-submitted a shared instrumentation (S10) grant proposal to acquire a new Thermo Bigfoot cell sorter (spectral and conventional laser instrument) in the FCCS core to replace the aging BD Biosciences Aria IIu cell sorter. As of February 2023, the proposal is awaiting a funding decision.
- Two new grants supported by the AIC were awarded (PI: Jon Jaggar).
- In general, individual core budgets require rebalancing within the constraints of the total operating budget, in order to reconcile budgets across cores so that they are aligned with projected operating expenses and revenues based upon several years of historical data.
- For the first time since these reports have been generated in FY16, the institutional cores operating budget was sufficient to operate the nine shared resource facilities. However, it should be noted that unfilled personnel positions contributed the most significantly to this surplus, and as the job market stabilizes, savings from unfilled positions cannot be relied upon to balance the operating budget.

-**Table 1** overviews FY over FY comparisons of the aggregated cores' operating budgets. **Appendices A-G** overview the details of each individual unit's operating budget for each individual FY since these reports have been generated, beginning with FY16 (**Appendix A**) and concluding with FY22 (**Appendix G**).

TABLE 1

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
COMPARISON FY2016, FY2017, FY2018, FY2019, FY2020, FY2021, FY2022

	EXPENSE BUDGET	INCOME BUDGET	NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *Income / (Subsidy) without MRC, if THEC rollover*	EXPENDITURES FUNDED BY OTHER SOURCES	TOTAL Income/(Subsidy)
FY2016 TOTAL ALL ACCOUNTS:	2,255,575	(275,000)	1,980,575	5,498,507	(3,444,744)	(73,188)	1,276,817	(1,350,005)
FY2017 TOTAL ALL ACCOUNTS:	2,141,183	(161,528)	1,979,655	5,615,825	(3,516,189)	(119,981)	387,243	(507,224)
FY2018 TOTAL ALL ACCOUNTS:	2,553,788	(306,393)	2,247,395	6,539,617	(2,876,389)	(1,447,171)	715,703	(2,162,874)
FY2019 TOTAL ALL ACCOUNTS:	2,678,048	(327,538)	2,350,510	6,272,412	(3,140,272)	(831,034)	-	(831,034)
FY2020 TOTAL ALL ACCOUNTS:	2,543,266	(61,373)	2,481,893	6,389,938	(3,396,176)	(560,140)	-	(560,140)
FY2021 TOTAL ALL ACCOUNTS:	$ 2,572,123	(95,850)	3,219,610	7,772,001	(4,231,048)	(172,357)	-	(172,357)
FY2022 TOTAL ALL ACCOUNTS:	$ 3,709,901	(142,570)	3,576,303	7,557,027	(4,169,375)	179,679	-	179,679

Increase (Decrease) Comparison FY2016 through FY2022

	EXPENSE BUDGET	INCOME BUDGET	NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *Income / (Subsidy) without MRC, if THEC rollover*	EXPENDITURES FUNDED BY OTHER SOURCES	FY over FY TOTAL NET SUBSIDY Increase/(Decrease)
Increase (Decrease) from FY2016 to FY2017	**(114,392)**	**(113,472)**	**(920)**	**117,318**	**71,445**	**46,793**	**(889,574)**	**(842,781)**
Increase (Decrease) from FY2017 to FY2018	**412,605**	**144,865**	**267,740**	**923,792**	**(639,800)**	**1,327,190**	**328,460**	**1,655,650**
Increase (Decrease) from FY2018 to FY2019	**124,260**	**21,145**	**103,115**	**(267,205)**	**263,883**	**(616,137)**	**(715,703)**	**(1,331,840)**

*FOOTNOTE: FY16 data is included as Appendix A, FY17 data as Appendix B, FY18 data as Appendix C and FY19 data as Appendix D, FY20 data as Appendix E and FY21 data as Appendix F and FY22 data as Appendix G.

-The institution allocated additional funding for core operations in FY22. The net total operating budget for the cores increased by $405,267 in FY22 ($3,576,303) over FY21 levels ($3,171,339) (**Appendix G**). As previously noted, in FY22, the reduction in operating expenses, primarily due to unfilled personnel positions, was the primary driver of the net surplus. Expenses also decreased from $7,772,008 in FY21 to $7,557,027 in FY22 (a reduction of ~$220,981). Revenues in FY22 ($4,169,375) decreased slightly (~1.4%) from FY21 levels ($4,231,048).

As indicated in **Table 1**, multiple sources of funding (subsidy) are necessary to supplement core revenues/external income from service fee recoveries. Since the vice chancellor for research startup funds were expended by the close of FY18, the only funds available in the FY19-FY20 budgets to invest in new core equipment were dollars from the indirect cost return to the Office of Research. Sponsored programs/research expenditures experienced record growth from FY19-FY22. The FY20 indirect cost return to the Office of Research (based on FY19 research expenditures) was used to purchase the Zeiss Elyra 7 super resolution microscope system for the Advanced Imaging Core, which began offering super resolution microscopy services to the research community in January of 2021. Although grants and contracts awards increased between FY20-FY22, there was a halt of indirect cost return to the Office of Research. Therefore, there is currently no budget for investments in new core equipment, or for the replacement of old/outdated equipment for the institutional core facilities.

The Office of Research continues to leverage its partnership with the UT Foundation Sr. Director of Development for UTHSC, and UTHSC Assistant Vice Chancellor for Strategic Initiatives & Advancement Services (Greg Harris) as a model to generate new sources of funding, such as directly fundraising for institutional core facility needs and building relationships with vendors to negotiate future gift-in-kind discounts. Since FY19, the Office of Research has been actively preparing multiple federal-level grant proposals focused on research infrastructure, including S10 shared instrumentation grants (submitted by the FCCS and PMC). In Q2 of FY22, an NIH R24 “Modern Equipment for Shared-use Biomedical Research Facilities” proposal was submitted by the LACU, and was awarded in Q1 of FY23. The goal of this R24 funding is to improve animal care facilities, leading to improved health of live animals. Modernized equipment that will be purchased includes automated watering, and new cage washers. In addition, the RBL received a G20 infrastructure award from NIAID that began in August of 2022. This funding will be used to purchase new scientific equipment to enhance existing services and to provide new services related to whole animal imaging and immunological assays. In addition, Dr. Goodman prepared a multi-million dollar US Department of Commerce, Economic Development Administration (EDA) “Good Jobs Challenge” proposal, which included new equipment/infrastructure for core facilities, as well as animal husbandry initiatives, which together would offer local workforce technical training opportunities. Although unfunded, these types of multi-million dollar proposals that leverage our growing relationships with our regional academic and industrial partners are novel approaches to upgrading our shared resource facilities, while also providing workforce development opportunities. The training of advanced degree students for long-term careers in shared resource facilities, which includes use of high-end instrumentation, is one key component of the current strategic plan of the Federation of American Societies for Experimental Biology (FASEB).

We hope that these reports are helpful to The University of Tennessee Health Science Center community.

APPENDIX A

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2016

Unrestricted

ACCT NO.	ACCOUNT NAME	FY16 EXPENSE BUDGET (includes PO carryover)	FY16 INCOME BUDGET	FY16 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)	TOTAL income/(subsidy)
E070160	LABORATORY ANIMAL CARE UNIT (LACU)	791,397	(150,000)	641,397	3,442,706	(2,795,576)	(5,733)		(5,733)
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	5,000	(5,000)	0	4,714	(12,832)	8,118		8,118
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	738,532	(120,000)	618,532	779,033	(195,120)	34,619		34,619
	PROTEOMICS AND METABOLOMICS CORE (PMC)	0	0	0	0	0	0	1,074,817	(1,074,817)
E070167001	MOLECULAR BIOINFORMATICS	71,531	0	71,531	101,967	(39,478)	9,042		9,042
	SUBTOTAL UNRESTRICTED ACCOUNTS	***1,606,460***	***(275,000)***	***1,331,460***	***4,328,420***	***(3,043,006)***	***46,046***	***1,074,817***	***(1,028,771)***

Restricted

ACCT NO.	ACCOUNT NAME	FY16 EXPENSE BUDGET		FY16 THEC FUNDED & ADJUSTED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *Rollover / (Subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)	TOTAL MRC THEC Rollover/(Subsidy)
R070167013	MOLECULR RESOURCE CENTER (MRC) of Excellence FY16	649,115		649,115	1,170,087	(401,738)	(119,234)	202,000	(321,234)
	SUBTOTAL RESTRICTED ACCOUNT	***649,115***	***-***	***649,115***	***1,170,087***	***(401,738)***	***(119,234)***	***202,000***	***(321,234)***
	TOTAL ALL ACCOUNTS:	**$ 2,255,575**	**$ (275,000)**	**$ 1,980,575**	**$ 5,498,507**	**$ (3,444,744)**	**$ (73,188)**	**$ 1,276,817**	**$ (1,350,005)**

(a) Funded by VC Research start-up

Orbitrap Lumos Mass Spectrometer for PMC	**1,027,150**
D. Kakhniashvili, PMC Director, salary 12/15/15 - 6/30/16	**47,667**
Total PMC:	**$1,074,817**
NexGen500 Sequencing System/Illumina, for MRC	202,000
Total MRC:	**$202,000**

APPENDIX B

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2017

Unrestricted

ACCT NO.	ACCOUNT NAME	FY17 EXPENSE BUDGET	FY17 INCOME BUDGET	FY17 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES *(a)*	TOTAL income/(subsidy)
E070160	LABORATORY ANIMAL CARE (LACU)	610,729	(20,300)	590,429	3,401,781	(2,805,431)	(5,921)	0	(5,921)
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	15,000	(15,000)	0	75,998	(24,320)	(51,678)	286,592	(338,270)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	697,204	(70,000)	627,204	784,798	(221,535)	63,941	0	63,941
E070170	PROTEOMICS AND METABOLOMICS CORE (PMC)	90,640	0	90,640	149,277	(26,470)	(32,167)	0	(32,167)
E070174	MOLECULAR BIOINFORMATICS (mBIO)	73,495	(5,000)	68,495	134,902	(30,006)	(36,401)	0	(36,401)
E070175	RESEARCH HISTOLOGY CORE (RHC)	5,000	(5,000)	0	35,290	0	(35,290)	0	(35,290)
	SUBTOTAL UNRESTRICTED ACCOUNTS	***1,492,068***	***(115,300)***	***1,376,768***	***4,582,046***	***(3,107,762)***	***(97,516)***	***286,592***	***(384,108)***

Restricted

ACCT NO.	ACCOUNT NAME	FY17 EXPENSE BUDGET (includes FY16 PO carryover)	FY16 PO carryover	FY17 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *Rollover / (Subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES *(a)*	TOTAL MRC THEC Rollover/(Subsidy)
R070167014	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY17	649,115	(46,228)	602,887	1,033,779	(408,427)	(22,465)	100,651	(123,116)
	SUBTOTAL RESTRICTED ACCOUNT	***649,115***	***(46,228)***	***602,887***	***1,033,779***	***(408,427)***	***(22,465)***	***100,651***	***(123,116)***
	TOTAL ALL ACCOUNTS:	**$ 2,141,183**	**$ (161,528)**	**$ 1,979,655**	**$ 5,615,825**	**$ (3,516,189)**	**$ (119,981)**	**$ 387,243**	**$ (507,224)**

(a) **Funded by VC Research start-up**

YETI Flow Cytometry Analyzer	286,592
Total FCCS:	**$286,592**
STARlet NexGen Sequencing System/Hamilton	100,651
Total MRC:	**$100,651**

APPENDIX C

INSTITUTIONAL CORE LAB BUDGET BALANCES VICE CHANCELLOR FOR RESEARCH

FISCAL YEAR END 2018

Unrestricted

ACCT NO.	ACCOUNT NAME	FY18 EXPENSE BUDGET	FY18 INCOME BUDGET	FY18 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)		TOTAL income/(subsidy)
E070160	LABORATORY ANIMAL CARE (LACU)	865,209	(150,000)	715,209	3,946,369	(2,351,047)	(880,113)	550,952	*	(1,431,065)
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	16,890	(16,890)	0	166,094	(28,892)	(137,202)	0		(137,202)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	807,969	(70,000)	737,969	1,170,295	(130,680)	(301,646)	0		(301,646)
E070170	PROTEOMICS AND METABOLOMICS CORE (PMC)	93,360	0	93,360	163,712	(37,827)	(32,525)	0		(32,525)
E070174	MOLECULAR BIOINFORMATICS (mBIO)	67,302	(5,000)	62,302	132,520	(30,046)	(40,172)	0		(40,172)
E070175	RESEARCH HISTOLOGY CORE (RHC)	77,937	(59,503)	18,434	94,718	(19,663)	(56,621)	0		(56,621)
E070176	MEDICINAL CHEMISTRY CORE (MedChem)	5,000	(5,000)	0	12,725	(13,833)	1,108	164,751	*	(163,643)
	SUBTOTAL UNRESTRICTED ACCOUNTS	***1,933,667***	***(306,393)***	***1,627,274***	***5,686,433***	***(2,611,988)***	***(1,447,171)***	***715,703***		***(2,162,874)***

Restricted

ACCT NO.	ACCOUNT NAME	FY18 EXPENSE BUDGET	FY17 PO carryover	FY18 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *Rollover / (Subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)		TOTAL MRC THEC Rollover/(Subsidy)
R079700143	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY18	620,121	-	620,121	853,184	(264,401)	31,338			31,338
	SUBTOTAL RESTRICTED ACCOUNT	***620,121***	***-***	***620,121***	***853,184***	***(264,401)***	***31,338***	***-***		***31,338***
	TOTAL ALL ACCOUNTS:	**$ 2,553,788**	**$ (306,393)**	**$ 2,247,395**	**$ 6,539,617**	**$ (2,876,389)**	**$ (1,415,833)**	**$ 715,703**	*	**$ (2,131,536)**
	OVERALL NET DEFICIT, EXCLUDING THEC ROLLOVER									**$ (2,162,874)**

*** Additional Institutional Support**

Funded by VC Research Start-up and UTHSC New	
and replacement Animal Caging	550,952
Total LACU:	**$550,952**
Funded by VC Research-MedChem Core Setup Salary	
Support-MedChem	80,000
Dell Desktop and Laptop	3,808
Discover SP Microwave System	19,967
Reveleris Prep System	53,123
Digital Melting Pot, Thermosci, Stirrer Mantle	7,854
Total MedChem:	**164,751**
TOTAL:	**715,703**

APPENDIX D

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2019

Unrestricted

ACCT NO.	ACCOUNT NAME	FY19 EXPENSE BUDGET	FY19 INCOME BUDGET	FY19 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES *(a)*		TOTAL income/(subsidy)
E070160	LABORATORY ANIMAL CARE (LACU)	894,864	(150,000)	744,864	3,791,590	(2,640,045)	(406,681)			(406,681)
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	18,513	(18,513)	0	126,532	(25,745)	(100,787)			(100,787)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	825,465	(70,000)	755,465	951,231	(108,047)	(87,719)			(87,719)
E070170	PROTEOMICS AND METABOLOMICS CORE (PMC)	95,694	0	95,694	139,814	(40,930)	(3,190)			(3,190)
E070174	MOLECULAR BIOINFORMATICS (mBIO)	126,971	(5,000)	121,971	163,119	(16,661)	(24,487)			(24,487)
E070175	RESEARCH HISTOLOGY CORE (RHC)	79,025	(79,025)	0	129,931	(11,018)	(118,913)			(118,913)
E070176	MEDICINAL CHEMISTRY CORE (MedChem)	5,000	(5,000)	0	119,438	(30,181)	(89,257)			(89,257)
	SUBTOTAL UNRESTRICTED ACCOUNTS	***2,045,532***	***(327,538)***	***1,717,994***	***5,421,655***	***(2,872,627)***	***(831,034)***	***0***		***(831,034)***

Restricted

ACCT NO.	ACCOUNT NAME	FY19 EXPENSE BUDGET	FY18 PO carryover	FY19 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *Rollover / (Subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES		TOTAL MRC THEC Rollover/(Subsidy)
R079700143	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY19	632,516	-	632,516	850,757	(267,645)	49,404	0		49,404
	SUBTOTAL RESTRICTED ACCOUNT	***632,516***	***-***	***632,516***	***850,757***	***(267,645)***	***49,404***	***-***		***49,404***
	TOTAL ALL ACCOUNTS:	**$ 2,678,048**	**$ (327,538)**	**$ 2,350,510**	**$ 6,272,412**	**$ (3,140,272)**	**$ (781,630)**	***0***	*	**$ (781,630)**
	OVERALL NET DEFICIT, EXCLUDING THEC ROLLOVER									**$ (831,034)**

APPENDIX E

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2020

Unrestricted

ACCT NO.	ACCOUNT NAME	FY20 EXPENSE BUDGET	FY20 INCOME BUDGET	FY20 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)		TOTAL income/(subsidy)
E070160002	LABORATORY ANIMAL CARE (LACU)	858,840	(30,000)	828,840	3,952,325	(2,891,915)	(231,570)			(231,570)
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	19,844	(19,844)	0	199,646	(30,499)	(169,147)	0		(169,147)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	755,371	(20,000)	735,371	888,434	(195,215)	42,152			42,152
E070179	PROTEOMICS AND METABOLOMICS CORE (PMC)/MPMS UNIT	97,608	0	97,608	230,744	(70,947)	(62,189)			(62,189)
E070182	MOLECULAR BIOINFORMATICS (mBIO)	128,980	(5,000)	123,980	156,125	(15,784)	(16,361)			(16,361)
E070184	RESEARCH HISTOLOGY CORE (RHC)	34,414	(34,414)	0	75,345	(24,136)	(51,209)			(51,209)
E070185	MEDICINAL CHEMISTRY CORE (MedChem)	6,312	(6,312)	0	85,546	(13,730)	(71,816)			(71,816)
						0				
	SUBTOTAL UNRESTRICTED ACCOUNTS	***1,901,369***	***(115,570)***	***1,785,799***	***5,588,165***	***(3,242,226)***	***(560,140)***	***0***		***(560,140)***

Restricted

ACCT NO.	ACCOUNT NAME	FY20 EXPENSE BUDGET	FY19 PO carryover	FY20 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *Rollover / (Subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES		TOTAL MRC THEC Rollover/(Subsidy)
R079700143	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY20	641,897	54,197	696,094	801,773	(153,950)	48,271	0		48,271
	SUBTOTAL RESTRICTED ACCOUNT	***641,897***	***54,197***	***696,094***	***801,773***	***(153,950)***	***48,271***	***-***		***48,271***
	TOTAL ACROSS ALL ACCOUNTS:	**$ 2,543,266**	**$ (61,373)**	**$ 2,481,893**	**$ 6,389,938**	**$ (3,396,176)**		***0***		
	OVERALL NET DEFICIT, EXCLUDING THEC ROLLOVER									**$ (560,140)**

APPENDIX F

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2021

Unrestricted

ACCT NO.	ACCOUNT NAME	FY21 EXPENSE BUDGET	FY21 INCOME BUDGET	FY21 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a)*	TOTAL income/(subsidy)
E070160002	LABORATORY ANIMAL CARE (LACU)	858,840	(30,000)	1,075,284	3,900,980	(3,064,422)	238,726	-	238,726
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	19,844	(20,570)	64,760	217,136	(32,824)	(119,552)	-	(119,552)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	755,371	(20,000)	1,029,459	1,838,975	(827,598)	18,082	-	18,082
E070179	PROTEOMICS AND METABOLOMICS CORE (PMC)-PROTEOMICS UNIT	98,535	0	138,942	110,341	(15,326)	43,927	-	43,927
E070182	MOLECULAR BIOINFORMATICS (mBIO)	128,980	(5,000)	150,538	111,321	(17,241)	56,458	-	56,458
E070184	RESEARCH HISTOLOGY CORE (RHC)	34,414	(34,414)	12,045	79,927	(23,568)	(44,314)	-	(44,314)
E070185	MEDICINAL CHEMISTRY CORE (MedChem)	6,312	(6,312)	26,070	96,384	(36,370)	(33,944)	-	(33,944)
E070186	METABOLIC PHENOTYPING MASS SPECTROMETRY (MPMS) UNIT OF PMC	22,000	(22,175)	7,828	80,841	(41,216)	(31,797)	-	(31,797)
E070187	ADVANCED IMAGING CORE (AIC)	0	(5,650)	18,586	481,567	(5,080)	(457,901)	-	(457,901)
						0			
	SUBTOTAL UNRESTRICTED ACCOUNTS	***1,924,296***	***(144,121)***	***2,523,512***	***6,917,472***	***(4,063,645)***	***(330,315)***	***0***	***(330,315)***
E070183	*ADDITIONAL OPERATIONAL FUNDS*			157,958					157,958
	NET SUBTOTAL UNRESTRICTED ACCOUNTS	**1,924,296**	**(144,121)**	**2,681,470**	**6,917,472**	**(4,063,645)**	**(330,315)**	**0**	**$ (172,357)**

Restricted

ACCT NO.	ACCOUNT NAME	FY21 EXPENSE BUDGET	FY20 THEC CARRYOVER	FY21 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES	TOTAL MRC THEC Rollover/(Subsidy)
R079700143	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY21, THEC appropriation	647,827	48,271	696,098	854,529	(167,403)	8,971	-	8,971
	SUBTOTAL RESTRICTED ACCOUNT	***647,827***	***48,271***	***696,098***	***854,529***	***(167,403)***	***8,971***	***-***	***8,971***
	TOTAL ACROSS ALL ACCOUNTS:	**$ 2,572,123**	**$ (95,850)**	**$ 3,219,610**	**$ 7,772,001**	**$ (4,231,048)**	**$ 8,971**	***0***	**$ 8,971**
	OVERALL NET DEFICIT, EXCLUDING THEC ROLLOVER								**$ (172,357)**

APPENDIX G

INSTITUTIONAL CORE LAB BUDGET BALANCES
VICE CHANCELLOR FOR RESEARCH
FISCAL YEAR END 2022

Unrestricted

ACCT NO.	ACCOUNT NAME	FY22 EXPENSE BUDGET	FY22 INCOME BUDGET	FY22 NET STATE FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES (*a*)	TOTAL income/(subsidy)
E070160002	LABORATORY ANIMAL CARE (LACU)	1,385,501	(30,000)	1,355,501	4,303,550	(3,245,108)	297,059	-	297,059
E070161	FLOW CYTOMETRY and CELL SORTING (FCCS)	29,442	(19,844)	9,598	192,206	(31,533)	(151,075)	-	(151,075)
E070165	REGIONAL BIOCONTAINMENT LAB (RBL)	1,178,859	(20,000)	1,158,859	1,528,661	(567,520)	197,718	-	197,718
E070179	PROTEOMICS AND METABOLOMICS CORE (PMC)-PROTEOMICS UNIT	150,325	0	150,325	130,261	(40,135)	60,199	-	60,199
E070182	MOLECULAR BIOINFORMATICS (mBIO)	196,580	(5,000)	191,580	159,347	(15,847)	48,080	-	48,080
E070184	RESEARCH HISTOLOGY CORE (RHC)	51,060	(34,414)	16,646	67,373	(13,261)	(37,466)	-	(37,466)
E070185	MEDICINAL CHEMISTRY CORE (MedChem)	13,253	(6,312)	6,941	71,943	(15,545)	(49,457)	-	(49,457)
E070186	METABOLIC PHENOTYPING MASS SPECTROMETRY (MPMS) UNIT OF PMC	32,642	(22,000)	10,642	53,358	(21,140)	(21,576)	-	(21,576)
E070187	ADVANCED IMAGING CORE (AIC)	7,418	(5,000)	2,418	120,922	(11,785)	(106,719)	-	(106,719)
						0			
	SUBTOTAL UNRESTRICTED ACCOUNTS	***3,045,080***	***(142,570)***	***2,902,510***	***6,627,621***	***(3,961,874)***	***236,763***	***0***	***236,763***
E070183	*ADDITIONAL OPERATIONAL FUNDS*			0					0
	NET SUBTOTAL UNRESTRICTED ACCOUNTS	**3,045,080**	**(142,570)**	**2,902,510**	**6,627,621**	**(3,961,874)**	**236,763**	**0**	**$ 236,763**

Restricted

ACCT NO.	ACCOUNT NAME	FY22 EXPENSE BUDGET	FY21 THEC CARRYOVER	FY22 THEC FUNDED BUDGET	Cumulative Actual Expenses	Cumulative Internal Recovery & External Income	THEC BUDGET BALANCE *income / (subsidy)*	EXPENDITURES FUNDED BY OTHER SOURCES	TOTAL MRC THEC Rollover/(Subsidy)
R079700143	MOLECULAR RESOURCE CENTER (MRC) of Excellence, FY21, THEC appropriation	664,821	8,972	673,793	929,406	(207,501)	(48,112)	-	(48,112)
	SUBTOTAL RESTRICTED ACCOUNT	***664,821***	***8,972***	***673,793***	***929,406***	***(207,501)***	***(48,112)***	***-***	***(48,112)***
	TOTAL ACROSS ALL ACCOUNTS:	**$ 3,709,901**	**$ (133,598)**	**$ 3,576,303**	**$ 7,557,027**	**$ (4,169,375)**	**$ (48,112)**	***0***	**$ (48,112)**

OVERALL NET DEFICIT, EXCLUDING THEC ROLLOVER	**$ 188,651**
OVERALL NET DEFICIT, INCLUDING FY21 ROLLOVER	**$ 179,679**

Lab Animal Care Unit (LACU) Institutional Research Core Facility Analysis Report- FY22

Written by David Hamilton, DVM; Detric Stigall; Joyce Jones; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?
The LACU core designation as an institutional core is appropriate since it served 103 internal users across 20 departments within five colleges (COM, COP, CON, COHP and COD) and three external users (US Biologic, Diatech Diabetics, and Dr. Joel Bumgardner of the University of Memphis and Diatech Diabetics).

2. Does the core pass the multi-departmental, multi-investigator litmus test?
Yes. Service was provided to 103 unique internal users across 20 departments within five colleges (COM, COP, CON, COHP and COD). The LACU also served three external users. The top four departments ranked by their contribution to FY22 core internal revenues were, in order, the Department of Physiology (20.65%, COM), the Department of Pediatrics (17.29%, COM), the Department of Genetics, Genomics and Informatics (13.65%, COM), and the Department of Anatomy and Neurobiology (9.70%, COM). The other 16 departments collectively accounted for 38.71% of all internal revenues. The top five users, based on FY22 invoices for completed services accounted for 23.88% of internal revenues. These investigators were: 1) Hao Chen (6.65%, Pharmacology, COM), 2) Rob Williams (6.12%, GGI, COM), 3) Adebiyi Adebowale (4.31%, Physiology, COM), 4) Amadeep Bajwa (3.50%, Transplant Surgery, COM) and 5) Zhongjie Sun (3.30%, Physiology, COM).

3. Is there sufficient intra- and inter-departmental use and if not, why?
Yes. There were 103 unique internal users who were served across 20 departments within five colleges at UTHSC.

4. Can the services for the core be outsourced more economically?
No. There is no competition for this institutional core facility since it is the only accredited unit that can provide services for animal care and welfare on the UTHSC campus. There are three other institutions in Memphis that support research using laboratory animals (the VA, the University of Memphis, and St. Jude Children's Research Hospital), but the majority of UTHSC investigators do not have faculty appointments at these institutions.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g., grants funded through investigator use, publications, etc.)?
Yes. In FY22, core activities led to 94 unique PubMed-indexed publications and supported 112 extramural grants and contracts. The LACU also provided training and orientation to animal use in research to 70 investigators and research staff in FY22.

6. Is the core currently self-sufficient, or is it subsidized by the Institution?
In FY22, the core was subsidized by the Institution. After accounting for the state appropriation ($1,355,501), the total net income was $297,058.

Accomplishments this past year:

- The LACU veterinary team continued regularly scheduled hands-on training classes for the campus. Two different hands-on labs are offered: one in basic rodent techniques and

one in aseptic surgical technique. A total of 23 rodent technique and 9 aseptic technique laboratories were held in FY22 for a total of 70 research staff trained.

- The LACU continued with its goal of technician training and education leading to certification by the American Association for Laboratory Animal Science (AALAS). As of FY22, 50% of husbandry technicians are AALAS certified, with those not certified being new hires who are attending training classes to achieve certification. In addition, several cage wash technicians have also obtained certification.
- Dr. Katy Phillip published the manuscript: **Phillip K**, Nair N, Samanta K, Azevedo JF, Brown GD, Petersen CA, Gomes-Solecki M. Maternal transfer of neutralizing antibodies to B. burgdorferi OspA after oral vaccination of the rodent reservoir. Vaccine. 2021 Jul 13;39(31):4320-4327. doi: 10.1016/j.vaccine.2021.06.025. Epub 2021 Jun 23. PMID: 34172332; PMCID: PMC8495753.
- Dr. Cameron Fili published the manuscript: **Fili CV**, Lin L, Chapman J, **Hamilton D**, Yates CR. Methylsulfonylmethane and Sesame Seed Oil Improve Dyslipidemia and Modulate Polyunsaturated Fatty Acid Metabolism in Two Mouse Models of Diabetes. J Med Food. 2022 Jun;25(6):607-617. doi: 10.1089/jmf.2021.0196. PMID: 35708633; PMCID: PMC9247677.
- Dr. Brianne Hibl presented two posters at the 72nd National American Association for Laboratory Animal Science (AALAS) Meeting in Kansas City, Missouri October 17-21, 2021:
    - **Hibl, Brianne M**; Perkins, Cheryl L.; Henderson, Kenneth S.; **Hamilton, David J**. *Shake-and-Bake Health Monitoring: An Alternative to Soiled Bedding Mouse Sentinels for Racks Not Compatible with Exhaust Plenum Sampling*
    - **Hibl, Brianne M**; Perkins, Cheryl L.; Henderson, Kenneth S.; **Hamilton, David J.** *Use of a modified external in-line exhaust collection device for detection of murine pathogens within a double-sided ventilated rack.*
- Dr. David Hamilton received notice of award for a $320,468 federal award (1R24OD033718-01), *Modernization of the UTHSC Animal Care Facility,* to help modernize the TriMetis animal facility. This grant will allow the installation of an automated watering system, to deliver quality water to all animals in the facility and decrease the reliance on water bottles. The budget will include the purchase of water drinking valves, to outfit all ventilated rodent racks already present in the facility.
- The LACU core supported numerous publications, abstract presentations and extramural and intramural awards. A total of 95 manuscripts were published in FY22 in which animal work was conducted on the UTHSC campus.
- The LACU continued its mission of education by participating in coursework related to animals in research, orienting new faculty and staff to the animal care facilities, and providing hands-on training to laboratory personnel.
- The LACU maintained its quality level of animal care and investigator support during the COVID-19 pandemic. The LACU instituted some procedural changes in terms of cage change out frequencies to permit an altered schedule for LACU technicians, to help support social distancing in order to decrease the risk of COVID-19 infection. No mandate to euthanize research animals in response to the pandemic was initiated at UTHSC, in contrast to many other research institutions in the country.

Financial overview:

TOTALS	FY19	FY20	FY21	FY22
Revenues	2,640,045	2,891,915	3,064,422	3,245,107
Expenses	(3,791,590)	(3,952,325)	(3,900,980)	(4,303,550)
Income (Subsidy)	(1,151,545)	(1,060,410)	(836,558)	(1,058,443)
Equipment	0	0	0	0
Net Income (Subsidy)	(1,151,545)	(1,060,410)	(836,558)	(1,058,443)
State Appropriation	744,864	828,840	1,075,284	1,355,501
Net Income (Subsidy)	(406,681)	(231,570)	238,726	297,058
Other Expense (Caging FY18)	0	0	0	0
Net Income (Subsidy)	(406,681)	(231,570)	238,726	297,058
Subsidy, % before State Appropriation	30.3%	26.8%	21%	25%
Subsidy, % after State Appropriation	10.72%	5.9%	0%	0%

7. Suggested outcomes:

It is recommended that the LACU continue as an institutional core.

Laboratory Animal Care Unit (LACU) Institutional Core Facility
Summary of institutional Core Activities for FY22

Written by David Hamilton, DVM; Detric Stigall; Joyce Jones; and Tiffany Seagroves, PhD

I. PUBLICATIONS (Journal publication dates: July 1, 2021 to June 30, 2022)
Full-length published articles (**UTHSC faculty investigators who used the LACU are indicated in boldt**; **LACU staff are underlined**)

Maron BJ, Desai MY, Nishimura RA, Spirito P, Rakowski H, **Towbin JA**, Rowin EJ, Maron MS, Sherrid MV. Diagnosis and Evaluation of Hypertrophic Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022 Feb 1;79(4):372-389. doi:10.1016/j.jacc.2021.12.002. PMID: 35086660.

Maron BJ, Desai MY, Nishimura RA, Spirito P, Rakowski H, **Towbin JA**, Dearani JA, Rowin EJ, Maron MS, Sherrid MV. Management of Hypertrophic Cardiomyopathy: JACC State-of-the-Art Review. J Am Coll Cardiol. 2022 Feb 1;79(4):390-414. doi:10.1016/j.jacc.2021.11.021. PMID: 35086661.

Kumar S, Kumar P, Kodidela S, Duhart B, Cernasev A, Nookala A, Kumar A, **Singh UP**, Bissler J. Racial Health Disparity and COVID-19. J Neuroimmune Pharmacol.2021 Dec;16(4):729-742. doi: 10.1007/s11481-021-10014-7. Epub 2021 Sep 9. PMID:34499313; PMCID: PMC8426163.

Williams EG, Pfister N, Roy S, Statzer C, Haverty J, Ingels J, Bohl C, Hasan M, Cuklina J, Buhlmann P, Zamboni N, **Lu L**, Ewald CY, **Williams RW**, Aebersold R. Multiomic profiling of the liver across diets and age in a diverse mouse population. Cell Syst. 2022 Jan 19;13(1):43-57.e6. doi:10.1016/j.cels.2021.09.005. Epub 2021 Oct 18. PMID: 34666007; PMCID: PMC8776606.

Conde-Dusman MJ, Dey PN, Ela-Zudaire, Rabaneda LG, Garcia-Lira C, Grand T,Briz V, Velasco ER, Andero R, Nierola S, Barco A, Paoletti P, Wesseling JF, Gardoni F, **Tavalin SJ**, Perez-Otao I. Control of protein synthesis and memory by GluN3A-NMDA receptors through inhibition of GIT1/mTORC1 assembly. Elife. 2021Nov 17;10:e71575. doi: 10.7554/eLife.71575. PMID: 34787081; PMCID: PMC8598234.

Liao FF, Lin G, Chen X, Chen L, Zheng W, Raghow R, **Zhou FM**, Shih AY, Tan XL. Endothelial Nitric Oxide Synthase-Deficient Mice: A Model of Spontaneous Cerebral Small-Vessel Disease. Am J Pathol. 2021 Nov;191(11):1932-1945. doi:10.1016/j.ajpath.2021.02.022. Epub 2021 Mar 10. PMID: 33711310; PMCID:PMC8647425.

Kumar V, Kiran S, **Kumar S**, **Singh UP**. Extracellular vesicles in obesity and its associated inflammation. Int Rev Immunol. 2022;41(1):30-44. doi:10.1080/08830185.2021.1964497. Epub 2021 Aug 23. PMID: 34423733; PMCID:PMC8770589.

Zhang L, Hu J, Meshkat BI, Liechty KW, **Xu J**. LncRNA MALAT1 ModulatesTGF-ß1-Induced EMT in Keratinocyte. Int J Mol Sci. 2021 Oct 30;22(21):11816.doi: 10.3390/ijms222111816. PMID: 34769245; PMCID: PMC8584148.

Kumari R, Irudayam MJ, Al Abdallah Q, Jones TL, Mims TS, **Puchowicz MA**, **Pierre JF**, **Brown CW**. SMAD2 and SMAD3 differentially regulate adiposity and the growth of subcutaneous white

adipose tissue. FASEB J. 2021 Dec;35(12):e22018. doi:10.1096/fj.202101244R. PMID: 34731499.

Ware SM, Bhatnagar S, Dexheimer PJ, Wilkinson JD, Sridhar A, Fan X, Shen Y, Tariq M, Schubert JA, Colan SD, Shi L, Canter CE, Hsu DT, Bansal N, Webber SA, Everitt MD, Kantor PF, Rossano JW, Pahl E, Rusconi P, Lee TM, **Towbin JA**, Lal AK, Chung WK, Miller EM, Aronow B, Martin LJ, Lipshultz SE; Pediatric Cardiomyopathy Registry Study Group. The genetic architecture of pediatric cardiomyopathy. Am J Hum Genet. 2022 Feb 3;109(2):282-298. doi: 10.1016/j.ajhg.2021.12.006. Epub 2022Jan 12. PMID: 35026164; PMCID: PMC8874151.

Trotter C, Kim H, Farage G, Prins P, **Williams RW**, Broman KW, Seno. Speeding up eQTL scans in the BXD population using GPUs. G3 (Bethesda). 2021 Dec8;11(12):jkab254. doi: 10.1093/g3journal/jkab254. PMID: 34499130; PMCID:PMC8664437.

Hama T, Nagesh PK, Chowdhury P, Moore BM 2nd, Yallapu MM, Regner KR, **Park F**. DNA damage is overcome by TRIP13 overexpression during cisplatin nephrotoxicity. JCI Insight. 2021 Nov 22;6(22):e139092. doi: 10.1172/jci.insight.139092. PMID:34806647; PMCID: PMC8663775.

Sharp BM, Fan X, Redei EE, **Mulligan MK**, Chen H. Sex and heredity are determinants of drug intake in a novel model of rat oral oxycodone self-administration. Genes Brain Behav. 2021 Nov;20(8):e12770. doi:10.1111/gbb.12770. Epub 2021 Sep 16. PMID: 34459088; PMCID: PMC8815756.

DeJarnette C, Meyer CJ, Jenner AR, Butts A, Peters T, Cheramie MN, Phelps GA, Vita NA, Loudon-Hossler VC, Lee RE, **Palmer GE**. Identification of Inhibitors of Fungal Fatty Acid Biosynthesis. ACS Infect Dis. 2021 Dec 10;7(12):3210-3223.doi: 10.1021/acsinfecdis.1c00404. Epub 2021 Nov 17. PMID: 34786940; PMCID:PMC8670506.

Sumida K, Han Z, Chiu CY, Mims TS, **Bajwa A**, Demmer RT, Datta S, Kovesdy CP, **Pierre JF**. Circulating Microbiota in Cardiometabolic Disease. Front Cell Infect Microbiol. 2022 May 3;12:892232. doi: 10.3389/fcimb.2022.892232. PMID: 35592652;PMCID: PMC9110890.

Skaar DA, Dietze EC, Alva-Ornelas JA, Ann D, Schones DE, Hyslop T, SistrunkC, Zalles C, Ambrose A, Kennedy K, Idassi O, **Miranda Carboni G**, Gould MN, Jirtle RL, Seewaldt VL. Epigenetic Dysregulation of KCNK9 Imprinting and Triple-Negative Breast Cancer. Cancers (Basel). 2021 Nov 30;13(23):6031. doi:10.3390/cancers13236031. PMID: 34885139; PMCID: PMC8656495.

Chintanaphol M, Orgil BO, Alberson NR, **Towbin JA**, **Purevjav E**. Restrictive cardiomyopathy: from genetics and clinical overview to animal modeling. Rev Cardiovasc Med. 2022 Mar 17;23(3):108. doi: 10.31083/j.rcm2303108. PMID:35345275.

Chen K, **Sun Z**. Estrogen inhibits renal Na-Pi Co-transporters and improves klotho deficiency-induced acute heart failure. Redox Biol. 2021 Nov;47:102173.doi: 10.1016/j.redox.2021.102173. Epub 2021 Oct 18. PMID: 34678656; PMCID:PMC8577443.

Singla B, Aithabathula RV, Kiran S, Kapil S, **Kumar S**, **Singh UP**. Reactive Oxygen Species in Regulating Lymphangiogenesis and Lymphatic Function. Cells.2022 May 26;11(11):1750. doi: 10.3390/cells11111750. PMID: 35681445; PMCID:PMC9179518.

Perkins RS, Suthon S, **Miranda-Carboni GA**, **Krum SA**. WNT5B in cellular signaling pathways. Semin Cell Dev Biol. 2022 May;125:11-16. doi:10.1016/j.semcdb.2021.09.019. Epub 2021 Oct 9. PMID: 34635443.

Xu F, Gao J, Orgil BO, Bajpai AK, Gu Q, **Purevjav E**, Davenport AS, **Li K**, **Towbin JA**, Black DD, **Pierre JF**, **Lu L**. Ace2 andTmprss2 Expressions Are Regulated by Dhx32 and Influence the Gastrointestinal Symptoms Caused by SARS-CoV-2. J Pers Med. 2021 Nov 16;11(11):1212. doi: 10.3390/jpm11111212.PMID: 34834564; PMCID: PMC8621576.

Pierre JF, Phillips GJ, Chandra LC, Rendina DN, Thomas-Gosain NF, Lubach GR, Lyte M, Coe CL, **Gosain A**. Lyticase Facilitates Mycobiome Resolution Without Disrupting Microbiome Fidelity in Primates. J Surg Res. 2021 Nov;267:336-341.doi: 10.1016/j.jss.2021.06.023. Epub 2021 Jun 26. PMID: 34186310; PMCID:PMC8678161.

Rich TC, **Xin W**, Leavesley SJ, Francis CM, Taylor M. Ion Channel-Based Reporters for cAMP Detection. Methods Mol Biol. 2022;2483:265-279. doi:10.1007/978-1-0716-2245-2_17. PMID: 35286682.

Shrestha AP, **Vaithianathan T**. Tracking the dynamics of single fused synaptic vesicle proteins from a single ribbon active zone in zebrafish retinal bipolar cells. STAR Protoc. 2022 Jan 20;3(1):101107. doi: 10.1016/j.xpro.2021.101107.PMID: 35098163; PMCID: PMC8783205.

Myers LK, Winstead M, Kee JD, Park JJ, Zhang S, **Li W**, **Yi AK**, Stuart JM, Rosloniec EF, Brand DD, Tuckey RC, Slominski AT, Postlethwaite AE, Kang AH.1,25-Dihydroxyvitamin D3 and 20-Hydroxyvitamin D3 Upregulate LAIR-1 and Attenuate Collagen Induced Arthritis. Int J Mol Sci. 2021 Dec 12;22(24):13342.doi: 10.3390/ijms222413342. PMID: 34948139; PMCID: PMC8709360.

Hala D, Petersen LH, Huggett DB, **Puchowicz MA**, Brunengraber H, Zhang GF. Overcompensation of CoA Trapping by Di(2-ethylhexyl) Phthalate (DEHP)Metabolites in Livers of Wistar Rats. Int J Mol Sci. 2021 Dec 16;22(24):13489.doi: 10.3390/ijms222413489. PMID: 34948286; PMCID: PMC8709406.

Goldberg LR, Yao EJ, Kelliher JC, Reed ER, Wu Cox J, Parks C, Kirkpatrick SL, Beierle JA, Chen MM, Johnson WE, Homanics GE, **Williams RW**, Bryant CD, **Mulligan MK**. A quantitative trait variant in Gabra2 underlies increased methamphetamine stimulant sensitivity. Genes Brain Behav. 2021 Nov;20(8):e12774.doi: 10.1111/gbb.12774. Epub 2021 Oct 22. PMID: 34677900; PMCID: PMC9083095.

Rybak JM, Sharma C, Doorley LA, Barker KS, **Palmer GE**, Rogers PD. Delineation of the Direct Contribution of Candida auris ERG11 Mutations to Clinical Triazole Resistance. Microbiol Spectr. 2021 Dec 22;9(3):e0158521. doi:10.1128/Spectrum.01585-21. Epub 2021 Dec 8. PMID: 34878305; PMCID: PMC8653815.

Samak G, Rao R, **Rao R**. Lactobacillus casei and Epidermal Growth Factor Prevent Osmotic Stress-Induced Tight Junction Disruption in Caco-2 Cell Monolayers. Cells. 2021 Dec 18;10(12):3578. doi: 10.3390/cells10123578. PMID:34944085; PMCID: PMC8700399.

Suthon S, Lin J, Perkins RS, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**. Estrogen receptor alpha and NFATc1 bind to a bone mineral density-associated SNto repress WNT5B in

osteoblasts. Am J Hum Genet. 2022 Jan 6;109(1):97-115. doi:10.1016/j.ajhg.2021.11.018. Epub 2021 Dec 13. PMID: 34906330; PMCID: PMC8764205.

Neilson DE, Zech M, Hufnagel RB, Slone J, Wang X, Homan S, Gutzwiller LM, Leslie EJ, Leslie ND, **Xiao J**, Hedera P, LeDoux MS, Gebelein B, Wilbert Feckenweiler M, Winkelmann J, Gilbert DL, Huang T. A Novel Variant of ATP5MC3Associated with Both Dystonia and Spastic Paraplegia. Mov Disord. 2022Feb;37(2):375-383. doi: 10.1002/mds.28821. Epub 2021 Oct 11. PMID: 34636445;PMCID: PMC8840961.

Sun QW, **Sun Z**. Stem cell therapy for pulmonary arterial hypertension: An update. J Heart Lung Transplant. 2022 Jun;41(6):692-703. doi:10.1016/j.healun.2022.02.020. Epub 2022 Mar 6. PMID: 35341679; PMCID:PMC9133091.

Dietrich P, Alli S, **Mulligan MK**, Cox R, **Ashbrook DG**, **Williams RW**, **Dragatsis I**. Identification of cyclin D1 as a major modulator of 3-nitropropionic acid-induced striatal neurodegeneration. Neurobiol Dis. 2022 Jan;162:105581. doi:10.1016/j.nbd.2021.105581. Epub 2021 Dec 3. PMID: 34871739; PMCID: PMC8717869.

Gu Q, Xu F, Orgil BO, Khuchua Z, Munkhsaikhan U, Johnson JN, Alberson NR, **Pierre JF**, Black DD, Dong D, Brennan JA, Cathey BM, Efimov IR, **Towbin JA**, **Purevjav E**, **Lu L**. Systems genetics analysis defines importance oTMEM43/LUMA for cardiac- and metabolic-related pathways. Physiol Genomics. 2022 Jan 1;54(1):22-35. doi: 10.1152/physiolgenomics.00066.2021. Epub2021 Nov 12. PMID: 34766515; PMCID: PMC8721901.

Kiran S, Rakib A, **Singh UP**. The NLRP3 Inflammasome Inhibitor Dapansutril Attenuates Cyclophosphamide-Induced Interstitial Cystitis. Front Immunol. 2022Jun 3;13:903834. doi: 10.3389/fimmu.2022.903834. PMID: 35720309; PMCID:PMC9205468.

Bhattacharya S, Yin J, Yang C, Wang Y, Sims M, **Pfeffer LM**, Chaum E. STAT3 suppresses the AMPK±/ULK1-dependent induction of autophagy in glioblastoma cells. J Cell Mol Med. 2022 Jul;26(14):3873-3890. doi: 10.1111/jcmm.17421. Epub2022 Jun 6. PMID: 35670018; PMCID: PMC9279602.

Meena AS, Shukla PK, Bell B, Giorgianni F, Caires R, Fernández-Peña C, Beranova S, Aihara E, Montrose MH, Chaib M, **Makowski L**, Neeli I, Radic MZ, **Vasquez V**, **Jaggar JH**, **Cordero-Morales JF**, **Rao R**. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID:PMC9250449.

Kumar A, Sinha N, Kodidela S, Zhou L, **Singh UP**, **Kumar S**. Effect of benzo(a)pyrene on oxidative stress and inflammatory mediators in astrocytes and HIV-infected macrophages. PLoS One. 2022 Oct 14;17(10):e0275874. doi:10.1371/journal.pone.0275874. PMID: 36240258; PMCID: PMC9565757.

Torres-Rojas C, Zhao W, Zhuang D, O'Callaghan JP, **Lu L**, **Mulligan MK**, **Williams RW**, **Jones BC**. Paraquat Toxicogenetics: Strain-Related Reduction of Tyrosine Hydroxylase Staining in Substantia Nigra in Mice. Front Toxicol.2021 Nov 11;3:722518. doi: 10.3389/ftox.2021.722518. PMID: 35295113; PMCID:PMC8915807.

Gunturkun MH, Flashner E, Wang T, **Mulligan MK**, **Williams RW**, Prins P, Chen H. GeneCup: mining PubMed and GWAS catalog for gene-keyword relationships. G3(Bethesda). 2022 May 6;12(5):jkac059. doi: 10.1093/g3journal/jkac059. PMID:35285473; PMCID: PMC9073678.

Luna-Tapia A, Parker JE, Kelly SL, **Palmer GE**. Species-Specific Differences in C-5 Sterol Desaturase Function Influence the Outcome of Azole Antifungal Exposure. Antimicrob Agents Chemother. 2021 Nov 17;65(12):e0104421. doi:10.1128/AAC.01044-21. Epub 2021 Sep 13. PMID: 34516249; PMCID: PMC8597749.

Flores-Torres AS, **Samarasinghe AE**. Impact of Therapeutics on Unified Immunity During Allergic Asthma and Respiratory Infections. Front Allergy. 2022Mar 25;3:852067. doi: 10.3389/falgy.2022.852067. PMID: 35386652; PMCID:PMC8974821.

Mitachi K, Mingle D, Effah W, Sanchez-Ruiz A, Hevener KE, **Narayanan R**, Clemons WM Jr, Sarabia F, Kurosu M. Concise Synthesis of Tunicamycin, ÄÖV and Discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID:35594368; PMCID: PMC9329268.

Bhuniya R, Yuan X, Bai L, Howie KL, Wang R, **Li W**, **Park F**, Yang CY. Design, Synthesis, and Biological Evaluation of Apcin-Based CDC20 Inhibitors. ACS Med Chem Lett. 2022 Jan 18;13(2):188-195. doi: 10.1021/acsmedchemlett.1c00544. PMID:35178174; PMCID: PMC8842116.

Shukla PK, Meena AS, **Pierre JF**, **Rao R**. Central role of intestinal epithelial glucocorticoid receptor in alcohol- and corticosterone-induced gut permeability and systemic response. FASEB J. 2022 Jan;36(1):e22061. doi:10.1096/fj.202101424R. PMID: 34861075; PMCID: PMC8647846.

Jha KA, Rasiah PK, Gentry J, Del Mar NA, Kumar R, **Adebiyi A**, **Reiner A**, **Gangaraju R.** Mesenchymal stem cell secretome protects against oxidative stress-induced ocular blast visual pathologies. Exp Eye Res. 2022 Feb;215:108930. doi:10.1016/j.exer.2022.108930. Epub 2022 Jan 10. PMID: 35016886.

Millet JRM, Romero LO, Lee J, Bell B, Vasquez V. C. elegans PEZO-1 is a mechanosensitive ion channel involved in food sensation. J Gen Physiol. 2022 Jan3;154(1):e202112960. doi: 10.1085/jgp.202112960. Epub 2021 Dec 2. PMID:34854875; PMCID: PMC8647359.

Xu J, Hu J, Idlett-Ali S, Zhang L, Caples K, Peddibhotla S, Reeves M, Zgheib C, Malany S, Liechty KW. Discovery of Small Molecule Activators of Chemokine Receptor CXCR4 That Improve Diabetic Wound Healing. Int J Mol Sci. 2022 Feb16;23(4):2196. doi: 10.3390/ijms23042196. PMID: 35216311; PMCID: PMC8879702.

Camors EM, Roth AH, Alef JR, Sullivan RD, Johnson JN, **Purevjav E**, **Towbin JA**. Progressive Reduction in Right Ventricular Contractile Function Attributable to Altered Actin Expression in an Aging Mouse Model of Arrhythmogenic Cardiomyopathy. Circulation. 2022 May 24;145(21):1609-1624. doi:10.1161/CIRCULATIONAHA.
120.049261. Epub 2022 Apr 19. PMID: 35437032; PMCID:PMC9133220.

Shukla PK, Meena AS, **Rao R**. Prevention and mitigation of alcohol-induced neuroinflammation by Lactobacillus plantarum by an EGF receptor-dependent mechanism. Nutr Neurosci. 2022

Apr;25(4):871-883. doi:10.1080/1028415X.2020.1819105. Epub 2020 Sep 18. PMID: 32945721; PMCID:PMC7969470.

Krutilina RI, Playa H, Brooks DL, Schwab LP, Parke DN, Oluwalana D, Layman DR, Fan M, Johnson DL, Yue J, Smallwood H, **Seagroves TN**. HIF-Dependent CKB Expression Promotes Breast Cancer Metastasis, Whereas Cyclocreatine Therapy Impairs Cellular Invasion and Improves Chemotherapy Efficacy. Cancers (Basel).2021 Dec 22;14(1):27. doi: 10.3390/cancers14010027. PMID: 35008190; PMCID:PMC8749968.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y, Vogel P, Channappanavar R, **Jonsson CB**, **Smith AM**. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infection during SARS-CoV-2Infection. bioRxiv [Preprint]. 2022 Mar 1:2022.02.28.482305. doi:10.1101/2022.02.28.482305. Update in: Front Immunol. 2022 May 12;13:894534.PMID: 35262077; PMCID: PMC8902874.

Broadbear JH, Depoortere RY, Vacy K, Ralph D, **Tunstall BJ**, Newman-Tancredi A. Discriminative stimulus properties of the 5-HT1A receptor biased agonistsNLX-101 and F13714, in rats trained to discriminate 8-OH-DPAT from saline. Behav Pharmacol. 2021 Dec 1;32(8):652-659. doi: 10.1097/FBP.0000000000000659. PMID:34751175; PMCID: PMC8589115.

Kallumadyil AMT, McClenahan T, De Filippis S, Vungarala A, Satyadev N, **Waters RS**, Kulkarni AL. Perspectives into the possible effects of the B.1.1.7variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on spermatogenesis. J Basic Clin Physiol Pharmacol. 2021 Nov 26;33(1):9-12. doi:10.1515/jbcpp-2021-0083. PMID: 34837491.

Sasani TA, **Ashbrook DG**, Beichman AC, **Lu L**, Palmer AA, **Williams RW**, Pritchard JK, Harris K. A natural mutator allele shapes mutation spectrum variation in mice. Nature. 2022 May;605(7910):497-502. doi: 10.1038/s41586-022-04701-5. Epub2022 May 11. PMID: 35545679; PMCID: PMC9272728.

Lin Y, **Sun Z**. Klotho deficiency-induced arterial calcification involves osteoblastic transition of VSMCs and activation of BMP signaling. J Cell Physiol. 2022 Jan;237(1):720-729. doi: 10.1002/jcp.30541. Epub 2021 Aug 8. PMID:34368951; PMCID: PMC8810603.

Mondal K, Takahashi H, Cole J 2nd, Del Mar NA, Li C, Stephenson DJ, Allegood J, Cowart LA, Chalfant CE, **Reiner A**, **Mandal N**. Systemic Elevation of n-3Polyunsaturated Fatty Acids (n-3-PUFA) Is Associated with Protection against Visual, Motor, and Emotional Deficits in Mice following Closed-Head Mild Traumatic Brain Injury. Mol Neurobiol. 2021 Nov;58(11):5564-5580. doi:10.1007/s12035-021-02501-y. Epub 2021 Aug 8. PMID: 34365584; PMCID: PMC8655834.

Yoon TW, **Fitzpatrick EA**, Snyder JD, Lee S, Kim YI, Zacheaus C, **Yi AK**. Contribution of Protein Kinase D1 on Acute Pulmonary Inflammation and Hypersensitivity Pneumonitis Induced by Saccharopolyspora rectivirgula. Immunohorizons. 2022 Mar 10;6(3):224-242. doi: 10.4049/immunohorizons.2200017.PMID: 35273098.

Gropler MRF, Lipshultz SE, Wilkinson JD, **Towbin JA**, Colan SD, Canter CE, Lavine KJ, Simpson KE. Pediatric and adult dilated cardiomyopathy are distinguished by distinct biomarker profiles. Pediatr Res. 2022Jul;92(1):206-215. doi: 10.1038/s41390-021-01698-x. Epub 2021 Aug 17. PMID:34404929.

Govatati S, Pichavaram P, Mani AM, Kumar R, Sharma D, Dienel A, Meena S, **Puchowicz MA**, Park EA, **Rao GN**. Novel role of xanthine oxidase-dependent H2O2 production in 12/15-lipoxygenase-mediated de novo lipogenesis, triglyceride biosynthesis and weight gain. Redox Biol. 2021Nov;47:102163. doi: 10.1016/j.redox.2021.102163. Epub 2021 Oct 12. PMID:34655995; PMCID: PMC8577505.

Ranea-Robles P, Chen H, Stauffer B, Yu C, Bhattacharya D, Friedman SL, **Puchowicz M**, Houten SM. The peroxisomal transporter ABCD3 plays a major role in hepatic dicarboxylic fatty acid metabolism and lipid homeostasis. J Inherit Metab Dis. 2021 Nov;44(6):1419-1433. doi: 10.1002/jimd.12440. Epub 2021 Oct 2.PMID: 34564857; PMCID: PMC8578467.

Thomas MH, Gui Y, Garcia P, Karout M, Gomez Ramos B, Jaeger C, Michelucci A,Gaigneaux A, Kollmus H, Centeno A, Schughart K, Balling R, Mittelbronn M, Nadeau JH, Sauter T, **Williams RW**, Sinkkonen L, Buttini M. Quantitative trait locus mapping identifies a locus linked to striatal dopamine and points to collagen IValpha-6 chain as a novel regulator of striatal axonal branching in mice. Genes Brain Behav. 2021 Nov;20(8):e12769. doi: 10.1111/gbb.12769. Epub 2021 Sep 28.PMID: 34453370.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, Yue J, Benya Z, **Tigyi GJ**. Pro metastatic Effect of ATX Derived from Alveolar Type II Pneumocytes andB16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi:10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.

Aksel H, Zhu X, Gauthier P, **Zhang W**, Azim AA, **Huang GT**. A new direction in managing avulsed teeth: stem cell-based de novo PDL regeneration. Stem Cell Res Ther. 2022 Jan 28;13(1):34. doi: 10.1186/s13287-022-02700-x. PMID: 35090556;PMCID: PMC8796335.

Suthon S, Perkins RS, Lin J, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**. GATA4 and estrogen receptor alpha bind at SNPs rs9921222 and rs10794639 to regulate AXIN1 expression in osteoblasts. Hum Genet. 2022 Jun 9. doi:10.1007/s00439-022-02463-8. Epub ahead of print. PMID: 35678873.

Kiran S, Rakib A, Moore BM, **Singh UP**. Cannabinoid Receptor 2 (CB2) Inverse Agonist SMM-189 Induces Expression of Endogenous CB2 and Protein Kinase A That Differentially Modulates the Immune Response and Suppresses Experimental Colitis. Pharmaceutics. 2022 Apr 26;14(5):936. doi:10.3390/pharmaceutics14050936. PMID: 35631522; PMCID: PMC9147685.

He Y, Yang C, Wang Y, Sacher JR, Sims MM, **Pfeffer LM**, Miller DD. Novel structural-related analogs of PFI-3 (SRAPs) that target the BRG1 catalytic subunit of the SWI/SNF complex increase the activity of temozolomide in glioblastoma cells. Bioorg Med Chem. 2022 Jan 1;53:116533. doi:10.1016/j.bmc.2021.116533. Epub 2021 Nov 27. PMID: 34863065.

Bonjour K, Palazzi C, Silva TP, Malta KK, Neves VH, Oliveira-Barros EG, Neves I, Kersten VA, Fortuna BT, **Samarasinghe AE**, Weller PF, Bandeira-Melo C, Melo RCN. Mitochondrial Population in Mouse Eosinophils: Ultrastructural Dynamics in Cell Differentiation and Inflammatory Diseases. Front Cell Dev Biol.2022 Mar 21;10:836755. doi: 10.3389/fcell.2022.836755. PMID: 35386204; PMCID:PMC8979069.

Guo H, **Zhang W**, Wang J, Zhao G, Wang Y, Zhu BM, Dong P, Watari H, Wang B, **Li W**, **Tigyi G**, Yue J. Cryptotanshinone inhibits ovarian tumor growth and metastasis by degrading c-Myc

and attenuating the FAK signaling pathway. Front Cell Dev Biol. 2022 Sep 28;10:959518. doi: 10.3389/fcell.2022.959518. PMID: 36247016;PMCID: PMC9554091.

Mozhui K, Lu AT, Li CZ, Haghani A, Sandoval-Sierra JV, Wu Y, **Williams RW**, Horvath S. Genetic loci and metabolic states associated with murine epigenetic aging. Elife. 2022 Apr 7;11:e75244. doi: 10.7554/eLife.75244. PMID: 35389339;PMCID: PMC9049972.

Huo X, **Zhang W**, Zhao G, Chen Z, Dong P, Watari H, **Narayanan R**, Tillmanns TD, **Pfeffer LM**, Yue J. FAK PROTAC Inhibits Ovarian Tumor Growth and Metastasis by Disrupting Kinase Dependent and Independent Pathways. Front Oncol. 2022 Apr28;12:851065. doi: 10.3389/fonc.2022.851065. PMID: 35574330; PMCID: PMC9095959.

Kiran S, Rakib A, Kodidela S, **Kumar S**, **Singh UP**. High-Fat Diet-Induced Dysregulation of Immune Cells Correlates with Macrophage Phenotypes and Chronic Inflammation in Adipose Tissue. Cells. 2022 Apr 13;11(8):1327. doi:10.3390/cells11081327. PMID: 35456006; PMCID: PMC9031506.

Gaur AH, Panetta JC, **Smith AM**, Dallas RH, Freeman BB 3rd, Stewart TB, Tang L, John E, Branum KC, Patel ND, Ost S, Heine RN, Richardson JL, Hammill JT, Bebrevska L, Gusovsky F, Maki N, Yanagi T, Flynn PM, McCarthy JS, Chalon S, Guy RK. Combining SJ733, an oral ATP4 inhibitor of Plasmodium falciparum, with the pharmacokinetic enhancer cobicistat: An innovative approach in antimalarial drug development. E BioMedicine. 2022 Jun;80:104065. doi: 10.1016/j.ebiom.2022.104065.Epub 2022 May 19. PMID: 35598441; PMCID: PMC9127571.

Zhou Q, Verne GN. Disruption of the Mucosal Serotonin Reuptake Transporter (SERT) Through Gut Dysbiosis. Gastroenterology. 2022 Jun;162(7):1833-1834. doi:10.1053/j.gastro.2022.03.029. Epub 2022 Mar 24. PMID: 35341788.

Yu W, **Mulligan MK**, **Williams RW**, Meisler MH. Correction of the hypomorphic Gabra2 splice site variant in mouse strain C57BL/6J modifies the severity of Scn8a encephalopathy. HGG Adv. 2021 Oct 8;3(1):100064. doi:10.1016/j.xhgg.2021.100064. PMID: 35047853; PMCID: PMC8756487.

Hitzemann R, Bergeson SE, Berman AE, Bubier JA, Chesler EJ, Finn DA, Hein M, Hoffman P, Holmes A, Kisby BR, Lockwood D, Lodowski KH, McManus M, Owen JA, Ozburn AR, Panthagani P, Ponomarev I, Saba L, Tabakoff B, Walchale A, **Williams RW**, Phillips TJ. Sex Differences in the Brain Transcriptome Related to Alcohol Effects and Alcohol Use Disorder. Biol Psychiatry. 2022 Jan 1;91(1):43-52. doi:10.1016/j.biopsych.2021.04.016. Epub 2021 May 1. PMID: 34274109; PMCID:PMC8558111.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, Yue J, **Zhang W**. Adipose-Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal Transition Through Activating the TGF-Œ≤ Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276;PMCID: PMC8727693.

Regan J, DeJarnette C, Luna-Tapia A, Parker JE, Reitler P, Barnett S, Tucker KM, Kelly SL, **Palmer GE**. Titration of C-5 Sterol Desaturase Activity Reveals Its Relationship to Candida albicans Virulence and Antifungal Susceptibility Is Dependent upon Host Immune Status. mBio. 2022 Apr 26;13(2):e0011522. doi:10.1128/mbio.00115-22. Epub 2022 Apr 5. PMID: 35380453; PMCID: PMC9040724.

Swanson ML, Regner KR, Moore BM, **Park F**. Cannabinoid Type 2 Receptor Activation Reduces the Progression of Kidney Fibrosis Using a Mouse Model of Unilateral Ureteral Obstruction. Cannabis Cannabinoid Res. 2022 Feb 23. doi:10.1089/can.2021.0127. Epub ahead of print. PMID: 35196117.

Wang Y, Yang C, Sims MM, Sacher JR, Raje M, Deokar H, Yue P, Turkson J, Buolamwini JK, **Pfeffer LM**. SS-4 is a highly selective small molecule inhibitor of STAT3 tyrosine phosphorylation that potently inhibits GBM tumorigenesis invitro and in vivo. Cancer Lett. 2022 May 1;533:215614. doi:10.1016/j.canlet.2022.215614. Epub 2022 Mar 1. PMID: 35245627.

Beasley MM, Gunawan T, **Tunstall BJ**, Kearns DN. Intermittent access training produces greater motivation for a non-drug reinforcer than long access training. Learn Behav. 2022 Feb 7. doi: 10.3758/s13420-022-00512-w. Epub ahead of print. PMID: 35132517.

Salman M, Ismael S, Li L, Ahmed HA, **Puchowicz MA**, **Ishrat T**. Acute Hyperglycemia Exacerbates Hemorrhagic Transformation after Embolic Stroke and Reperfusion with tPA: A Possible Role of TXNIP-NLRP3 Inflammasome. J Stroke Cerebrovasc Dis. 2022 Feb;31(2):106226. doi:10.1016/j.jstrokecerebrovasdis.2021.106226. Epub 2021 Nov 27. PMID: 34847489;PMCID: PMC8792268.

Liu J, Vogel AK, Miao J, Carnahan JA, Lowes DJ, Rybak JM, **Peters BM**. Rapid Hypothesis Testing in Candida albicans Clinical Isolates Using a Cloning-Free, Modular, and Recyclable System for CRISPR-Cas9 Mediated Mutant and Revertant Construction. Microbiol Spectr. 2022 Jun 29;10(3):e0263021. doi:10.1128/spectrum.02630-21. Epub 2022 May 25. PMID: 35612314; PMCID: PMC9241802.

Ranea-Robles P, Pavlova NN, Bender A, Pereyra AS, Ellis JM, Stauffer B, Yu C, Thompson CB, Argmann C, **Puchowicz M**, Houten SM. A mitochondrial long-chain fatty acid oxidation defect leads to tRNA uncharging and activation of the integrated stress response in the mouse heart. Cardiovasc Res. 2022 Apr7:cvac050. doi: 10.1093/cvr/cvac050. Epub ahead of print. PMID: 35388887.

Chen K, Wang S, **Sun Z**. In Vivo Cardiac-specific Expression of Adenylyl Cyclase 4 Gene Protects against Klotho Deficiency-induced Heart Failure. Transl Res. 2022 Jun;244:101-113. doi: 10.1016/j.trsl.2022.01.006. Epub 2022 Jan 31.PMID: 35114419; PMCID: PMC9119924.

Senko AN, Overall RW, Silhavy J, Mlejnek P, Malansk H, Hattl M, Markov I, Fabel KS, **Lu L**, Stuchlik A, **Williams RW**, Pravenec M, Kempermann G. Systems genetics in the rat HXB/BXH family identifies Tti2 as a pleiotropic quantitative trait gene for adult hippocampal neurogenesis and serum glucose. PLoS Genet.2022 Apr 4;18(4):e1009638. doi: 10.1371/journal.pgen.1009638. PMID: 35377872;PMCID: PMC9060359.

Honig MG, Del Mar NA, Henderson DL, O'Neal D, Yammanur M, Cox R, Li C, Perry AM, Moore BM, **Reiner A**. Raloxifene, a cannabinoid type-2 receptor inverse agonist, mitigates visual deficits and pathology and modulates microglia after ocular blast. Exp Eye Res. 2022 May;218:108966. doi: 10.1016/j.exer.2022.108966.Epub 2022 Feb 7. PMID: 35143834.

Regan J, **Palmer GE**. Identifying Specific Small Molecule-Protein Interactions Using Target Abundance-Based Fitness Screening (TAFiS). Methods Mol Biol.2022;2542:115-126. doi: 10.1007/978-1-0716-2549-1_8. PMID: 36008660.

Adhikari P, Shukla PK, Alharthi F, **Rao R**, Pradhan P. Photonic technique to study the effects of probiotics on chronic alcoholic brain cells by quantifying their molecular specific structural alterations via confocal imaging. J Biophotonics. 2022 Mar;15(3):e202100247. doi: 10.1002/jbio.202100247. Epub 2021Dec 2. PMID: 34786860.

Han X, **Sun Z**. Adult Mouse Kidney Stem Cells Orchestrate the De Novo Assembly of a Nephron via Sirt2-Modulated Canonical Wnt/ß-Catenin Signaling. Adv Sci (Weinh). 2022 May;9(15):e2104034. doi: 10.1002/advs.202104034. Epub 2022 Mar22. PMID: 35315252; PMCID: PMC9130916.

Smoum R, Grether U, Karsak M, Vernall AJ, **Park F**, Hillard CJ, Pacher P. Editorial: Therapeutic potential of the cannabinoid CB2 receptor. Front Pharmacol. 2022 Oct 7;13:1039564. doi: 10.3389/fphar.2022.1039564. PMID:36278235; PMCID: PMC9585503.

Phillip K, Nair N, Samanta K, Azevedo JF, Brown GD, Petersen CA, Gomes-Solecki M. Maternal transfer of neutralizing antibodies to B. burgdorferi OspA after oral vaccination of the rodent reservoir. Vaccine. 2021 Jul 13;39(31):4320-4327. doi: 10.1016/j.vaccine.2021.06.025. Epub 2021 Jun 23. PMID: 34172332; PMCID: PMC8495753.

Fili CV, Lin L, Chapman J, **Hamilton D**, Yates CR. Methylsulfonylmethane and Sesame Seed Oil Improve Dyslipidemia and Modulate Polyunsaturated Fatty Acid Metabolism in Two Mouse Models of Diabetes. J Med Food. 2022 Jun;25(6):607-617. doi: 10.1089/jmf.2021.0196. PMID: 35708633; PMCID: PMC9247677.

II. PRESENTATIONS GIVEN TO PROMOTE CORE USAGE

A. New Faculty Orientation

One of the LACU veterinarians attends each of the UTHSC new faculty orientation days and meets with investigators who plan to use animals as part of their research. Information is provided regarding LACU contact information, facility locations, services provided and a copy of the current LACU per diem rate sheet is distributed.

B. Courses

CMED711 Essentials of Animal Experimentation – Department of Comparative Medicine. This graduate course is offered every fall semester and nine students enrolled in 2021. The course is a requirement for the Laboratory Research and Management Program in the College of Graduate Health Sciences. The course involves didactic and hands-on training and covers the animal species most used in research. Students learn handling and common techniques for rats and mice and perform a practice surgery. They also receive a tour of one of the animal facilities, learn how to write an IACUC protocol and are introduced the various regulations surrounding the use of animals in research.

C. Facility Orientations

The training coordinator, Leadra Williford, conducts facility orientations and meets with all new investigators and all new research staff prior to granting card access to an

animal facility. This is generally the first introduction of new research staff to the LACU and allows LACU to become familiar with the lab's research focus and to offer expertise and training, if necessary. The facility orientation consists of a PowerPoint presentation followed by a tour of the animal facility in the building in which the lab is located. The entire orientation lasts 1-1.5 hours and provides information on:

- LACU contact information for each animal facility, including after hour phone numbers
- LACU services (e.g., animal ordering, animal imports, technical services)
- Available equipment for research use (e.g., ultrasound machine, x-ray unit, micro CT)
- Rodent cage types and drinking water options
- Animal facility traffic patterns
- IACUC policies (e.g., animal transport, euthanasia, animal density)
- LACU policies (e.g., personal protective equipment, animal ordering, reporting sick animals, animal bites)
- Census management training and cage card printing

The orientation is followed by a tour of the facility by the supervisor where the research staff get to meet other members of the LACU, including the area supervisor and learn where to find equipment, store feed, etc. Proper cage changing practices using microisolator techniques are also demonstrated during the tour. At the end of the orientation, a copy of the presentation, along with the various policies and documents that were discussed during the orientation, are emailed to the individual.

For FY22, a total of 60 orientations were presented for research staff training.

III. SUMMARY OF ACTIVITIES FOR FY22

A. Personnel

In FY22, the LACU consisted of 42 permanent and four temporary staff members:

- **Director:** Dr. David Hamilton, DVM (100%)
- **Clinical Veterinarian:** Dr. Tyler Aycock and Dr. Brianne Hibl (100% effort)
- **Post-Doctoral Veterinarians:** (1) Dr. Monica Sidhu
- **Operations Management:** (2) Stanley Latocha (100% effort) and Casey Inman (100% effort)
- **Administrative Staff:**
  Business Manager: Detric Stigall (100% effort)
  Financial Coordinator: Joyce Jones (100% effort)
  Accounting Assistant: Trinica Collins (100% effort)
- **Supervisors:**
  Husbandry: (3) Sherry Frazier (100% effort), Brad Stevens (100% effort) and Tyler Patterson (100% effort),
- **Training Coordinator:** Leadra Williford (100% effort)
- **Veterinary Technicians**: (1) Kadijah Wainwright (100% effort)
- **Husbandry Technicians**: 17 @ 100% effort
- **Cage Wash Technicians**: 10 @ 100% effort
- **Service Assistants**: 2 @ 100% effort
- **Temporary Service Assistants:** 1 @ 100% effort

There were 6 buildings on campus which contain animal facilities:

- Cancer Research Building (CRB)
- Coleman Building
- Translational Sciences Research Building (TSRB)
- TriMetis
- Wittenborg Building
- Regional Biocontainment Laboratory
-

B. Advisory Board

The Laboratory Animal Care Unit Internal Advisory Board consisted of the following members for FY22:

- Ade Adebiyi (Physiology, COM)
- Kevin Freeman (GGI, COM)
- Detlef Heck (Anatomy and Neurobiology, COM)
- Joseph Pierre (Pediatrics, COM); *CHAIR*

C. Equipment

Equipment currently housed in the LACU core for shared investigator use

Equipment	Cost	Funding Source	Date Purchased
VisualSonics Vevo 2100 ultrasound machine	$400,013.00	J07002200	01/23/2009
Starr MouseOx pulse oximeter	$4,950.00	LACU Core	06/06/2008
Sedecal/Idexx X-ray machine	$103,500.00	J07002200	01/25/2010
Anesthetic Machines (5)	$25,000	LACU Core	multiple

D. Service Contracts, FY22

Contract Type:	Vendor:	Expense:
Andersen Sterilizers Preventive Maintenance	Andersen Products, Inc.	$719
Automatic Watering System: Coleman, Wittenborg, TSRB & CRB	Avidity Sciences LLC	$25,631
ATS Annual Hood Certifications	Air Technical Services	$9,600
Avidity (Edstrom) PM Service Renewal for TriMetis facility	Avidity Sciences, LLC	$18,196
Maintenance Service Contract TriMetis Facility / TSRB Facility	Getinge/Castle Inc.	$74,659

SHL Periodic Maintenance Service Agreement	Adam Stonaker DBA Stonaker Hospital & Lab, LLC	$62,208
Tecniplast Service Agreement Equipment in TSRB	Tecniplast	$85,632
TOTAL		**$276,645**

E. Core Revenues by Department, FY22

Department	Total Amount, $
NOT REPORTED	38,085.29
ANATOMY & NEUROBIOLOGY	321,502.28
BIOSCIENCE RESEARCH	2,882.47
CLINICAL LAB SCIENCES	5,260.31
CLINICAL PHARMACY	36,867.37
COMPARATIVE MEDICINE	51,292.36
GGI	452,687.56
MEDICINE	86,812.92
MEDICINE (GASTROENTEROLOGY)	55,040.35
MEDICINE (HEMATOLOGY)	46,047.07
MEDICINE (NEPHROLOGY)	10,254.75
MIB	200,692.19
NEUROLOGY	34,845.46
OPTHALMOLOGY	173,664.68
ORTHODONTICS	2,979.33
ORTHOPAEDIC SURGERY	6,971.32
PATHOLOGY	25,301.80
PEDIATRICS	573,236.94
PHARMACEUTICAL SCIENCES	172,917.47
PHARMACOLOGY	266,089.82
PHYSICAL THERAPY	51,152.85
PHYSIOLOGY	684,775.63
SURGERY	15,616.40
SUBTOTAL, INTERNAL REVENUES	**3,315,890.42**
EXCLUDED from service fees*	**(199.55)**
TOTAL INTERNAL REVENUES INVOICED FOR LACU, FY22	**3,315,690.87**

*Charges for LACU training or sentinel cages and for RBL per diems credited to RBL budget

F. Core Invoices for External Users, FY22

Vendor:	PI/Contact:	Invoiced:
US Biologics	Jolieke Van Oosterwijk	10,597.68
University of Memphis	Joel Bumgardner	263.40
Diatech	Tyler Aycock	4,635.19
TOTAL		**$15,496.27**

G. Multi-year trends

Mouse care days, total (all types of caging)

Year	Care days	Total revenues
FY22	2,102,674	$2,055,480
FY21	2,260,818	$2,154,520
FY20	2,218,366	$2,054,958
FY19	1,962,365	$1,760,552
FY18	1,890,148	$1,648,515

Rat care days, total (all types of caging)

Year	Care days	Total revenues
FY22	234,276	$366,362
FY21	157,061	$239,240
FY20	118,681	$175,517
FY19	95,641	$137,051
FY18	110,509	$154,825

Rabbit care days

Year	Care days	Total revenues
FY22	4,643	$9,988
FY21	4,314	$9,320
FY20	3,599	$7,432
FY19	1,626	$3,135
FY18	5,004	$9,655

Pig care days

Year	Care days	Total revenues
FY22	1,549	$14,263
FY21	736	$6,605
FY20	1,230	$11,248
FY19	938	$7,938
FY18	905	$7,425

Hamster care days

Year	Care days	Total revenues
FY22	3,913	$8,343
FY21	5,594	$10,952
FY20	3,813	$7,133
FY19	86	$132
FY18	264	$420

Peromyscus care days

Year	Care days	Total revenues
FY22	5,039	$4,888
FY21	6,345	$6,183
FY20	3,702	$2,629
FY19	10,268	$7,889
FY18	6,458	$6,367

Zebrafish care days

Year	Care days	Total revenues
FY22	17,432	$4,471
FY21	17,894	$3,980
FY20	7,225	$959
FY19	2,960	$69
FY18	0	$0

Total Veterinarian or Technical Service Fee Revenues

Year	Total revenues
FY22	$149,055
FY21	$117,306
FY20	$113,526
FY19	$125,892
FY18	$149,544

Total LACU Animal and Supplies Orders Revenues

Year	Total revenues
FY22	$718,742
FY21	$629,601
FY20	$618,082
FY19	$626,428
FY18	$462,029

Top 5 Internal Users, FY22

PI	Charges, $	% of Total LACU Internal Revenues
Hao Chen	$220,629.71	6.65%
Robert Williams	$202,861.89	6.12%
Adebiyi Adebowale	$142,865.48	4.31%
Amandeep Bajwa	$116,080.59	3.50%
Zhongjie Sun	$109,378.57	3.30%

Top 5 Departments, FY22

Department	Charges, $	% of Total LACU Internal Revenues
Physiology	684,775.63	20.65%
Pediatrics	573,236.94	17.29%
Genetics, Genomics and Informatics	452,687.56	13.65%
Anatomy & Neurobiology	321,502.28	9.70%
Pharmacology	266,089.82	8.03%

H. FY22 Fee Structure

LACU revenue is primarily generated through per diem rates and charges for special services. Animal housing is billed through a daily per diem charge, depending on the species, animal size and cage type. Management and veterinary staff submit charge tickets/material orders through the internal ACIM system to invoice for special services such as veterinary procedures, animal transport or equipment usage.

FY22 Per Diem Rates

Mouse Per Diem, Standard box (75 in^2):	
Microisolator box*:	$0.97/box/day
IVC box**:	$0.97/box/day
IVC box + water bottle:	$1.07/box/day
Sterile microisolator care***:	$1.56/box/day
Biocontainment (ABSL2)****:	$1.21/box/day
Sterile microisolator care, ABSL2:	$1.87/box/day
Diabetic Mouse Per Diem, Standard box (75 in^2):	
Microisolator box*:	$1.15/box/day
IVC box**:	$1.15/box/day
IVC box + water bottle:	$1.27/box/day
Sterile microisolator care***:	$1.87/box/day
Biocontainment (ABSL2)****:	$1.46/box/day
Sterile microisolator care, ABSL2:	$2.25/box/day
Mouse Per Diem, Metabolism Box:	$1.41/box/day
Mouse Per Diem, Large box (157 in^2):	
Microisolator box*:	$1.55/box/day
IVC box**:	$1.55/box/day
IVC box + water bottle:	$1.67/box/day
Biocontainment (ABSL2)****:	$1.85/box/day
Diabetic Mouse Per Diem, Large box (157 in^2):	
Microisolator box*:	$1.86/box/day
IVC box**:	$1.86/box/day
Biocontainment (ABSL2)****:	$2.24/box/day
Rat Per Diem:	
Standard box*:	$1.55/box/day
IVC box**:	$1.55/box/day
IVC box + water bottle:	$1.67/box/day
Sterile microisolator care***:	$2.06/box/day
Biocontainment (ABSL2)****:	$1.86/box/day
Diabetic Rat Per Diem:	
Standard box*:	$1.86/box/day
IVC box**:	$1.86/box/day
IVC box + water bottle:	$1.98/box/day
Sterile microisolator care***:	$2.48/box/day
Biocontainment (ABSL2)****:	$2.24/box/day
Rat Per Diem, Metabolism Box:	$2.33/box/day

Rodent care descriptions:

*Standard box refers to standard charges for husbandry practices for a given facility or room, which includes caging, standard diet, standard bedding and a water bottle.

**IVC box refers to a box placed on a ventilated rack system with an automatic watering system. The per diem rate includes caging, standard diet, standard bedding and automatic water.

***Sterile microisolator care is provided at the request of the PI. The box is fully assembled (lid, grill, bottom, standard bedding) prior to autoclaving as a unit.

****ABSL2 is required for animals inoculated with human-derived materials (cells, tissue fragments, etc.), or for animals exposed to viral particles or other hazards deemed to require ABSL2 care.

Standard bedding:	Standard Feed:
Mice: Shepherd's Cob	Mice: Envigo 7912 or 7904 (breeder diet)
Rats: Shepherd's Cob	Rats: Envigo 7912

To request the use of non-standard bedding/feed, or special handling (e.g. autoclaving) of feed/bedding, please complete a LACU Resource Request Form and submit to the LACU director of operations, Stan Latocha (slatocha@uthsc.edu), as the above per diem rates will require adjustment.

Rabbits:	
<2 kg:	$2.08/animal/day
2-5.4 kg:	$2.24/animal/day
>5.4 kg:	$2.35/animal/day
Swine:	
Neonate:	$9.18/animal/day
< 25 lbs.:	$10.00/animal/day
25-75 lbs.:	$10.80/animal/day
> 75 lbs.:	$11.59/animal/day
Guinea Pig:	$2.34/enclosure/day
Hamster:	
Microisolator Box*:	$1.48/box/day
Biocontainment (ABSL2)****:	$1.78/box/day
Ferret:	
Standard:	$7.16/animal/day
Biocontainment (ABSL2):	$8.58/animal/day
Zebrafish:	
1.0 Liter tank:	$0.08/tank/day
3.5 Liter tank:	$0.26/tank /day
8.0 Liter tank:	$0.42/tank/day
Xenopus Frog:	$2.49/tank/day

For other species not listed above, please consult with LACU Director

Veterinarian, Vet Tech and Husbandry Tech Services:

Veterinarian services (M-F, 8am-5pm):	$69.82/hr
Veterinarian services, after-hrs/weekends and holidays:	$104.76/hr (2hr min)
Veterinary Tech services (M-F, 8am-5pm):	$27.99/hr
Veterinary Tech services, after-hrs/weekends and holidays:	$41.98/hr (2hr min)
Husbandry Tech services (M-F, 8am-5pm):	$18.89/hr
Husbandry Tech services, after-hrs./weekends and holidays:	$28.35/hr (2h min)

Other services:

Rodent ultrasound:	$92.74/hr
Rodent anesthesia:	$46.37/day
Surgery room, with sterile surgery pack:	$115.93/use
Gas sterilization:	$34.77
Steam sterilization:	$34.77
Radiography:	$34.77/hr
Specialty room use:	$32.25/day
Surgery Room Cleaning charge:	$52.17

Custom projects or services: Please consult the LACU Director

Purchasing surcharges:

Animal order late fee (after 5pm Tuesday):	$57.97
Ordering fee, non-approved vendors:	$57.97
Drug and other supply orders*:	15% above cost

The LACU no longer routinely orders drugs and supplies for research needs. All investigators are encouraged to obtain the necessary licenses to order drugs and supplies from medical distributors

Transportation services surcharges:

Airport Pickup/Order	$69.56
Feed & Bedding Delivery/Trip	$69.56
Special Animal Transport/Trip	$69.56

External users rate surcharge, per service: 30%

Projected per diem and services charges, FY23 - beyond: 3% annually over prior FY basis

IV. EXTRAMURAL GRANTS SUPPORTED BY THE CORE, FY22

Adebiyi, Adebowale

USPHS NIH Grant 1R01DK120595, Vascular ion channels and microcirculation in neonatal urinary tract obstruction

USPHS NIH Grant 1R01HL151735, Control of microvascular function by ion channels

USPHS NIH Grant 1R01DK127625, Urotensin II and renal insufficiency in growth-restricted infants.

Alway, Stephen

Department of Defense, US Army Medical Research and Material Command, W81XWH2110187, Using mitochondria therapy to improve restoration of neuromuscular function following injury

Bajwa, Amandeep

USPHS NIH Grant 7R01DK117183-02, Mitochondrial Therapy for Kidney Injury

Boughter, John

USPHS NIH Grant 1R01DC016833, Spatial taste coding in mouse gustatory cortex

Bukiya, Anna

USPHS NIH Grant 1R03AA028380, Fatty acid and alcohol modulation of cerebral artery diameter

Carson, James

USPHS NIH Grant, 1R21CA231131, The Regulation of Physical Function and Skeletal Muscle Metabolic Signaling After Cessation of 5-Fluorouracil Treatment

Chen, Guoyun

USPHS NIH Grant 1R01AI137255, Targeting Siglec-9/E for therapy of sepsis

Chen, Hao

USPHS NIH Grant 1R01DA048017, Reduced complexity mapping of oxycodone self-administration and stress responsiveness in rats

USPHS NIH Grant 1U01DA047638, System genetics of menthol and nicotine addiction

USPHS NIH Grant Subcontract to University of California, San Diego (UCSD), Integrated GWAS of Complex Behavioral and Gene Expression Traits in Outbred Rats

Chizhikov, Viktor

USPHS NIH Grant 5R01NS093009, Mesenchymal-neuroepithelial interactions in the developing telencephalon.

Collier, Daniel

USPHS NIH Grant 4R00HL133451, Trauma Induced Endothelial Cell Ca2+ Signaling

Cordero-Morales, Julio

USPHS NIH Grant 1R01GM125629, The Role of Bioactive Lipids in Transient Receptor Potential Channels Gating

Dale, James

USPHS NIH Grant 1R01AI132117, Structure-Based Design of a Broadly Protective Group A Streptococcal Vaccine

Dopico, Alejandro

USPHS NIH Grant 5R37AA011560, Ethanol Actions on SLO Channels from Arteries vs. Brain

USPHS NIH Grant 1R01HL147315, Regulation of arterial diameter through specific sensing of endogenous steroids and novel nonsteroidal analogs by BK channel subunits.

USPHS NIH Grant 1R01HL14894, Cholesterol regulation of smooth muscle BK channel proteins and consequent control of cerebral artery diameter

Dragatsis, Ioannis

USPHS NIH Grant 1R21NS111097, Cholesterol and sonic hedgehog signaling in alobar holoprosencephaly

USPHS NIH Grant 1R21NS112989, Genetic restoration of IKAP as a tool to study Familial Dysautonomia

Du, Jianyang

USPHS NIH Grant 7R01MH113986, CO2 inhalation enhances the lability of fear memory.

Fletcher, Max

USPHS NIH Grant 5R01DC013779, Cholinergic modulation of olfactory bulb glomerular sensitivity

Foehring, Robert

USPHS NIH Grant 2R01NS044163, Dynamics of Kv channel function in identified populations of pyramidal neurons in neocortex

Fortwendel, Jarrod

USPHS NIH Grant 1R21AI142509, Control of Antifungal Drug Tolerance through the Aspergillus fumigatus Kinome

USPHS NIH Grant 1R01AI158442, Unlocking the cidal activity of echinocandins against Aspergillus fumigatus

Freeman, Kevin

USPHS NIH Grant 7R01CA216394, Dissecting the contribution of the transcriptional regulators of SNS fate to neuroblastoma oncogenesis

Gadiparthi, Rao

USPHS NIH Grant 2R01EY014856, Mechanisms of retinal angiogenesis

USPHS NIH Grant 5R01HL069908, NFATs and Vascular Injury

USPHS NIH Grant 2R01HL103575, GPCR Signaling and Vascular Wall Remodeling

USPHS NIH Grant 2R01HL074860, Lipid mediators and vascular diseases

Gomes-Solecki, Maria

University Iowa -Subcontract USPHS NIH Grant 5R01AI139267, Field trial and modeling of transmission-blocking vaccine to prevent Lyme disease

Gosain, Ankush

USPHS NIH Grant 1R01DK125047, Dysbiosis in Hirschsprung Associated Enterocolitis Pathogenesis

Gu, Weikuan

Contract with Qiqhar Hospital, GU 20-5009

Hamre, Kristin

USPHS NIH Grant 5R01AA023508, Maternal genotype, choline intervention, & epigenetics in Fetal Alcohol Syndrome

Heck, Detlef

USPHS NIH Grant 3R01MH112143, Neuronal mechanisms of cerebellar cognitive function

Memorial Sloan Kettering Cancer Center Subcontract to NIH USPHS Grant MH-085726, Engrailed genes and cerebellum morphology, spatial gene expression and circuitry

Hole, Cameron

USPHS NIH Grant 1K22AI148724, Cryptococcal Chitin Synthase 3 and Host Immune Responses

Ishrat, Tauheed

USPHS NIH Grant 7R01NS097800, Mechanisms and therapeutic targets of neurovascular injury in hyperglycemic stroke

Jablonski, Monica

USPHS NIH Grant 2R01EY021200, Genetic Modulation of Glaucoma

USPHS NIH Grant 5R24EY029950, Novel Extended Release Glaucoma Therapy for Once Daily Dosing

Jaggar, Jonathan

USPHS NIH Grant 5R01HL133256, Blood pressure regulation by smooth muscle cell ion channels

USPHS NIH Grant 1R01HL137745, Endothelial cell potassium channels

USPHS NIH Grant 1R01HL155180, PKD proteins in endothelial cells

Jiang, Jianxiong

USPHS NIH Grant 7R01NS100947, Inflammatory regulation of neurotrophin signaling in epileptogenesis

USPHS NIH Grant 1R21NS109687, Targeting Prostaglandin Receptor EP2 for Glioma and Associated Epilepsy

Jones, Byron

USPHS NIH Grant 1R01ES031656, Genetics of epigenetic response to high circulating glucocorticoids and organophosphorus compounds

Jonsson, Colleen

US Food and Drug Administration Grant 75F40121P00322, FDA/NCTR Inactivation of Hamster Covid-19 tissues for the FDA

USPHS NIH Grant 5U19AI142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

US Food and Drug Administration Grant, Evaluation of Small Animal Models for COVID-19 and their application in Nonclinical Safety and Efficacy Studies of Investigational Therapeutics

Kassan, Modar

USPHS NIH Grant 7R01HL150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Khan, Mohammad Moshahid

USPHS NIH Grant 1R03NS114616, Examining Progression of a Neurodegenerative Disorder

Kim, Il Hwan

USPHS NIH Grant 1R01MH117429, Genes, Neural Circuits and Behavior

Laizure, Steven

USPHS NIH Grant 1R03NS116229, The inhibition and transesterification of dimethyl fumarate by ethanol

Leo, Marie Dennis

USPHS NIH Grant 1R01HL149662, Chloride channels in diabetic vascular disease

Li, Wei

USPHS NIH Grant 5R01CA148706, Targeting the colchicine site in tubulin for advanced melanoma

Liao, Francesca-Fang

USPHS NIH Grant 1RF1AG058467, Novel mechanistic link between metabolic changes and dementia potential role of miRNA21

USPHS Grant 1RF1NS120327, Blood-brain-barrier and white matter mechanisms underlying dementia

Makowski, Liza

USPHS NIH Grant 1R01CA253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

Mary Kay Foundation, PKC agonism reprograms innate immune suppression in TNBC

Malik, Kafait

USPHS NIH Grant 2R01HL019134, Angiotensins, Prostaglandins, Adrenergic Interactions

Mancarella, Salvatore

USPHS NIH Grant 1R56HL142631, Role of Orai in pathological cardiac remodeling

USPHS Grant 1R01HL153638, Defining the roles of Orai3 channel in cardiomyocytes and cardiomyopathy

Mandal, Nawajes

USPHS NIH Grant 1R01EY031316, Sphingolipids and their Impact in Corneal Wound Healing

US Department of Defense, Army Grant W81XWH2010900, Therapeutic Potential of n-3 PUFAs TBI Mediated Visual Dysfunction

Meibohm, Bernd

Colorado State University (CSU) G-45858-1, Aerosol spectinamide-1599 therapy against tuberculosis

St Jude Children's Research Hospital 112821010-7955678, Spectinomycins for Non-tuberculous Mycobacterial Infections

USPHS NIH Grant 5U19AI142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

St Jude Children's Research Hospital subcontract to USPHS NIH Grant 5R01AI090810, Development of Novel Proteins Synthesis Inhibitors for MDR Tuberculosis

Colorado State University (CSU) G-03441-01, Inhaled tigecycline therapy for pulmonary M. abscessus infections

Miranda-Carboni, Gustavo

Beckman Research Institute-City Hope Subcontract to USPHS Grant CA189283, Combined Breast MRI/Biomarker Strategies to identify Aggressive Biology

Narayanan, Ramesh

USPHS NIH Grant 1R01CA229164, Novel Degraders of the Androgen Receptor (AR) and AR Splice Variants (AR-SVs)

Nowak Jr, Thaddeus S

USPHS NIH Grant 1R01NS113957, Genetics of stroke vulnerability in C57BL/6 mouse substrains

Palmer, Glen

USPHS NIH Grant 1R21AI156611, Examining the importance of folate biosynthetic enzymes in infectious fungi

USPHS NIH Grant 5R33AI127607, Broad spectrum antifungals targeting fatty acid biosynthesis

USPHS NIH Grant 1R01AI152067, Antifungal antagonism as a cause of treatment failure for invasive mycoses

Parfenova, Elena

USPHS NIH Grant 1R01NS105655, Endothelial Vasoprotection by Hypothermia

Peters, Brian

USPHS NIH Grant 1R01AI134796, Candidalysin: a key mediator of Candida vaginitis immunopathology

USPHS NIH Grant 1R21AI141829, Targeted and forward genetic approaches to decipher the pathogenesis of symptomatic vulvovaginal candidiasis

Pierre, Joseph

USPHS NIH Grant 1R01CA253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

Quarles, Leigh Darryl

USPHS NIH Grant 1R01AR071930, Skeletal Functions of Polycystins and TAZ

USPHS NIH Grant 1R01DK121132, Optimization of Novel Small Molecules to Antagonize FGF-23

USPHS NIH Grant 1R01DK120567, Genetic and Environmental Determinants of GPRC6A Regulation of Energy Metabolism Using Genetically Engineered Mice and Systems Biology

USPHS NIH Grant 4R33AR073518, Polycystins/TAZ as a novel therapeutic target to treat osteoporosis

Rao, Radhakrishna

USPHS NIH Grant 5R01DK055532, Intestinal Mucosal Protection by Epidermal Growth Factor

USPHS NIH Grant 1R01AA029270, Defining the Role of Intestinal Calcium Channels in Alcoholic Liver Damage

Sakata, Kazuko

USPHS NIH Grant 1R21NS101703, Heat shock factor HSF1 regulation of promoter-specific BDNF transcription

Samarasinghe, Amali

USPHS NIH Grant 1R02AI125481, Eosinophils as Regulators of Host Immunity against Influenza Infections

American Lung Association, ALA Innovation Award IA-694036

Seagroves, Tiffany

University of Minnesota Subcontract to USPHS NIH Grant C-192178-05, Inducible PTK6 Expression Drives Oncogenic Signaling in Breast Cancer

US Department of Defense, Army Grant W81XWH2010019 (Partnering PI), Discovery of Orally Bioavailable Tubulin Inhibitors to Overcome Taxane Resistance in Metastatic Breast Cancer

Sharp, Burt

USPHS NIH Grant to 1U01DA053672, Genetics of oxycodone intake in a hybrid rat diversity panel

Singh, Udai

USPHS NIH Grant R01AI140405, Adipose T cell microRNAs (miRs) regulate macrophage function during obesity

Smith, Amber

USPHS NIH Grant 1R01AI139088, Predictive Modeling of Influenza-Pneumococcal Coinfection

Sun, Zhongjie

USPHS NIH Grant 7R01AG049780, Investigation into Heart Aging

USPHS NIH Grant 1R01AG062375, Epigenetic Regulation of Kidney Function and Blood Pressure

USPHS NIH Grant 1R01HL154147, Investigation into Arterial Stiffness and Hypertension

Tigyi, Gabor

USPHS NIH Grant 2R01CA092160 Anticancer Strategies Targeting the Autotaxin-LPA Receptor Axis

University of Maryland Subcontract to USPHS Grant AI150574, Intercollaborative Radiation Countermeasure (INTERACT) Consortium for Advanced Development of Medical Counter-measures to Mitigate/Treat Acute and Delayed Radiation Syndromes

RxBio Subcontract 21-4900-RXB, IND-Enabling Development of Rx100 as a Medical Countermeasure for Gastrointestinal Acute Radiation Syndrome

Towbin, Jeffrey Allen

USPHS NIH Grant 1R01HL151438, Discovery of modifier genes in cardiomyopathy

Tsao, Jack

USPHS NIH Grant 1R01HD094588, Investigations into the Etiology of Phantom Limb Sensations and Phantom Limb Pain

Vaithianathan, Thirumalini

USPHS NIH Grant 1R01EY030863, Dynamics of calcium signals control neurotransmitter release in retinal ribbon synapses

Vasquez, Valeria

USPHS NIH Grant 1R01GM133845, Regulation of mechanosensitive ion channels by membrane lipids

Verne, G. Nicholas

National Institute of Diabetes and Digestive and Kidney Diseases, Mechanisms of Gastrointestinal Post-Inflammatory Disease

Waters, Robert

USPHS NIH Grant 7R01DK118959, Investigations into the Etiology of Phantom Limb Sensations and Phantom Limb Pain

Williams, Robert

USPHS NIH Grant 1R01AG070913, Imaging Genetics of Brain Structure and Cognitive Aging in Murine Models of Alzheimer's Disease

Xiao, Jianfeng

USPHS NIH Grant 1R03NS119967, Identification and characterization of the gene associated with the spontaneous autosomal recessive Spinning mice

Xin, Wenkuan

USPHS NIH Grant 7R01DK106964, Role of TRP Channels in human detrusor function and dysfunction

Xu, Junwang

USPHS NIH Grant 7R01GM128660, The role of long non-coding RNA GAS5 in diabetic wounds

Zhou, Fuming

USPHS NIH Grant 5R01NS097671, Ion channel mechanisms of striatal dopaminergic motor stimulation

V. BUSINESS DEVELOPMENT SUMMARY

A. Market Assessment – Business in the LACU increased in FY22, with an increase in total value of services to $3,315,890 (including sentinel/training fees and RBL animal recharges prior to transfer to the RBL base budget) and in total service fees invoiced (internal and external) to $149,055. Revenues from internal use increased by $138,152 over FY21 while revenues from service fees, animal/supplies orders and per diem charges increased by $31,749, $88,871, and $33,031, respectively. We also saw an increase in the use of common equipment, particularly the VisualSonics Vevo 2100 ultrasound machine (+$6,479.65). Along with the other new hires in the LACU, the revised training provided to the staff will increase productivity and efficiency and, therefore, will lead to better quality research data.

B. Competitive Analysis – The LACU is the only core on the UTHSC campus that provides animal research services. Of all animal research cores in the Memphis area, we are the primary one which can offer services to outside entities, particularly with regards to large animal surgical projects. We already perform collaborative work with the Memphis VA, the University of Memphis, Le Bonheur Children's Hospital and St. Jude Children's Research Hospital. We offer very competitive pricing and per diem rates and a flexibility with regards to resources, which does not exist with other animal research service providers in the area. We have an established working relationship with the Medical Education and Research Institute in Memphis, which provides fluoroscopic equipment available for use in specialized cardiovascular studies. We also created a working relationship with the University of Alabama at Birmingham (UAB) transgenic core so that UTHSC investigators are charged UAB prices for transgenic mouse creation. We also provide dedicated transport of the transgenic mice from UAB so that the animals do not require quarantine upon arrival at UTHSC, thus saving investigators valuable time and resources.

C. Marketing Plans to Obtain New Business – Most of our customers hear about our services through word of mouth from other investigators who have utilized services provided by the LACU. For investigators on campus, or new to the UTHSC campus, much of the information about the core and its services are relayed either through word-of-mouth, during new faculty orientations or though the facility orientations as outlined in section II. An updated one-page LACU brochure is created each year through the Office of Research and is available for download through the Office of Research "Research Resources" webpage or directly from the LACU website. This brochure is distributed to new faculty and research staff as part their orientation to the campus or animal facility. The LACU webpage has been extensively updated and highlights the level of expertise within the core, the various services available to investigators and a Frequently Asked Questions section. The LACU has a Listserv email which is used to notify investigators of changes in procedures and policies and is also used to advertise new or updated services as they become available. The LACU has also created shared Outlook calendars for the animal procedure rooms throughout the facilities, so that researchers can reserve rooms in advance for their needs. A shared calendar has also been created that outlines veterinary technician availability to assist with research projects (a billable service).

D. Forecasted Volumes for New Business — It is difficult to forecast volumes for new business, as most researchers do not provide advance notice of their projects. Relative

to FY22, we expect an overall increase in the number of animals used on campus in FY23. As large animal projects practically came to a halt with the COVID-19 pandemic, we expect work using large animals (e.g. pigs, etc.) to increase. There was no revenue from large animal work in FY21 and a total of $6,215.92 in FY22. Large animal work is expected to increase significantly in FY23 as pandemic restrictions have loosened and there is already planned work with pigs, non-human primates, and rabbits. Work with the VisualSonics Vevo 2100 ultrasound machine is expected to remain strong and to further increase in the next fiscal year as other investigators realize the power in this imaging modality. Revenues from fees for quarantine, ultrasound use, drug purchases and anesthetic machine rental also increased in FY22 and are expected to further increase in FY23. LACU was without one of its two veterinary technicians from January 2021 to June 2022 resulting in a decreased billing revenue of $11,346.52 compared to FY21. A new veterinary technician hire, Kayla Hopper, started June 7, 2022. Dr. Zhongjie Sun joined UTHSC as the new chair in Physiology in 2018 and has made new hires in FY22 which will provide additional revenue in FY23. The Department of Pharmacology hired two new faculty in FY21, Drs. Brendan Tunstall and Dean Kirson, both of whom use rats as part of their research and commenced animal studies in FY22. LACU was not successful in obtaining a new veterinary resident for FY22, as an increase in pet ownership in the pandemic drove more graduating veterinarians into private practice instead of pursing further education. LACU therefore plans to hire two residents to start July 2023 as our current resident, Monica Sidhu, will finish her residency at the end of June 2023.

VI. Budget

FY22 Actual Budget (July 1, 2021- June 30, 2022)

FY2022	DEBITS	CREDITS
Salaries (Including Temporary Employees)	2,194,812	
Supplies	1,493,179	
Service Contracts	299,021	
Equipment (> $5,000)	0	
Other Expenses*	316,538	
TOTAL EXPENSES	***4,303,550***	
FY21 Internal Recoveries		3,230,382
FY21 External Recoveries*		14,725
TOTAL CREDITS		***3,245,107***
Income / (Subsidy)	(1,058,443)	
State Appropriation	1,355,501	
Net Income / (Subsidy)	**297,058**	

*Payments received prior to FY22 closeout

*Other expenses consist of the following categories: Communications, Travel, Maintenance/Repairs, Memberships, Copier Rental and Registration Fees.

Subsidy, % before state Appropriation	25%
Subsidy, % after state appropriation	0%

Research Biocontainment Laboratory (RBL) Institutional Research Core Facility Analysis Report - FY22

Written by Colleen Jonsson, PhD; Elizabeth Fitzpatrick PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?

The RBL core designation as an institutional core is appropriate since it served 24 internal users across 11 departments and three colleges (COM, COP, and COHP), and eight external users. The top five users of RBL services, based upon the value of completed services in FY22, excluding animal orders and per diems, were: 1) Sina Bavari (14.48%, external, Healion Bio) 2) Prasann Bavaniya (12.75%, external, APPILI Therapeutics), 2) Jay Han (12.40%, external, MICO BIOMED), 4) Colleen Jonsson (9.72%, Microbiology, Immunology and Biochemistry, COM), and 5) Kui Li (6.58%, Microbiology, Immunology and Biochemistry, COM).

2. Does the core pass the multi-departmental, multi-investigator litmus test?

Yes. In FY22, this core supported 2,229 units of RBL services procured from 24 unique internal users across 11 departments, three colleges, and multiple external academic institutions or commercial entities.

3. Is there sufficient intra- and inter-departmental use and if not, why?

Yes.

4. Can the services for the core be outsourced more economically?

No. It should also be noted that BSL-3/ABSL-3 research requires specialized containment which the UTHSC RBL provides. The RBL was specifically constructed by NIH to meet the research needs of BSL-3 users who require this level of biocontainment, and it should be noted that there are only 11 RBL facilities in the United States. The RBL is a regional facility, providing UTHSC and external users in the Memphis area with the appropriate engineering controls, facilities and resources for BSL-3 and ABSL-3 research.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g., grants funded through investigator use, publications, etc.)?

Yes. Dr. Jonsson leveraged the institutional support offered by the campus and the Office of Research in the awarded NIH U19 Center of Excellence for Encephalitic Alphavirus Therapeutics for which she is the program leader. In addition, in FY22, the RBL supported 49 publications and 23 extramural grants or contracts. Services available in the RBL are unique and essential for investigators to maintain their research programs using BSL-3/ABSL-3 infectious or select agents. Importantly, the RBL enhances UTHSC's ability to compete for research projects in virology, bacterial pathogenesis, bacterial generated toxins and immunology, with a focus on emerging infectious diseases and select agents.

6. Is the core currently self-sufficient, or is it subsidized by the institution?

In FY22, the core was subsidized by the institution. After the state appropriation of $1,158,859, the net income for the core was $197,718.

Accomplishments this past year:
RBL Director, Colleen Jonsson and Associate Director, Elizabeth Fitzpatrick, have continued to revamp the existing RBL services to be more robust and to provide enhanced targeted services for ABSL-2 and ABSL-3 studies. In addition, the team has:

1. Increased faculty membership in the Institute for the Study of Host Pathogen Systems to support faculty research activities on campus through promotion of interdisciplinary research and faculty recruitment.
2. Revised the RBL marketing strategy to enhance, to promote and to increase the *in vivo* and after life studies performed in the RBL, thus creating more collaborative partnerships with internal, external, commercial and government agencies.
3. Designed and offered new RBL services related to the SARS COV-2 (COVID-19) pandemic, including drug discovery services.
4. Served over 30 external users from FY21-FY22, the highest volume of external users since the RBL opened.
5. Completed training on the Janus robot instruments to streamline high throughput screening using SARS CoV-2 and variants.
6. Began offering histology services in-house to increase specimen turnaround time and to remain compliant with biohazard inactivation protocols.
7. Awarded a facilities grant (G20 award) in FY22 to upgrade existing RBL infrastructure and to purchase new scientific equipment to enhance the existing services and to provide new services.

Financial Overview – FY22:

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues	130,680	108,048	195,215	827,598	567,520
Expenses	(1,170,295)	(951,232)	(888,434)	(1,838,975)	(1,528,661)
Income (Subsidy)	(1,039,615)	(843,184)	(693,219)	(1,011,377)	(961,141)
Other Costs	0	0	0	0	0
Income (Subsidy)	(1,039,165)	(843,184)	(693,219)	(1,011,377)	(961,141)
State Appropriation	737,969	755,465	735,371	1,029,459	1,158,859
Net Income (Subsidy)	(301,646)	(87,719)	42,152	18,082	197,718
Subsidy, % before State Appropriation	89%	88.6%	78%	55%	63%
Subsidy, % after State Appropriation	25.7%	9.2%	--	--	--

7. Suggested outcomes:
It is recommended that RBL continue as an institutional core.

Regional Biocontainment Laboratory (RBL) Institutional Core Facility Summary of Institutional Core Activities for FY22

Written by Colleen Jonsson, PhD; Elizabeth Fitzpatrick, PhD; Na Yeon; Natalie Smith, MS; and Tiffany Seagroves, PhD

I. PUBLICATIONS (Journal publication dates: July 1, 2021 to June 30, 2022)

Full length published articles (UTHSC faculty investigators using the RBL in FY22 are indicated in bold)

Kumar S, Kumar P, Kodidela S, Duhart B, Cernasev A, Nookala A, Kumar A, **Singh UP**, Bissler J. Racial Health Disparity and COVID-19. J Neuroimmune Pharmacol. 2021 Dec;16(4):729-742. doi: 10.1007/s11481-021-10014-7. Epub 2021 Sep 9. PMID: 34499313; PMCID: PMC8426163.

Kumar V, Kiran S, Kumar S, **Singh UP**. Extracellular vesicles in obesity and its associated inflammation. Int Rev Immunol. 2022;41(1):30-44. doi: 10.1080/08830185.2021.1964497. Epub 2021 Aug 23. PMID: 34423733; PMCID: PMC8770589.

Liao FF, Lin G, Chen X, Chen L, Zheng W, Raghow R, Zhou FM, Shih AY, Tan XL. Endothelial Nitric Oxide Synthase-Deficient Mice: A Model of Spontaneous Cerebral Small-Vessel Disease. Am J Pathol. 2021 Nov;191(11):1932-1945. doi: 10.1016/j.ajpath.2021.02.022. Epub 2021 Mar 10. PMID: 33711310; PMCID: PMC8647425.

Sumida K, Han Z, Chiu CY, Mims TS, Bajwa A, Demmer RT, Datta S, **Kovesdy CP**, Pierre JF. Circulating Microbiota in Cardiometabolic Disease. Front Cell Infect Microbiol. 2022 May 3;12:892232. doi: 10.3389/fcimb.2022.892232. PMID: 35592652; PMCID: PMC9110890.

DeJarnette C, Meyer CJ, Jenner AR, Butts A, Peters T, Cheramie MN, Phelps GA, Vita NA, Loudon-Hossler VC, Lee RE, **Palmer GE**. Identification of Inhibitors of Fungal Fatty Acid Biosynthesis. ACS Infect Dis. 2021 Dec 10;7(12):3210-3223. doi: 10.1021/acsinfecdis.1c00404. Epub 2021 Nov 17. PMID: 34786940; PMCID:PMC8670506.

Kovesdy CP, Adebiyi A, Rosenbaum D, Jacobs JW, Quarles LD. Novel Treatments from Inhibition of the Intestinal Sodium-Hydrogen Exchanger 3. Int J Nephrol Renovasc Dis. 2021 Dec 1;14:411-420. doi: 10.2147/IJNRD.S334024. PMID: 34880650; PMCID: PMC8646223.

Sharp BM, Fan X, Redei EE, Mulligan MK, **Chen H**. Sex and heredity are determinants of drug intake in a novel model of rat oral oxycodone self- administration. Genes Brain Behav. 2021 Nov;20(8):e12770. doi: 10.1111/gbb.12770. Epub 2021 Sep 16. PMID: 34459088; PMCID: PMC8815756.

Nagy-Szakal D, Couto-Rodriguez M, Wells HL, Barrows JE, Debieu M, Butcher K, Chen S, Berki A, Hager C, Boorstein RJ, Taylor MK, **Jonsson CB**, Mason CE, O'Hara NB. Targeted Hybridization Capture of SARS-CoV-2 and Metagenomics Enables Genetic Variant Discovery and Nasal Microbiome Insights. Microbiol Spectr. 2021 Oct 31;9(2):e0019721. doi: 10.1128/Spectrum.00197-21. Epub 2021 Sep 1. PMID: 34468193; PMCID: PMC8557865.

Wohlgemuth N, Whitt K, Cherry S, Kirkpatrick Roubidoux E, Lin CY, Allison KJ, Gowen A, Freiden P, Allen EK; St. Jude Investigative Team,, Gaur AH, Estepp JH, Tang L, Mori T, Hijano DR, Hakim H, McGargill MA, Krammer F, **Whitt MA**, Wolf J, Thomas PG, Schultz-Cherry S. An Assessment of Serological Assays for SARS- CoV-2 as Surrogates for Authentic Virus

Neutralization. Microbiol Spectr. 2021 Oct 31;9(2):e0105921. doi: 10.1128/Spectrum.01059-21. Epub 2021 Oct 27. PMID: 34704832; PMCID: PMC8549747.

Xue Y, Yang D, Vogel P, Stabenow J, Zalduondo L, Kong Y, Ravi Y, Sai-Sudhakar CB, Parvathareddy J, Hayes E, Taylor S, **Fitzpatrick E**, **Jonsson CB**. Cardiopulmonary Injury in the Syrian Hamster Model of COVID-19. Viruses. 2022 Jun 27;14(7):1403. doi: 10.3390/v14071403. PMID: 35891384; PMCID: PMC9316644.

Xu F, Gao J, Orgil BO, Bajpai AK, Gu Q, Purevjav E, Davenport AS, **Li K**, Towbin JA, Black DD, Pierre JF, Lu L. Ace2 and Tmprss2 Expressions Are Regulated by Dhx32 and Influence the Gastrointestinal Symptoms Caused by SARS-CoV-2. J Pers Med. 2021 Nov 16;11(11):1212. doi: 10.3390/jpm11111212. PMID: 34834564; PMCID: PMC8621576.

Rybak JM, Sharma C, Doorley LA, Barker KS, **Palmer GE**, Rogers PD. Delineation of the Direct Contribution of Candida auris ERG11 Mutations to Clinical Triazole Resistance. Microbiol Spectr. 2021 Dec 22;9(3):e0158521. doi: 10.1128/Spectrum.01585-21. Epub 2021 Dec 8. PMID: 34878305; PMCID: PMC8653815.

Bansal S, **Jonsson CB**, Taylor SL, Figueroa JM, Dugour AV, Palacios C, Vega JC. Iota-carrageenan and xylitol inhibit SARS-CoV-2 in Vero cell culture. PLoS One. 2021 Nov 19;16(11):e0259943. doi: 10.1371/journal.pone.0259943. PMID: 34797868; PMCID: PMC8604354.

Kneller DW, Li H, Phillips G, Weiss KL, Zhang Q, Arnould MA, **Jonsson CB**, Surendranathan S, Parvathareddy J, Blakeley MP, Coates L, Louis JM, Bonnesen PV, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors of SARS-CoV-2 main protease. Nat Commun. 2022 Apr 27;13(1):2268. doi: 10.1038/s41467-022-29915-z. PMID: 35477935; PMCID: PMC9046211.

Almeida C, Pongilio RP, Móvio MI, Higa GSV, Resende RR, **Jiang J**, Kinjo ER, Kihara AH. Distinct Cell-specific Roles of NOX2 and MyD88 in Epileptogenesis. Front Cell Dev Biol. 2022 Jul 4;10:926776. doi: 10.3389/fcell.2022.926776. PMID: 35859905; PMCID: PMC9289522.

Fischer MJ, Streja E, Hsiung JT, Crowley ST, **Kovesdy CP**, Kalantar-Zadeh K, Kourany WM. Depression screening and clinical outcomes among adults initiating maintenance hemodialysis. Clin Kidney J. 2021 Jun 25;14(12):2548-2555. doi: 10.1093/ckj/sfab097. PMID: 34950466; PMCID: PMC8690052.

Adams A, Murphy QM, Dougherty OP, Sawyer AM, Bai F, Edholm CJ, Williams EP, Allen LJS, **Jonsson CB**. Data-driven models for replication kinetics of Orthohantavirus infections. Math Biosci. 2022 Jul;349:108834. doi: 10.1016/j.mbs.2022.108834. Epub 2022 May 19. PMID: 35598641.

Kiran S, Rakib A, **Singh U**P. The NLRP3 Inflammasome Inhibitor Dapansutrile Attenuates Cyclophosphamide-Induced Interstitial Cystitis. Front Immunol. 2022 Jun 3;13:903834. doi: 10.3389/fimmu.2022.903834. PMID: 35720309; PMCID: PMC9205468.

Kumar A, Sinha N, Kodidela S, Zhou L, **Singh UP**, Kumar S. Effect of benzo(a)pyrene on oxidative stress and inflammatory mediators in astrocytes and HIV-infected macrophages. PLoS One. 2022 Oct 14;17(10):e0275874. doi: 10.1371/journal.pone.0275874. PMID: 36240258; PMCID: PMC9565757.

Banerjee S, Yadav S, Banerjee S, Fakayode SO, Parvathareddy J, Reichard W, Surendranathan S, Mahmud F, Whatcott R, Thammathong J, **Meibohm B**, Miller DD, **Jonsson CB**, Dubey KD. Drug Repurposing to Identify Nilotinib as a Potential SARS-CoV-2 Main Protease Inhibitor: Insights from a Computational and In Vitro Study. J Chem Inf Model. 2021 Nov 22;61(11):5469-5483. doi: 10.1021/acs.jcim.1c00524. Epub 2021 Oct 20. PMID: 34666487; PMCID: PMC8547516.

Hou R, Yu Y, Sluter MN, Li L, Hao J, Fang J, Yang J, **Jiang J**. Targeting EP2 receptor with multifaceted mechanisms for high-risk neuroblastoma. Cell Rep. 2022 Jun 21;39(12):111000. doi: 10.1016/j.celrep.2022.111000. PMID: 35732130; PMCID: PMC9282716.

Xu X, Zhang C, **Jiang J**, Xin M, Hao J. Effect of TDP43-CTFs35 on Brain Endothelial Cell Functions in Cerebral Ischemic Injury. Mol Neurobiol. 2022 Jul;59(7):4593-4611. doi: 10.1007/s12035-022-02869-5. Epub 2022 May 18. PMID: 35581521.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y, Vogel P, Channappanavar R, **Jonsson CB**, **Smith AM**. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infections During SARS-CoV-2. Front Immunol. 2022 May 12;13:894534. doi: 10.3389/fimmu.2022.894534. PMID: 35634338; PMCID: PMC9134015.

Luna-Tapia A, Parker JE, Kelly SL, **Palmer GE**. Species-Specific Differences in C-5 Sterol Desaturase Function Influence the Outcome of Azole Antifungal Exposure. Antimicrob Agents Chemother. 2021 Nov 17;65(12):e0104421. doi: 10.1128/AAC.01044-21. Epub 2021 Sep 13. PMID: 34516249; PMCID: PMC8597749.

Wu Y, Yang D, **Chen GY**. The role of the Siglec-G ITIM domain during bacterial infection. Cell Mol Biol (Noisy-le-grand). 2022 Jan 2;67(4):163-169. doi: 10.14715/cmb/2021.67.4.18. PMID: 35809291.

Nagib MM, Zhang S, Yasmen N, Li L, Hou R, Yu Y, Boda VK, Wu Z, Li W, **Jiang J**. Inhibition of TRPC3 channels by a novel pyrazole compound confers antiseizure effects. Epilepsia. 2022 Apr;63(4):1003-1015. doi: 10.1111/epi.17190. Epub 2022 Feb 18. PMID: 35179226; PMCID: PMC9007831.

Wu Y, Yang D, **Chen GY**. Targeted disruption of Gdi2 causes early embryonic lethality. Placenta. 2022 Aug;126:17-25. doi: 10.1016/j.placenta.2022.05.005. Epub 2022 May 13. PMID: 35689892.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y, Vogel P, Channappanavar R, **Jonsson CB**, **Smith AM**. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infection during SARS-CoV-2 Infection. bioRxiv [Preprint]. 2022 Mar 1:2022.02.28.482305. doi: 10.1101/2022.02.28.482305. Update in: Front Immunol. 2022 May 12;13:894534. PMID: 35262077; PMCID: PMC8902874.

Kneller D, Li H, Phillips G, Weiss K, Zhang Q, Arnould M, **Jonsson C**, Surendranathan S, Parvathareddy J, Blakeley M, Coates L, Louis J, Bonnesen P, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors of SARS-CoV-2 main protease: room-temperature X-ray and neutron crystallography, binding thermodynamics, and antiviral activity. Res Sq [Preprint]. 2022 Feb 11:rs.3.rs-1318037. doi: 10.21203/rs.3.rs-1318037/v1. Update in: Nat Commun. 2022 Apr 27;13(1):2268. PMID: 35169792; PMCID: PMC8845512.

Munkhsaikhan U, Kwon Y, Sahyoun AM, Ait-Aissa K, Kassan A, **Kassan M**. The microsomal triglyceride transfer protein inhibitor lomitapide improves vascular function in mice with obesity. Obesity (Silver Spring). 2022 Apr;30(4):893-901. doi: 10.1002/oby.23389. Epub 2022 Mar 6. PMID: 35253407; PMCID: PMC8957593.

Yoon TW, **Fitzpatrick EA**, Snyder JD, Lee S, Kim YI, Zacheaus C, Yi AK. Contribution of Protein Kinase D1 on Acute Pulmonary Inflammation and Hypersensitivity Pneumonitis Induced by Saccharopolyspora rectivirgula Immunohorizons. 2022 Mar 10;6(3):224-242. doi: 10.4049/immunohorizons.2200017. PMID: 35273098.

Li L, Yasmen N, Hou R, Yang S, Lee JY, Hao J, Yu Y, **Jiang J**. Inducible Prostaglandin E Synthase as a Pharmacological Target for Ischemic Stroke. Neurotherapeutics. 2022 Jan;19(1):366-385. doi: 10.1007/s13311-022-01191-1. Epub 2022 Jan 31. PMID: 35099767; PMCID: PMC9130433.

Kneller DW, Li H, Galanie S, Phillips G, Labbé A, Weiss KL, Zhang Q, Arnould MA, Clyde A, Ma H, Ramanathan A, **Jonsson CB**, Head MS, Coates L, Louis JM, Bonnesen PV, Kovalevsky A. Structural, Electronic, and Electrostatic Determinants for Inhibitor Binding to Subsites S1 and S2 in SARS-CoV-2 Main Protease. J Med Chem. 2021 Dec 9;64(23):17366-17383. doi: 10.1021/acs.jmedchem.1c01475. Epub 2021 Oct 27. PMID: 34705466; PMCID: PMC8565456.

Ahmed HA, Ismael S, Salman M, Devlin P, McDonald MP, **Liao FF**, Ishrat T. Direct AT2R Stimulation Slows Post-stroke Cognitive Decline in the 5XFAD Alzheimer's Disease Mice. Mol Neurobiol. 2022 Jul;59(7):4124-4140. doi: 10.1007/s12035-022-02839-x. Epub 2022 Apr 29. PMID: 35486224.

Merigeon EY, Yang D, Ihms EA, Bassit LC, **Fitzpatrick EA**, **Jonsson CB**, Schinazi RF, Block DS, Olsen HS. An ACE2-IgG4 Fc Fusion Protein Demonstrates Strong Binding to All Tested SARS-CoV-2 Variants and Reduced Lung Inflammation in Animal Models of SARS-CoV-2 and Influenza. Pathog Immun. 2022 Aug 23;7(1):104-121. doi: 10.20411/pai.v7i1.491. PMID: 36072571; PMCID: PMC9438944.

Fu H, Wang J, Wang J, Liu L, **Jiang J**, Hao J. 4R-cembranoid protects neuronal cells from oxygen-glucose deprivation by modulating microglial cell activation. Brain Res Bull. 2022 Feb;179:74-82. doi: 10.1016/j.brainresbull.2021.12.007.Epub 2021 Dec 20. PMID: 34942325; PMCID: PMC8849140.

Ryan MC, Kim E, Cao X, Reichard W, Ogorek TJ, Das P, **Jonsson CB**, Baudry J, Chung D, Golden JE. Piperazinobenzodiazepinones: New Encephalitic Alphavirus Inhibitors via Ring Expansion of 2-Dichloromethylquinazolinones. ACS Med Chem Lett. 2022 Mar 14;13(4):546-553. doi: 10.1021/acsmedchemlett.1c00539. PMID: 35450382; PMCID: PMC9014857.

Kiran S, Rakib A, Moore BM, **Singh UP**. Cannabinoid Receptor 2 (CB2) Inverse Agonist SMM-189 Induces Expression of Endogenous CB2 and Protein Kinase A That Differentially Modulates the Immune Response and Suppresses Experimental Colitis. Pharmaceutics. 2022 Apr 26;14(5):936. doi: 10.3390/pharmaceutics14050936. PMID: 35631522; PMCID: PMC9147685.

Zhang C, Sajith AM, Xu X, **Jiang J**, Phillip Bowen J, Kulkarni A, Hao J. Targeting NLRP3 signaling by a novel-designed sulfonylurea compound for inhibition of microglial inflammation. Bioorg Med Chem. 2022 Mar 15;58:116645.doi: 10.1016/j.bmc.2022.116645. Epub 2022 Jan 31. PMID: 35151118; PMCID:
PMC8895276.

åKiran S, Rakib A, Kodidela S, Kumar S, **Singh UP**. High-Fat Diet-Induced Dysregulation of Immune Cells Correlates with Macrophage Phenotypes and Chronic Inflammation in Adipose Tissue. Cells. 2022 Apr 13;11(8):1327. doi: 10.3390/cells11081327. PMID: 35456006; PMCID: PMC9031506.

Gaur AH, Panetta JC, **Smith AM**, Dallas RH, Freeman BB 3rd, Stewart TB, Tang L, John E, Branum KC, Patel ND, Ost S, Heine RN, Richardson JL, Hammill JT, Bebrevska L, Gusovsky F, Maki N, Yanagi T, Flynn PM, McCarthy JS, Chalon S, Guy RK. Combining SJ733, an oral ATP4 inhibitor of Plasmodium falciparum, with the pharmacokinetic enhancer cobicistat: An innovative approach in antimalarial drug
development. EBioMedicine. 2022 Jun;80:104065. doi: 10.1016/j.ebiom.2022.104065. Epub 2022 May 19. PMID: 35598441; PMCID: PMC9127571.

Wang D, Wang R, **Li K**. Impaired Antiviral Responses to Extracellular Double- Stranded RNA and Cytosolic DNA, but Not to Interferon-α Stimulation, in TRIM56-Deficient Cells. Viruses. 2022 Jan 5;14(1):89. doi: 10.3390/v14010089. PMID: 35062293; PMCID: PMC8777648.

Regan J, DeJarnette C, Luna-Tapia A, Parker JE, Reitler P, Barnett S, Tucker KM, Kelly SL, **Palmer GE**. Titration of C-5 Sterol Desaturase Activity Reveals Its Relationship to Candida albicans Virulence and Antifungal Susceptibility Is Dependent upon Host Immune Status. mBio. 2022 Apr 26;13(2):e0011522. doi: 10.1128/mbio.00115-22. Epub 2022 Apr 5. PMID: 35380453; PMCID: PMC9040724.

Kassan A, Ait-Aissa K, **Kassan M**. Gut Microbiota Regulates the Sympathetic Nerve Activity and Peripheral Serotonin Through Hypothalamic MicroRNA-204 in Order to Increase the Browning of White Adipose Tissue in Obesity. Cureus. 2022 Feb 4;14(2):e21913. doi: 10.7759/cureus.21913. PMID: 35155042; PMCID: PMC8820388.

Fili CV, Lin L, Chapman J, **Hamilton D,** Yates CR. Methylsulfonylmethane and Sesame Seed Oil Improve Dyslipidemia and Modulate Polyunsaturated Fatty Acid Metabolism in Two Mouse Models of Diabetes. J Med Food. 2022 Jun;25(6):607-617. doi: 10.1089/jmf.2021.0196. PMID: 35708633; PMCID: PMC9247677.

Liu J, Vogel AK, Miao J, Carnahan JA, Lowes DJ, Rybak JM, **Peters BM**. Rapid Hypothesis Testing in Candida albicans Clinical Isolates Using a Cloning-Free, Modular, and Recyclable System for CRISPR-Cas9 Mediated Mutant and Revertant Construction. Microbiol Spectr. 2022 Jun 29;10(3):e0263021. doi: 10.1128/spectrum.02630-21. Epub 2022 May 25. PMID: 35612314; PMCID: PMC9241802.

Regan J, **Palmer GE**. Identifying Specific Small Molecule-Protein Interactions Using Target Abundance Based Fitness Screening (TAFiS). Methods Mol Biol. 2022;2542:115-126. doi: 10.1007/978-1-0716-2549-1_8. PMID: 36008660.

Ye X, Pan T, Wang D, Fang L, Ma J, Zhu X, Shi Y, Zhang K, Zheng H, Chen H, **Li K**, Xiao S. Corrigendum: Foot-and-Mouth Disease Virus Counteracts on Internal Ribosome Entry Site

Suppression by G3BP1 and Inhibits G3BP1-Mediated Stress Granule Assembly via Post-Translational Mechanisms. Front Immunol. 2021 Nov 4;12:702530. doi: 10.3389/fimmu.2021.702530. Erratum for: Front Immunol. 2018 May 25;9:1142. PMID: 34804006; PMCID: PMC8600380.
Taylor MK, Williams EP, Wongsurawat T, Jenjaroenpun P, Nookaew I, **Jonsson CB**. Corrigendum: Amplicon-Based, Next-Generation Sequencing Approaches to Characterize Single Nucleotide Polymorphisms of Orthohantavirus Species. Front Cell Infect Microbiol. 2022 Jan 24;11:804914. doi: 10.3389/fcimb.2021.804914. Erratum for: Front Cell Infect Microbiol. 2020 Oct 14;10:565591. PMID: 35141171; PMCID: PMC8819723.

II. PRESENTATIONS GIVEN TO PROMOTE CORE USAGE:

The amount of work coming into the RBL resulted in the directors and staff being at capacity. Hence, we have not made any presentations during the pandemic. We will resume advertisement in FY23 through UTHSC and at national meetings.

III. SUMMARY OF ACTIVITIES

A. Personnel (% Salary/ Effort, until 6/30/2022)

Director: Colleen Jonsson (40%)
Assistant Director: Elizabeth Fitzpatrick (13.25%)
Facility Manager: Jennifer Stabenow (100%); salary coverage to 06.17.2022
Building Superintendent: Robert Benson (100%); salary coverage until 05.04.2022
Building Superintendent: Terry Bruckman (100%), salary coverage starting 04.01.2022
Supervisor (ABSL-3): Lillian Zalduondo (100%)
Assistant Building Superintendent: John Burns (100%); salary coverage until June 17, 2022
Sr. Lab Animal Care Technician: Fu Zeng (100%)
Lab Animal Care Technician: Crystal Murphy (100%); salary coverage
Lab Animal Care Technician: Arlandis Clayton (100%); salary coverage until October 27, 2021
Lab Animal Care Technician: Mercedes Carter's hire date was May 9, 2022. She is 100% salary coverage from this date.
Grants and Contracts Coordinator: Na Seung Yeon (50%)
Assistant Director/RBL Business Manager: Natalie Smith (50% effort, paid by the Office of Research under a separate budget)
Financial Coordinator: Wendy Love (100%)
Sr. Research Specialist: Jyothi Parvathareddy (100%)
Sr. Research Specialist: Surekha Surendranatha (100%)
Sr. Research Specialist: Yuting Zhang (100%)
RBL Research Program Manager: Dong Yang (100%)
RBL Facility Technician: Hayden Anderson (100%)

B. Oversight Committee: University of Tennessee RBL Executive Committee (UTREC)

UTREC consisted of the following members in FY22:
Steven Youngentob, PhD (Sr. Associate Vice Chancellor for Research, Dept. of Anatomy and Neurobiology) *UTREC Chair*
Michael Whitt, PhD (Dept. of Microbiology, Immunology & Biochemistry)

Mark Miller, PhD (Dept. of Microbiology, Immunology & Biochemistry)
Tiffany Seagroves, PhD (Associate Vice Chancellor for Research-Core Facilities, and Dept. of Pathology and Laboratory Medicine)
David Hamilton, DVM (Lab Animal Care Unit)
Jennifer Stabenow, MS, RVT (RBL)
Robert Benson (RBL)
Jacqueline Toney (RBL)
Lillian Zalduondo (RBL)
Dong Yang (RBL)

C. Equipment (> $10K)

Responsible cost center:	Equipment Description:	Cost:	Capitalized on:
E070165001	FACS Aria II Special order system	367,940.00	01/21/2009
E070165001	IVIS Spectrum Imaging System	344,708.00	12/11/2008
E070165	JANUS Intergrator Platform	225,952.00	01/06/2010
E070165	Delta Vision personal DV Live Cell Imaging System	191,598.76	09/14/2009
E070165	MiSeq System	95,931.00	07/16/2018
E070165	CH Technologies BANG unit	92,690.00	05/11/2010
E070165	Minidox-M Chlorine Dioxide Gas Generator	75,158.92	09/02/2009
E070165	EnVision Multilabel Reader	69,825.00	06/11/2010
E070165	EnVision Multilabel Reader	67,620.00	01/06/2010
E070165	CH Technologies BANG unit	63,965.40	07/21/2010
E070165	Millipore Luminex 200 3.1 x Ponent	45,591.00	12/21/2009
E070165	MDT Disposable Tip Head	44,700.00	07/24/2018
E070165001	BioPROtect lll Bio-Containment Enclosure for BD	44,400.00	05/08/2009
E070165	BCU 2000 Housing System for Mice	41,350.00	02/10/2012
E070165	BCU 2000 Housing System for Mice	41,350.00	02/10/2012
E070165002	QSTUDIO 6 FLX system	38,844.78	12/20/2017
E070165	CFX96 Realtime PCR Detection System	35,900.00	11/16/2009
E070165001	Cage Mouse Bio-Containment Unit #1	30,068.21	12/10/2008
E070165001	Synergy 2 SLFA Model Plate Reader	28,630.50	03/30/2009
E070165	Synergy 2 SLFA Model Dr. Byrne	28,630.50	10/15/2009
E070165	42-Cage mouse Bio containment unit	27,098.46	09/02/2010
E070165	42-Cage mouse Bio containment unit	27,098.46	09/02/2010
E070165	42-Cage mouse Bio containment unit	27,098.46	09/02/2010
E070165002	MAGPIX with XPONENT 4.2	23,660.00	11/13/2017
E070165	Synergy HT RDR - (Miller)	23,605.00	09/18/2006
E070165	DiaSys Chemistry System Analyzer	22,696.99	04/23/2018
E070165	42-Cage Bio containment unit w/ blower and battery	22,364.50	06/19/2012
E070165002	Multiflo Fx with Peri Washer	19,472.79	09/02/2010
E070165	softWoRx Computer Server 3.7.0 (Linux)	19,163.95	01/13/2010

E070165001	Eddy Jet Automatic Plater for Spiral Spreading	18,954.00	09/12/2008
E070165	2014 POLARIS GEM TRUCK	18,192.32	01/16/2014
E070165002	Infinite M200 PRO # Monochromator	16,234.00	06/18/2014
E070165001	Ventilated Animal Transport Unit	13,812.60	05/14/2009
E070165001	Axiovert 40 cfl	11,865.00	06/22/2009
E070165	Axiovert 40 CFL	11,865.00	07/14/2009
E070165002	ULT FZ TSX60086A 115V/60HZ PMO	11,367.20	05/01/2018
E070165	Upright -86 Ultralow Freezer	11,034.00	05/05/2017
E070165002	Fastprep-24 Instrument Homogenizer	10,950.00	08/09/2013
E070165	DiaSys Hematology Analyzer	10,849.04	04/23/2018
E070165	ATI Model 2HA Digital Photometer 120V w/attachment CTL Immunospot	10,547.83 128,000.00	02/19/2010
R070165024 (G20)	Cytek Aurora Cytometer	242,138.00	11/23/2021
R070165024 (G20 grant)	Fujifilm Echo vivo system incl mouse bed and probe	375,125.00	11/22/2022

D. RBL Service Contracts, FY22

Vendor	**Equipment**	**Cost/yr.**
Perkin Elmer	Janus BSL2/BSL3	$22,116.00
Specialty Underwriters	Various Equipment	$41,790.00
Illumina, Inc.	MiSeq System	$18,390.00
Agilent Technologies	2100 Bioanalyzer	$2,548.79
Life Technologies	Quantstudio 6 Flex	$6,120.00
Total costs, all service contracts		**$90,964.79**

E. Advertisement of the Core

Due to the large and ever-increasing demand for SARS-CoV-2 research by public and private institutes nationwide during the pandemic of FY21/FY22, the UTHSC RBL became more recognizable. The RBL performed, and continues to perform, several promotional activities to provide awareness of RBL expertise and services. (1) Website updates: The website updates continued through FY22 and included restructuring of service pages with updated pricing, service descriptions and images, and information about SARS CoV-2 specific services. It also developed a new page to help clients submit a service request directly through the link on the website. (2) Personal contacts / word of mouth: The RBL director and others at UTHSC recommended the UTHSC RBL to individuals and companies around the globe bringing in numerous new clients. Additionally, new clients provided our information to others bringing in additional clients to the UTHSC RBL. (3) NIAID resource: The UTHSC RBL has a webpage on the NIAID biocontainment facilities resource website (Biocontainment Laboratory—University of Tennessee | NIH: National Institute of Allergy and Infectious Diseases) which attracted additional new customers. (4) Collaboration/Contribution with local community: The UTHSC RBL became visible to many members of the local community due to its continued participation in regional COVID 19 activities, such as sequencing variants for

the City of Memphis, interviews of Dr. Jonsson by local news media outlets, etc., resulting in new clients and greater visibility in our region.

F. Usage in FY22 By Service

FY22 usage of RBL by internal UTHSC investigators:

Department/PI	Value of Completed Services, $
Anatomy and Neurobiology	**1,521.00**
Robert W. Williams	1,521.00
CLINICAL PHARMACY & TRANSLATIONAL SCIENC	**13,288.31**
Brian Peters	2,724.64
Glen Palmer	5,087.84
Ted Cory	5,475.83
COMPARATIVE MEDICINE-GHS	**974.10**
David Hamilton	974.10
MEDICINE-NEPHROLOGY	**557.43**
Csaba Kovesdy	557.43
Microbiology, Immunology, and Biochemistry	**99,361.29**
Amber Smith	2,120.22
Colleen Jonsson	50,383.23
Elizabeth A Fitzpatrick	2,444.39
Kui Li	34,110.34
Ying Kong	9670.72
Michael Whitt	404.41
Tayebeh Pourmotabbed	228.48
ORTHOPAEDIC SURGERY	**139.20**
Hongsik Cho	139.20
PEDIATRICS-RESEARCH	**14,642.21**
Guoyun Chen	14,642.21
PHARMACEUTICAL SCIENCES	**3,848.21**
Bernd Meibohm	3,630.44
Jianxiong Jiang	195.91
Udai Singh	21.86
PHARMACOLOGY	**4,130.74**
Francesca-Fang Liao	4,130.74
PHYSIOLOGY	**17,758.80**
Gabor Tigyi	16,331.10
Modar Omar Kassan	1,427.70
Regional Biocontainment laboratory	**175.00**
	175.00
Grand Total, Internal	**156,396.26**

FY22 usage of the RBL by external clients:

External Client	Value of Completed Services, $
MICO BIOMED (Commercial)	64,272.67
Rutgers University (Academic: Fan, Simon, Welsh)	2,719.20
Amcyte Pharma (Commercial)	1,548.80
Anavex (Commercial)	13,133.21
Appili Therapeutics (Commercial)	66,084.90
BIOMED DIAGNOSTICS (Commercial)	20,453.07
FDA NCTR (Government)	6,385.56
FUJIFILM Pharmaceuticals (Commercial)	9,604.08
Harvard (Academic)	18,434.80
Healion Bio (Commercial)	75,000.00
Kansas State University (Academic)	2,472.00
Oak Ridge National Laboratory (Academic)	9,000.00
PROVECTUS (Commercial)	9,277.10
Pusan National University, S. Korea (Academic)	1,302.00
St. John's Cancer Institute (Academic)	865.20
St. Jude Children's Research Hospital (Academic)	23,689.56
University of Arkansas at Fort Smith (UAFS, Academic)	494.40
UCHS	13,905.53
University of Michigan (Academic)	15,889.88
University of North Carolina at Charlotte (Academic)	2,472.00
University of South Carolina (Academic)	4,120.00
Yale University (Academic)	610.80
Grand Total, External	**361,914.76**

G. FY22 Fee Structure

PER DIEM ANIMAL CHARGES:

Item	Cost	Unit
Mice (4 per cage):		
ABSL2 per diem, internal	$1.04	cage/day
ABSL2 per diem, commercial	$1.53	cage/day
ABSL3 per diem, internal	$1.14	cage/day
ABSL3 per diem, commercial	$3.23	cage/day
Rats (2 per cage):		
ABSL2 per diem, internal	$2.60	cage/day
ABSL2 per diem, commercial	$3.85	cage/day
ABSL3 per diem, internal	$3.33	cage/day
ABSL3 per diem, commercial	$4.93	cage/day

Hamster (1-2 per cage):		
ABSL2 per diem, internal	$2.60	cage/day
ABSL2 per diem, commercial	$3.85	cage/day
ABSL3 per diem, internal	$3.33	cage/day
ABSL3 per diem, commercial	$4.93	cage/day
Guinea Pig or Cotton Rat (1 per cage):		
ABSL2 per diem, internal	$2.60	cage/day
ABSL2 per diem, commercial	$3.85	cage/day
ABSL3 per diem, internal	$3.33	cage/day
ABSL3 per diem, commercial	$4.93	cage/day
Ferret (2 per cage):		
ABSL2 per diem, internal	$6.35	cage/day
ABSL2 per diem, commercial	$11.34	cage/day
ABSL3 per diem, internal	$7.62	cage/day
ABSL3 per diem, commercial	$14.74	cage/day

PPE-ROOM CHARGES: BSL2, BSL3 or ABSL3:

INTERNAL

Item	Cost	Unit
BSL-2 PPE	$5.00	day
BSL-3/ABSL-2 PPE Fee	$9.84	day
ABSL-3 PPE Fee	$30.61	day
Dedicated ABSL-2 Suite-per PI	$30.61	day
Pathogen Storage (long term):	$3.09	day

COMMERCIAL

Item	Cost	Unit
BSL-2/ABSL-2 PPE Fee	$54.65	day
BSL-3/ABSL-3 PPE Fee	$109.28	day
BSL-3 Facility Use	$47.84	day
Vivarium Facility Usage fee	$61.81	day
Sample Storage (long term)	$3.83	day

INSTRUMENTATION

Cost estimates for instrumentation. NOTE: Costs do not include consumables, labor or PPE.

Item	Cost	Unit
QuantStudio 6 qPCR		
Internal	$10.93	per run
Commercial	$17.71	per run

EnVision Microplate Reader		
Internal	$10.93	per run
Commercial	$17.71	per run
Synergy 2 Microplate Reader:		
Internal	$5.46	per run
Commercial	$8.85	per run
Luminex FX-200:		
Internal	$10.93	per run
Commercial	$41.53	per run
MagPix:		
Internal	$27.32	per run
Commercial	$54.64	per run
Illumina MiSeq System:		
Internal	$114.73	per run
Commercial	$149.15	per run
MultiFlo FX:		
Internal	$10.93	per run
Commercial	$27.32	per run
Janus high-throughput robot:		
Internal	$87.42	per run
Commercial	$114.73	per run
BioAnalyzer:		
Internal	$10.93	per run
Commercial	$41.53	per run
CLC Software:		
Internal	$10.30	per run
Commercial	$13.39	per run
Bead Mill		
Internal	$10.93	per run
Commercial	$27.32	per run
IVIS Spectrum Bio-Imager:		
Unassisted, internal	$109.27	per hour
Operator assisted, internal	$139.94	per hour
Operator assisted, commercial	$227.23	per hour
BANG (aerosol delivery device):		
Setup charge, internal	$54.64	run
Setup charge, commercial	$88.51	run
Decon. charge, internal	$54.64	run
Decon. charge, commercial	$88.51	run

IN VITRO SERVICES

Virology services

Item	Cost/unit	Unit
Virus Isolation, internal:	$223.51	sample
Virus Isolation, commercial:	$362.09	sample
Virus Plaque Assay, internal (labor not included)	$52.10	sample
Virus Plaque Assay, commercial, (labor not included)	$67.72	sample
Virus PRNT (titer reduction) Assay, internal	$824.00	5 samples plus controls
Virus PRNT (titer reduction) Assay, commercial	$1,071.20	5 samples plus controls
Viral TCID CPE Assay, internal:	$54.61	96-well
Viral TCID CPE Assay, commercial:	$70.99	96-well
Viral TCID HI Assay, internal	$54.61	sample
Viral TCID HI Assay, commercial	$70.99	sample
RNA Isolation (Qiagen-Kingfisher) internal	$29.87	sample
RNA Isolation (Qiagen-Kingfisher) commercial	$38.11	sample
RNA Isolation (Trizol) \qRTPCR , internal	$54.86	sample
RNA Isolation (Trizol)/ qRTPCR , commercial	$71.32	sample
Viral Neutralization Test, internal:	$580.50	Plate (1-20 samples-duplicate)
Viral Neutralization Test, commercial:	$937.30	Plate (1-20 samples-duplicate)
Viral Antiviral HTS Test, internal:	$206.00	1 compound
Viral Antiviral HTS Test, commercial:	$267.80	1 compound
Viral Antiviral HTS Test, internal:	$123.60	3-7 compounds
Viral Antiviral HTS Test, commercial:	$154.50	3-7 compounds
Viral Antiviral HTS Test, internal:	$61.80	8 plus compounds
Viral Antiviral HTS Test, commercial:	$80.34	8 plus compounds
Custom Viral Antiviral HTS Test, internal:	$257.50	1 compound
Custom Viral Antiviral HTS Test, commercial:	$319.30	1 compound
Custom Viral Antiviral HTS Test, internal:	$175.10	3-7 compounds
Custom Viral Antiviral HTS Test, commercial:	$216.30	3-7 compounds
Custom Viral Antiviral HTS Test, internal:	$162.74	8 plus compounds
Custom Viral Antiviral HTS Test, commercial:	$175.10	8 plus compounds
Custom SARS-CoV-2 Variant screening and Antiviral HTS, internal:	$610.80	For 4 viruses
Custom SARS-CoV-2 Variant Screening and Antiviral HTS, commercial:	$800.34	For 4 viruses

IMMUNOLOGY SERVICES - full service multiplex bead based assay (Cytokines)

Item	Cost	Unit
Samples (40-80) and kit provided by PI		
Luminex		
internal	$293.55	per plate
commercial	$381.62	per plate

Magpix-BSL2		
internal	$320.85	per plate
commercial	$417.10	per plate
Magpix-BSL3 (includes PPE)		
internal	$341.63	per plate
commercial	$526.28	per plate

Tissue Homogenization

Item	Cost	Unit
BSL2		
per 40 samples		
internal	$61.65	(6.50/tissue)
commercial	$402.53	(9.80/tissue)
BSL3		
per 40 samples		
internal	$267.65	(6.50/tissue)
commercial	$457.22	(11.10/tissue)

Flow cytometry prep — Includes labor and materials for single cell isolation, counting and aliquoting to flow tubes - NO PPE

Item	Cost	Unit
Internal		
Spleen	$25.75	sample
Inguinal lymph nodes	$25.75	sample
Lung	$56.65	sample
Brain	$56.65	sample
Intestine	$56.65	sample
Commercial $400 minimum (or 10 sample minimum)		
Spleen	$25.75	sample
Inguinal lymph nodes	$25.75	sample
Lung	$56.65	sample
Brain	$56.65	sample
Intestine	$56.65	sample

Flow Cytometry staining - using our flow cytometry panels (quotes for other markers will be customized)		
Internal	$2.06	sample
Commercial	$32.96	sample
Flow cytometer run		
Internal	ILAB	
Commercial	$81.08	hour

PATHOLOGY (BSL3 Tissues Only- Limited Availability)

Item	Cost	Unit
Decalcification	$8.74	specimen
Paraffin processing only (no embedding):	$2.74	cassette
Paraffin process and embedding:	$3.28	block
First and additional unstained slides:	$2.74	slide
Unstained slides, but *levels requested**:	$6.56	slide
Recut of previously faced paraffin block:	$2.74	slide
H&E staining of cut slides:	$3.83	slide
Trichrome staining of cut slides:	$19.67	slide
PAS staining of cut slides:	$16.39	slide
Other special stains of cut slides:	TBD	slide
Antibodies	purchase cost	unit

CLINICAL CHEMISTRY AND HEMATOLOGY SERVICES:

Item	Cost	Unit
Clinical Chemistry:		
Chemistry panels (internal)	$26.06	per sample
Set-Up charge (internal)	$24.08	per run
Chemistry panels (commercial)	$48.15	per sample
Set-Up charge (commercial)	$31.20	per run
Hematology:		
Sample analyses (internal)	$15.45	per sample
Set-Up Charge (internal)	$10.61	per run
Sample Analyses (commercial)	$23.02	per sample
Set-Up charge (commercial)	$13.79	per run

SARS-CoV-2 NEXT GENERATION SEQUENCING SERVICES:

Item	Cost	Unit
Variant Calling – minimum 80 samples per run		
SARS-CoV-2 (internal)	$75.00	per sample
SARS-CoV-2 (commercial)	$300.00	per sample
Deep Sequencing >400 nt – minimum 20 samples (up to 22 per run)		
SARS-CoV-2 (internal)	$98.00	per sample
SARS-CoV-2 (commercial)	$400.00	per sample

ISO/ASTM and GLP are available but will incur additional costs.

IV: GRANTS SUPPORTED BY THE CORE

Chen, Guoyun
USPHS NIH Grant AI-137255-01, Targeting Siglec-9/E for therapy of sepsis

Li, Kui
UPHS NIH Grant I-142044, Molecular mechanisms governing the regulation of innate antiviral immunity by the SRMS kinase

Jiang, Jianxiong
USPHS NIH Grant NS-100947, Inflammatory regulation of neurotrophin signaling in epileptogenesis

Jonsson, Colleen
CFD Research Corp/DOD - Jonsson, Producing Biosynthetic Therapeutics from Extreme Microbiomes

Jonsson, Colleen
FDA 75F40121C00154, Evaluation of Small Animal Models for COVID-19 and their application in Nonclinical Safety and Efficacy Studies of Investigational Therapeutics

Jonsson, Colleen
Univ Wisconsin Subcontract to USPHS NIH Grant AI-161232, Accelerated discovery of cell-active SARS-CoV-2 polymerase inhibitors via molecular dynamic guided screening and optimization

Jonsson, Colleen
USPHS Grant NIH AI-142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

Kassan, Modar
USPHS NIH Grant HI-150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Kong, Ying
Farmspace Systems, contract AT21T00000028, COVID Finder (CF)/Phase 1

Liao, Francesca-Fang
USPHS NIH Grant AG058467, Novel mechanistic link between metabolic changes and dementia potential role of miRNA21

Liao, Francesca-Fang
USPHS NIH Grant NS-120327-01, Blood-brain-barrier and white matter mechanisms underlying dementia

Meibohm, Bernd
St Jude Subcontract to USPHS NIH Grant AI090810, Development of Novel Proteins Synthesis Inhibitors for MDR Tuberculosis

Palmer, Glen
USPHS NIH Grant AI-156611, Examining the importance of folate biosynthetic enzymes in infectious fungi
Palmer, Glen
USPHS NIH Grant AI-127607, Broad spectrum antifungals targeting fatty acid biosynthesis

Palmer, Glen
USPHS NIH Grant AI-152067, Antifungal antagonism as a cause of treatment failure for invasive mycoses

Peters, Brian
USPHS NIH Grant AI-134796-01, Candidalysin: a key mediator of Candida vaginitis immunopathology

Singh, Udai
USPHS NIH Grant AI-140405, Adipose T cell microRNAs (miRs) regulate macrophage function during obesity

Smith, Amber
USPHS NIH Grant AI-139088, Predictive Modeling of Influenza-Pneumococcal Coinfection

Sumida, Keiichi
USPHS NIH Grant DK-125586, Circulating microbiome and premature mortality in hemodialysis patients

Tigyi, Gabor
RxBio Subcontract to USPHS NIH Grant DK-125208, Targeted Therapies for the Treatment of GI-ARS Diarrhea

Tigyi, Gabor
RxBio BAA 2017-1, IND-Enabling Development of Rx100 as a Medical Countermeasure for Gastrointestinal Acute Radiation Syndrome

Tigyi, Gabor
USPHS NIH Grant CA-092160, Anticancer Strategies Targeting the Autotaxin-LPA Receptor Axis

Whitt, Michael
ModernaXi - Whitt - UTRF, MTA - Development of VSV SARS CoV-2 Pseudotypes

V. BUSINESS DEVELOPMENT

A. Market Assessment

During FY22, RBL services were provided to several departments within the COM, COP and COHP, as well as external users at other academic institutions and commercial entities (refer to “RBL Users 2020 to Present” table, following page). Throughout FY21, Dr. Jonsson continued to focus on recruiting new internal and external users for those investigators whose research programs require RBL services. In FY21, the director built several service units (based on her own research strengths) to be leveraged by both academic and industry users to support the submission of new grants or contracts. The RBL was highly responsive to the SARS COV-2 (COVID-19) pandemic. Numerous services were added specifically addressing the needs of government, academic and commercial entities to fight the COVID pandemic. These included high-throughput screening workflows for SARS CoV-2 and variants, sequencing of viral variants, continued development of mouse and hamster models for SARS CoV-2 infection; including pathology consults for companies needing that service. In Q1 of FY22, Dr. Jonsson was awarded facilities grant (AI-167349-01) submitted in FY21 that will upgrade caging and will make additional upgrades to other core units of the facility. The grant also provides funds for several pieces of new equipment that will make the RBL more competitive in FY22 and beyond for existing and new users. The first new piece of equipment is the Cytek Aurora Spectral flow cytometer, which greatly increases the number of probes that can be detected, allowing users to perform sophisticated immunophenotyping that is necessary to be competitive for NIH grants. It will also reduce the sample size needed for analysis, allowing PIs to obtain more raw data from each animal per experiment. The system is designed for a multi-user environment with automated set up and quality control and, therefore, will not require a dedicated technician to operate or to maintain. The second piece of equipment is the CTL ImmunoSpot® S6 Universal Analyzer, which is capable of analyzing single- and dual-

color enzymatic ELISPOT in both clear and white 96-well and 384-well plate formats using an automatic plate loader- for walk-away detection. This instrument will provide an additional service option for academic and commercial users who need to monitor the immune response to viral infection, such as for vaccine development. The BioSpot Software for enumerating viral plaque assays improves the speed of processing plaque assays, which currently requires a significant amount of labor hours by our scientific staff. The Universal Analyzer is also equipped with an ImmunoCompliance™ package, which includes an integrated barcode reader and IQ reference plate and software package to comply with GLP regulations (21 CFR part 11). These new instruments will provide valuable new resources for UTHSC PIs as well as to external customers.

RBL Users 2020 to Present

Company	Location	
	City	State
ADH Public Health Laboratory Alkansas Government	Little Rock	AR
Akron Biotechnology LLC	Boca Raton	FL
Amcyte Pharma Inc	Cambridge	MA
Anavex Life Sciences Corp.	New York	NY
Anivive Lifesciences	Long Beach	CA
Apex laboratories private limited	Chennai TamilNadu	India
Appili Therapeutics Inc	Halifax	Canada
Apros Therapeutics/GHDDI	San Diego	CA
Arrowhead Pharma	Pasadena	CA
Arcturus Therapeutics Inc.	San Diego	CA
AVer Information Inc.USA	Fremont	CA
Baylor University	Waco	TX
Berghealth	Framingham	MA
Biomed Diagnostics Inc.	White City	OR
BioSkryb Inc	Durham	NC
Biotia Inc	New York	NY
Brilliant Health LLC	Tucson	AZ
CFD Research Corporation	Huntsville	AL
City of Memphis	Memphis	TN
Clemson	Clemson	SC
Cleveland Diagnostics Inc	Cleveland	OH
Coral Genomics	San Francisco	CA
CytaCoat Ab	Solna	Sweden
Dabur Research Foundation	Ghaziabad	India
Dvant Pharma_Univ. of Michigan	Ypsilanti	MI
Dynamics Inc	Pittsburgh	PA
EDP Biotech	Knoxville	TN
Emory University	Atlanta	GA
Emphycorp Inc	Flemington	NJ

EsperoVax	Plymouth	MI
Eutropics Pharmaceuticals	Cambridge	MA
Farmington Pharma Development	Cheshire	CT
Farmspace Systems LLC	Alamo	TN
FDA NCTR	Jefferson	AR
Fujifilm Pharmaceuticals	Cambridge	MA
Gliknik Inc	Baltimore	MD
Hansoh Bio LLC	Rockville	MD
Harvard University	Cambridge	MA
Healion Bio	Frederick	MD
Heel	Baden-Baden	Germany
Immuneering Corp.	Cambridge	MA
IntraMont Technologies Inc	Hackensack	NJ
Johns Hopkins Bloomberg School of Public Health	Baltimore	MD
Kenall.com	Kenosha	WI
Knowbio	Durham	NC
Koru Lifescience Ltd.	Auckland	New Zealand
Leidos Inc	Reston	VA
Leinco Technologies Inc.	St. Louis	MO
Loliware	New York	NY
Lumen Catheters LLC	Manchester	CT
MiCo BioMed Co., Ltd.	Skillman	NJ
Microban Products Company	Huntersville	NC
Missouri State University	Springfield	MO
Natural MA Inc	Cochrane Alberta	Canada
Nextcea	Woburn	MA
NIH NCI	Bethesda	MD
Northeastern University	Boston	MA
Novobiotic Pharmaceuticals LLC	Cambridge	MA
Old Dominion University	Norfolk	VA
OP Innovates.LLC	Lexington	KY
Oregon State University	Corvallis	OR
ORNL	Oak Ridge	TN
Otter Products LLC	Fort Collins	CO
Path BioAnalytics Inc	Chapel Hill	NC
Penn State University	University Park	PA
PhoneSoap LLC	Provo	UT
Pliant Therapeutics Inc.	South San Francisco	CA
POLYVISION	Atlanta	GA
Poplar Health	Memphis	TN
Pressure Profile INC	Hawthorne	CA
Primus Pharmaceuticals Inc	Scottsdale	AZ

Provectus Biopharmaceuticals Inc	Knoxville	TN
Providence Saint John's Health Center	Santa Monica	CA
Quantum Innovations Inc.	Central Point	OR
Red Queen Therapeutics (Appletreepartners)	Cambridge	MA
RedHill Biopharma Ltd.	Tel-Aviv	Israel
RETROVIROX INC.	San Diego	CA
ROWPAR INC.	Scottsdale	AZ
Rutgers Robert Wood Johnson Medical School	New Brunswick	NJ
Rutgers University	New Brunswick	NJ
Shelby County government	Memphis	TN
Speed Laboratory Inc	Gwinnett County	GA
spotLESS Materials inc	State College	PA
SRL Enterprises LLC.	Jersey City	NJ
St.Jude Childrens Hospital	Memphis	TN
Synexis LLC	Lenexa	KS
TES and Associates	Long Beach	CA
The University of Alabama in Huntsville	Huntsville	AL
Tiba Bio	Cambridge	MA
UConn Health	Farmington	CT
University of Arkansas	Fayetteville	AR
University of California San Francisco (UCSF)	San Francisco	CA
University of Colorado Denver	Denver	CO
University of Kentucky	Lexington	KY
University of Louisville	Louisville	KY
University of Memphis	Memphis	TN
University of South Carolina	Columbia	SC
University of New Mexico	Albuquerque	NM
University of South Carolina	Columbia	SC
University of Toledo	Toledo	OH
UNM	Albuquerque	NM
US Biologic	Memphis	TN
UT Chat College of Medicine	Chattanooga	TN
UTHSC	Memphis	TN
UTMB	Galveston	TX
Vast Therapeutics Inc	Durham	NC
Veru Inc	Miami	FL
ViroDefense	Maryland	MD
Vironova Medical AB	Stockholm	Sweden
Vivi-Biologics	Kurnool	India
Wondfo	Willowbrook	IL
Yale University	New Haven	CT
YewSavin Inc.	Fort Collins	CO
Zoetis	Parsippany	NJ

In conjunction with Lee Ferguson, Dr. Jonsson has continued to revise the RBL website, which has been updated with new marketing materials. The website will continue to be updated throughout FY23.

The RBL has expanded its base of regional customers, including researchers at the University of Memphis, Le Bonheur Children's Hospital, St. Jude Children's Research Hospital, and the Oak Ridge National Laboratories and other commercial and academic partners located in the state of Tennessee. Many of these entities were new customers in FY21, and several users have returned to complete additional studies in FY22, and they will continue working with the RBL throughout FY23. During FY22, with the assistance of Na Yeon, Dr. Jonsson refined the RBL user database to more efficiently track RBL usage from internal and external users (discriminating between academic vs. commercial external users); maintaining this database is one of Na's primary responsibilities.

The RBL also acquired new government customers, such as the US Food and Drug Administration (FDA) and the National Cancer Institute; we will continue to work with these clients through FY23. Likely new government clients for FY23 include the Department of Defense, the Navy, the Defense Threat Reduction Agency, the Medical CBRN Defense Consortium (MCDC), the Biomedical Advanced Research and Development Authority (BARDA), the Federal Bureau of Investigations, the National Advisory Council (NAC), the Centers for Disease Control and Prevention (CDC), and the US Department of Agriculture (USDA). Funding mechanisms offered by government agencies include contracts and grants of various types, such as IDIQ (Indefinite Delivery, Indefinite Quantity) and OTA (Other Transactional Authority) contracts. Within these opportunities, we will continue to attempt to secure contracts that use our RBL facilities for pathogen discovery, pathogen diagnostics or animal model development. We have also recently implemented COVID-19 drug discovery as a new service.

The RBL has acquired new external academic customers in FY22 which has led to numerous collaborations, including the inclusion of the UTHSC RBL as an animal core for several external groups submitting U19 proposals for Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern during FY22. Additional collaborations with PIs at other academic institutions, such as the University of Michigan (Dr. Duxin Sun) and Emory University (Dr.Ray Schinazi), have led, and will continue to lead, to RBL inclusion on R01 and other funding mechanism proposals.

Additional future customers may include inter-institutional collaborators ("friends" in the UT System, such as Dr. Klaus Schughart) and short-term academic PI visitors to our campus. A PI may wish to send to the RBL a student and/or themselves to execute a research project or to provide direct oversight. The RBL will develop approaches to facilitate short-term visits to train scientists in new technologies or to use our specialized service units within the RBL Core. The PI may also wish to have a person trained at our RBL to facilitate execution of their experiments since most research is highly technical and requires a great deal of background and expertise in the pathogen of interest.

Large and small commercial entities continue to move towards outsourcing when a technology or service capability is expensive to maintain, either due to limited use or level of specialization relative to the overall mandate of the company. For example, a

company may have an adjuvant and may desire testing it against BSL-2 and BSL-3 agents. The company may have BSL-2 facilities, but it would not be profitable for the company to devote resources to building BSL-3 capacity. Similarly, for drug discovery, many small biotech companies have one lead compound, and in order to build their patent portfolio, they will seek services to define the use of their compound against an array of pathogens. Opportunities likely exist to partner with biotechnology to create a larger group effort that neither partner could manage alone. For example, most larger companies would rather the drug discovery aspects of a project be brought to the preclinical phase or to phase 1 prior to acquisition by licensing agreements. Companies may wish to partner under a right of first refusal for inventions discovered at the RBL.

State of Tennessee agencies, such as hospitals and public health laboratories, are likely to continue to use services that are provided by the RBL, such as the SARS CoV-2 variant sequencing performed for the city of Memphis in FY21-FY22. These services include, but are not limited to, the growth of additional viruses and bacteria for identification (e.g., via sequencing, SNPs) from general population surveys, to developing new methods for isolating organisms for detection, or to providing a testing ground for new concepts in multiplexing pathogen detection arrays. In general, the RBL will seek to provide state-of-the-art technologies to facilitate public health in our state. The RBL is capable of providing support for environmental surveys for human and animal outbreaks of pathogens, and storage and tracking of select agents in order to provide the state with the ability to create panels for disease diagnosis and detection. This capacity is particularly important given that these labs are typically not allowed to store specimens after they are identified, if they are select agents.

B. Competitive Analysis

There are two national and 11 regional biocontainment facilities in the US. Because the RBL grants from the National Institute of Allergy and Infectious Diseases were used to build the facilities but did not supply any operational budget for the RBLs, it has become necessary for the UTHSC RBL, and all other RBLs, to identify several approaches for generating revenue to offset the considerable operational costs to staff and to maintain these facilities. The approaches include attracting federally-funded academic researchers, or private sector researchers, to perform their work in the RBL facilities, as well as contract, fee-for-service research conducted by RBL staff. There are a number of issues that have made it difficult to attract research activities to the UTHSC RBL:

1. Each of the RBLs are under the same financial pressures, and they can be in direct competition with each other for attracting research (e.g., the University of Alabama, Birmingham and the University of Louisville are direct competitors of the UTHSC RBL).
2. There are numerous other containment facilities around the country that are also competing for users/projects. Many of these facilities are located at academic institutions, and others are either commercial (e.g., Battelle) or are government-funded (e.g., Lawrence Livermore National Lab, and United States Army Medical Research Institute of Infectious Diseases, USAMRIID) operations. It is especially difficult to compete with large commercial and governmental laboratories because they are very well-staffed with research teams with dedicated expertise, and they have a wide array of core research facilities. Therefore, it is to our advantage to

understand what other the RBLs and BSL-3 labs have to offer and to then focus on our unique strengths or areas that are not widely available. For example, host-pathogen systems biology (i.e., through ISHPS) is one of the areas that focuses on UTHSC's unique strengths.

3. Since the RBL was constructed, there has been a paucity of recruitment for researchers whose research programs require BSL-3/ABSL-3 containment laboratory space, and the university has failed to retain several funded researchers whose work required BSL-3/ABSL-3 containment.
4. Lack of a dedicated project coordinator (i.e., "salesperson") with a virology background. Consulting with customers who want to use our services is essentially a full-time job. Our customers often need to be educated in the techniques we use, and then, most often, our standard procedures have to be customized to fit the client's particular project goals. No two projects are identical. Once a study design is agreed upon, quotes must then be generated and research service agreements initiated within the university, which are highly customized for each client. These activities are time-consuming and we have lost clients when we cannot respond quickly enough.

Overall, external, academic (outside university) customers will typically be principal investigators who have been awarded a government grant or contract who do not have BSL-3 or ABSL-3 facilities, and/or have access to the specialized equipment managed locally at their institution.

C. Marketing Plans to Obtain New Business

For each of the "units" areas of service at the UTHSC RBL, we need to understand the value proposition to win "business." Each of the units within the RBL should, and will, be described with a snapshot of current capability, gaps and value proposition that explains:

- how our core capability and capacity solve customers' problems or improves their situation (relevancy)
- explains how our core capability and capacity delivers specific benefits (quantified value)
- tells the ideal customer why they should work with us and not with the competition (unique differentiation)

Overall value proposition

Relevancy:

The RBL is the only facility available to UTHSC or to external users in the Memphis area on a collaborative or fee-for-service basis that has the appropriate engineering controls, facilities, and resources for BSL-3/ABSL-3 research. Agents that may cause serious or lethal disease through the inhalation route of exposure will benefit from the type of engineering controls, resources, and facilities that the UTHSC RBL offers. As an academic, not-for-profit entity, our services cannot make a profit. This provides commercial partners with a low-cost alternative to a corporate research organization or CRO.

Unique differentiation:

The availability of unique *in vitro* assays and *in vivo* small animal models will deliver added value for customers. The RBL has developed a new full-service menu to support animal studies, from experimental design, to animal procurement, to a wide array of animal services, and after-life endpoints. The RBL will stand up a wide

inventory of techniques in virology, bacteriology, and immunology, with a focus on emerging infectious diseases and select agents, which will be an important discriminator with our competition.

Small Animal Model-Pathogen Evaluation Unit
Government and commercial clients will seek service partners that can provide a wide array of services. We have and will continue to position ourselves to support clients in efficacy testing studies that provide them with critical capability that sets their studies apart and helps them evaluate their product fast. For example, we will help customers evaluate small molecules prior to embarking on an efficacy study, so that they have the best information available on compound formulation, route of administration and animal model.

Pathogen and Molecular Discovery Unit
Relevancy:
The high throughput robotic instrumentation currently located in the BSL-3 is not widely available nationwide. Our goal will be to have highly trained staff that provide the highest quality of service in the shortest time for the lowest price. The RBL will provide services to improve assays to be ready for high throughput screening (HTS), offering highly qualified staff, reproducible results and a documented track record in this area advertised in new marketing materials.

To support this unit, we offer the Perkin-Elmer Janus HTS robots, an Envision multi-modal plate reader (Synergy 2), chemical libraries procured through partnerships and PI-based material transfer agreements and siRNA libraries.

Based on current vivarium staffing, the UTHSC could provide: two full-service animal studies every month with downstream *in vitro* analyses which can take up to eight weeks - Target: 10-12 studies per year. This is up from 8-10 studies in FY21.

The brand strategy is the long-term plan for the development of the RBL as a recognizeable collaborative unit and a center of excellence for conducting studies that lead to greater biological understanding of pathogenic organisms and approaches for evaluation of antivirals, therapeutics and vaccines. This is the major purpose of our brand.

To move forward in FY23, the core plans to utilize a mass promotion platform and to create promotional campaigns to achieve the following three aims on a regular basis. The first aim is to keep existing clients informed about new services, or updated prices, to increase the return rate, measured using a customer database. The second aim is to introduce the RBL services to potential new clients with targeted email campaigns customized for the potential client. Finally, the third aim is to increase visibility of the RBL to both internal and external customers (regional and national) with an email campaign containing general information that may include some of our success stories, highlighting our facility’s contributions to the COVID pandemic and to advertise our expertise and services.

VI. Budget

FY2022	DEBITS	CREDITS
Salaries	987,635	
Supplies	339,643	
Service Contracts	79,797	
Equipment (> $5,000)	10,148	
Other Expenses*	111,438	
TOTAL EXPENSES	***1,528,661***	
FY22 Internal Recoveries FY22 External Recoveries		523,246 44,274
TOTAL CREDITS		***567,520***
Income / (Subsidy)**	(961,141)	
FY22 State Appropriation	1,158,859	
Net Income/ (Subsidy)* **	**197,718**	

*Other expenses consist of the following categories: Media/Communications, Travel, Maintenance/Repairs, Memberships, Copier Rental, Registration Fees and UT Direct Cost Sharing in the amount of $586.77.

**Subsidy, % before state appropriation 63%

***Subsidy, % after state appropriation ---

Medicinal Chemistry Core (MedChem) Institutional Research Core Facility Analysis Report – FY22

Written by Jiawang Liu, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?
The MedChem Core's designation as an institutional core is appropriate since it served six UTHSC laboratories across five departments and two colleges (COM and COP), and one external user in South Korea (Pusan National University, PNU).

2. Does the core pass the multi-departmental, multi-investigator litmus test?
Yes. In FY22, this core processed custom synthesis projects and performed analytical services for six unique laboratories across five departments and two colleges (COM and COP). The top five users of the core, based on the percentage of service fees invoiced for completed services were: 1) Dr. Il-Ho Jang (PNU, external, 44.07%), 2) Dr. Kirk Hevener (Pharmaceutical Sciences, COP, 20.07%), 3) Dr. Gabor Tigyi (Physiology, COM, 19.59%), 4) Dr. Jianxiong Jiang (Pharmaceutical Sciences, COP, 7.21%), and 5) Dr. Qi Zhao (Preventive Medicine, COM, 5.34%). The other users accounted for 3.72% of core invoices.

3. Is there sufficient intra- and inter-departmental use and if not, why?
Yes. Six unique laboratories were served across five departments and two colleges. Current internal use is almost evenly divided between the COM and the COP.

4. Can the services for the core be outsourced more economically?
No. The services available through an academic core facility are more economical than use of commercial vendors.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting? (e.g., grants funded through investigator use, publications, etc.)?
Yes. **1)** The core director's salary (31.7%) was partially offset in FY22 by three awarded NIH RO1 projects that require core services. **2)** The director participated in preparation of four NIH grant applications as either co-Investigator or multi-PI in FY22; of these, one NIH U19 grant and an NIH RO1 grant were funded. The two new awards require core services, including metabolite quantitation analysis, and will compensate an additional 20% of core director's salary in FY23. **3)** The director provided six letters of support for new grant applications on behalf of five unique investigators. **4)** The director authored five publications in FY22.

6. Is the core currently self-sufficient or is it subsidized by the institution?
In FY22, the core was subsidized by the institution. Overall, FY22 ended with a net subsidy of $56,398 (78%).

Accomplishments in FY22

- The core net subsidy required for operations has decreased since the core was established, excluding FY22. During this time, the state appropriation decreased from $26,070 in FY21 to $6,941 in FY23.
- In FY22, the core supported three NIH RO1 awards; for these awards, the director was listed as co-investigator and there was dedicated salary support.

- For the NIH RO1 project, “Optimization of Novel Small Molecules to Antagonize FGF-23”, promising drug candidates synthesized by the core were recognized by UTRF, and a provisional patent was prepared in FY22. This is the first intellectual property outcome for the core since it was established.
- In FY22, the director participated in the preparation of four NIH proposals as either a compensated co-Investigator, or as a multi-PI in FY22. One NIH U19 and one NIH RO1 proposal were awarded. Thus, core director’s salary will be offset in FY23 by a total of four awarded NIH RO1 projects and one NIH U19 project. This is contrast to the majority of other institutional cores, except for the RBL, since the other core directors’ salaries were not offset by external funding.
- The core also provided six letters of support for new grant applications.
- The core supported 19 internal user Pub-Med indexed publications.

Financial Overview – FY22:

TOTALS	FY18*	FY19	FY20	FY21	FY22
Revenues	13,833	30,181	13,730	36,370	15,545
Expenses	(92,725)	(119,438)	(85,546)	(96,384)	(71,943)
Income (Subsidy)	1,108	(89,257)	(71,816)	(60,014)	(56,398)
Other Costs	84,752	0	0	0	0
Income (Subsidy)	(163,643)	(89,257)	(71,816)	(60,014)	(56,398)
State Appropriation	0	0	0	26,070	6,941
Net Income (Subsidy)	(163,643)	(89,257)	(71,816)	(33,944)	(49,457)
Subsidy, % before State Appropriation	---	75%	84%	62%	78%
Subsidy, % after State Appropriation	92.2%	75%	84%	35%	69%

*The Medicinal Chemistry Core opened in Q3 of FY18.

7. Suggested outcomes:

It is recommended that the MedChem Core continue as an institutional core. The state appropriation allocated to the MedChem Core should be increased back to the FY21 levels.

Medicinal Chemistry (MedChem) Institutional Core Facility
Summary of Institutional Core Activities for FY22

Written by Jiawang Liu, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

I. PUBLICATIONS (Journal publication dates: July 1, 2021 to June 30, 2022)
Full-length published articles (UTHSC investigators are indicated in bold, the core director is underlined)

DeJarnette C, Meyer CJ, Jenner AR, Butts A, Peters T, Cheramie MN, Phelps GA, Vita NA, Loudon-Hossler VC, Lee RE, **Palmer GE**. Identification of Inhibitors of Fungal Fatty Acid Biosynthesis. ACS Infect Dis. 2021 Dec 10;7(12):3210-3223. doi: 10.1021/acsinfecdis.1c00404. Epub 2021 Nov 17. PMID: 34786940; PMCID: PMC8670506.

Rybak JM, Sharma C, Doorley LA, Barker KS, **Palmer GE**, Rogers PD. Delineation of the Direct Contribution of Candida auris ERG11 Mutations to Clinical Triazole Resistance. Microbiol Spectr. 2021 Dec 22;9(3):e0158521. doi: 10.1128/Spectrum.01585-21. Epub 2021 Dec 8. PMID: 34878305; PMCID: PMC8653815.

Almeida C, Pongilio RP, Móvio MI, Higa GSV, Resende RR, **Jiang J**, Kinjo ER, Kihara AH. Distinct Cell-specific Roles of NOX2 and MyD88 in Epileptogenesis. Front Cell Dev Biol. 2022 Jul 4;10:926776. doi: 10.3389/fcell.2022.926776. PMID: 35859905; PMCID: PMC9289522.

Hou R, Yu Y, Sluter MN, Li L, Hao J, Fang J, Yang J, **Jiang J**. Targeting EP2 receptor with multifaceted mechanisms for high-risk neuroblastoma. Cell Rep. 2022 Jun 21;39(12):111000. doi: 10.1016/j.celrep.2022.111000. PMID: 35732130; PMCID: PMC9282716.

Xu X, Zhang C, **Jiang J**, Xin M, Hao J. Effect of TDP43-CTFs35 on Brain Endothelial Cell Functions in Cerebral Ischemic Injury. Mol Neurobiol. 2022 Jul;59(7):4593-4611. doi: 10.1007/s12035-022-02869-5. Epub 2022 May 18. PMID: 35581521.

Luna-Tapia A, Parker JE, Kelly SL, **Palmer GE**. Species-Specific Differences in C-5 Sterol Desaturase Function Influence the Outcome of Azole Antifungal Exposure. Antimicrob Agents Chemother. 2021 Nov 17;65(12):e0104421. doi: 10.1128/AAC.01044-21. Epub 2021 Sep 13. PMID: 34516249; PMCID: PMC8597749.

Mitachi K, Mingle D, Effah W, Sánchez-Ruiz A, **Hevener KE**, Narayanan R, Clemons WM Jr, Sarabia F, Kurosu M. Concise Synthesis of Tunicamycin V and Discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug 1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID: 35594368; PMCID: PMC9329268.

Zhao Q, Shen H, **Liu J**, Chiu CY, Su KJ, Tian Q, Kakhniashvili D, Qiu C, Zhao LJ, Luo Z, Deng HW. Pathway-based metabolomics study of sarcopenia-related traits in two US cohorts. Aging (Albany NY). 2022 Mar 2;14(5):2101-2112. doi: 10.18632/aging.203926. Epub 2022 Mar 2. PMID: 35235538; PMCID: PMC8954970.

Nagib MM, Zhang S, Yasmen N, Li L, Hou R, Yu Y, Boda VK, Wu Z, Li W, **Jiang J**. Inhibition of TRPC3 channels by a novel pyrazole compound confers antiseizure effects. Epilepsia. 2022 Apr;63(4):1003-1015. doi: 10.1111/epi.17190. Epub 2022 Feb 18. PMID: 35179226; PMCID: PMC9007831.

Li L, Yasmen N, Hou R, Yang S, Lee JY, Hao J, Yu Y, **Jiang J**. Inducible Prostaglandin E Synthase as a Pharmacological Target for Ischemic Stroke Neurotherapeutics. 2022 Jan;19(1):366-385. doi: 10.1007/s13311-022-01191-1. Epub 2022 Jan 31. PMID: 35099767; PMCID: PMC9130433.

Fu H, Wang J, Wang J, Liu L, **Jiang J**, Hao J. 4R-cembranoid protects neuronal cells from oxygen-glucose deprivation by modulating microglial cell activation. Brain Res Bull. 2022 Feb;179:74-82. doi: 10.1016/j.brainresbull.2021.12.007. Epub 2021 Dec 20. PMID: 34942325; PMCID: PMC8849140.

Liu H, Lin X, Gong R, Shen H, Qu Z, **Zhao Q**, Shen J, Xiao H, Deng H. Identification and Functional Characterization of Metabolites for Skeletal Muscle Mass in Early Postmenopausal Chinese Women. J Gerontol A Biol Sci Med Sci. 2022 Mar 30:glac075. doi: 10.1093/gerona/glac075. Epub ahead of print. PMID: 35352111.

Zhang C, Sajith AM, Xu X, **Jiang J**, Phillip Bowen J, Kulkarni A, Hao J. Targeting NLRP3 signaling by a novel-designed sulfonylurea compound for inhibition of microglial inflammation. Bioorg Med Chem. 2022 Mar 15;58:116645. doi: 10.1016/j.bmc.2022.116645. Epub 2022 Jan 31. PMID: 35151118; PMCID: PMC8895276.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, Yue J, Benyó Z, **Tigyi GJ**. Prometastatic Effect of ATX Derived from Alveolar Type II Pneumocytes and B16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi: 10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.

Guo H, Zhang W, Wang J, Zhao G, Wang Y, Zhu BM, Dong P, Watari H, Wang B, Li W, **Tigyi G**, Yue J. Cryptotanshinone inhibits ovarian tumor growth and metastasis by degrading c-Myc and attenuating the FAK signaling pathway. Front Cell Dev Biol. 2022 Sep 28;10:959518. doi: 10.3389/fcell.2022.959518. PMID: 36247016; PMCID: PMC9554091.

Tylavsky FA, Han L, Sims Taylor LM, Mason WA, Carroll KN, Bush NR, LeWinn KZ, Melough MM, Hartman TJ, **Zhao Q**. Oxidative Balance Score during Pregnancy Is Associated with Oxidative Stress in the CANDLE Study. Nutrients. 2022 Jun 1;14(11):2327. doi: 10.3390/nu14112327. PMID: 35684127; PMCID: PMC9182929.

Zhang Q, Meng XH, Qiu C, Shen H, **Zhao Q**, Zhao LJ, Tian Q, Sun CQ, Deng HW. Integrative analysis of multi-omics data to detect the underlying molecular mechanisms for obesity in vivo in humans. Hum Genomics. 2022 May 14;16(1):15.doi: 10.1186/s40246-022-00388-x. PMID: 35568907; PMCID: PMC9107154.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, Yue J, Zhang W. Adipose- Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal Transition Through Activating the TGF-β Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276; PMCID: PMC8727693.

Regan J, DeJarnette C, Luna-Tapia A, Parker JE, Reitler P, Barnett S, Tucker KM, Kelly SL, **Palmer GE**. Titration of C-5 Sterol Desaturase Activity Reveals Its Relationship to Candida albicans Virulence and Antifungal Susceptibility Is Dependent upon Host Immune Status. mBio.

2022 Apr 26;13(2):e0011522. doi: 10.1128/mbio.00115-22. Epub 2022 Apr 5. PMID: 35380453; PMCID: PMC9040724.

II. PRESENTATIONS GIVEN TO PROMOTE CORE USAGE

10/26/2021: UTHSC Hot Topics in Research, “How to Use the MedChem Core to Achieve Your Research Goals”

III. SUMMARY OF ACTIVITIES

A. Personnel

Director: Jiawang Liu, PhD (100% effort)

B. Oversight Committee (Internal Advisory Board)

The following faculty were members of the FY22 Medicinal Chemistry Internal Advisory Board:

Wei Li, PhD (Pharmaceutical Sciences, COP), *CHAIR*
Len Lothstein, PhD (Pathology, COM)
Bernd Meibohm, PhD (Pharmaceutical Sciences, COP)
Duane Miller PhD (Pharmaceutical Sciences, COP)
Ramesh Narayanan, PhD (Pathology, COM)
Gabor Tigyi, PhD (Physiology, COM)

C. Equipment

Equipment currently maintained in the core facility (all functional):

Equipment:	Cost:	Funding Source:	Purchase Date:
Flash column system	$52,857	Office of Research	10/01/2017
Microwave Reactor	$19,967	Office of Research	10/01/2017
Rotation Evaporator	$5,000	Office of Research	08/01/2020
Labconco Freeze Dry System	$2,000	Office of Research	08/01/2020
-80 °C Ultra-Low Freezer	$8,653	Office of Research	10/12/2020

D. Service Contracts

No service contracts were purchased in FY22 for equipment maintenance.

E. Usage Volume

Usage Volumes, FY22, for invoiced completed projects

By PI Name (Department):	Total Service Fees:	Percentage of Internal Use:
Gabor Tigyi (Physiology)	$5,288.91	35.0%

Jianxiong Jiang (Pharmaceutical Sciences)	$1,945.04	12.9%
Kirk Hevener (Pharmaceutical Sciences)	$5,416.74	35.9%
Leonard Lothstein (Pathology)	$87.42	0.6%
Qi Zhao (Preventive Medicine)	$1,442.43	9.6%
Glen Palmer (Clinical Pharmacy and Translational Science)	$917.91	6.1%
TOTAL INVOICED, FY22	**$15,098.45**	100.00%

Revenues by Department, FY22

Department	Total Charges	Percentage of Total Internal Use
COM		
Pathology	$87.42	0.6%
Physiology	$5,288.91	35.0%
Preventive Medicine	$1,442.43	9.6%
COP		
Clinical Pharmacy and Translational Science	$917.91	6.1%
Pharmaceutical Sciences	$7,361.78	48.8%
Total	**$15,098.45**	100.0%

F. FY22 Service Fee Structure

Fees for services were developed by the director based on a market-based comparison of peer academic institutions and placement in the bottom-half to the bottom-third tier relative to peer academic institutions.

i.) Core Support Services

Service Code	Service Description	Price, $
P010	Support letter	No charge
P020	Experimental design/outline	No charge
P030	Chemical structure figure and synthetic route scheme	No charge
P040	3D Protein and ligand images	No charge

ii.) Research Strategy Assistance

Service Code	Service Description	Price, $
R010	Literature search for compounds	No charge
R020	Literature search for targets or pathways	No charge
R030	Oral literature search report	No charge
R040	Well-written, literature search report provided in Word (Font: Arial; 12; Page size; Letter)	$54.64/page
R050	Synthetic route design	$21.86/reaction
R060	Drug screening method determination	$109.28 /method

iii.) Small Molecule Synthesis

Service Code	Service Description	Price, $
S010	Reaction (10 – 500 mg)	$32.78/hour *
S014	Reaction (0.5 – 1.0 gram)	$32.78/hour *
S020	General workup (10 – 500 mg)	$131.13/step
S024	General workup (0.5 – 1.0 gram)	$218.55/step
S030	Column chromatography (10 – 500 mg)	$131.13/step
S034	Column chromatography (0.5 – 1.0 gram)	$218.55/step

* The maximum charge for a reaction is $262.24 (8 hours).

iv.) Instrumental Analysis services:

Service Code	Service Description	Price, $
S040	^{1}H and ^{13}C NMR	$43.71/sample
S050	MS (ESI) or LC/MS	$43.71/sample
S055	HPMS	$43.71/sample
S060	Melting point	No Charge
S070	Specific rotation	No Charge

Service fee calculation examples:

A typical 5-step synthesis project (0.5-1 gram):
[$33.76/hour x 6 hours (mean reaction time for one reaction) + $225.11/step x 2 steps + $45.02/analytical assay x 2 assays = $742.8/step] x 5 steps = $3,714 + costs of starting materials and special reagents.

A typical 5-step synthesis project (20-50 mg):
[$32.78/hour x 6 hours (mean reaction time for one reaction) + $131.13/step x 2 steps + $43.71/analytical assay x 2 assays =$546.36/step] x 5 steps =$2,731.8 + costs of starting materials and special reagents.

Note: The example service fee for a 5-step synthesis protocol does not include the costs of starting materials, anhydrous solvents, or any special reagents. Users must pay for these costs before synthesis services are initiated. A list of common solvents and regular reagents that are included in service fees is provided to core customers prior to initiation of services.

v.) Write-ups for Reports, Publications, and other Purposes

Service Code	Service Description	Price, $
W010	Write-up for publication(s), including supporting information (Times New Roman, 11; Double spacing; Letter)	$109.28/page
W020	Compound identity and purity report	No charge
W030	NMR and MS spectrum copy	No charge

vi.) Chemical Mailing and Processing Services

Service Code	Service Description	Price, $
M010	Product handling and delivery fee	No charge (internal) $54.64 (domestic) $218.55 (int'l)
M020	Starting material quotation	No charge
M030	Chemical storage and processing	No charge

In addition to these fee-for-service options, the following services are provided to UTHSC investigators at no charge:

1) Face-to-face initial consultation with investigators on needs related to their grant applications and/or proposed experimental design. Extended consultations incur an hourly service fee.
2) Seminars and workshops provided to campus in order to advertise the services and expertise offered by the core.

IV. GRANTS SUPPORTED BY THE CORE, FY22

A. Current grants and contracts that supported the core in FY22

Grants that provided salary coverage for the director, FY22

Quarles, L. Darryl
USPHS NIH Grant DK-121132, Optimization of Novel Small Molecules to Antagonize FGF-23 (16.7% effort for Dr. Liu)

Zhao, Qi & Shen, Hui
USPHS NIH Grant AG-061917, Identification of Metabolomic Profiles for Sarcopenia Traits in Older Whites and Blacks (10% effort for Dr. Liu)

Zhao, Qi & Johnson, Karen
USPHS NIH Grant AG-068232, Intensive Lifestyle Intervention, Metabolomics, and Risk of Frailty Fracture in Overweight or Obese Patients with Type 2 Diabetes.
(5% effort for Dr. Liu)

Other Grants:
Zhao, Qi
USPHS NIH Grant AG-061917, Identification of Metabolomic Profiles for Sarcopenia Traits in Older Whites and Blacks

Hevener, Kirk
Army Grant W81XWH2010296, Development and evaluation of inhibitors of the C. difficile enzyme, FabK, as microbiome-sparing antibacterials

Palmer, Glen
USPHS NIH Grant AI-152067, Antifungal antagonism as a cause of treatment failure for invasive mycoses

B. Letters of Support that were Provided for Grant Applications:

Six letters of support were written in support of grant applications on behalf of four internal investigators, Drs. Gabor Tigyi, Jianxiong Jiang (2 applications), Kirk Hevener, and Zhousheng Xiao, and one external investigator, Dr. Yaguang Xi (Louisiana State University).

C. MedChem Pending Grant Applications in FY22

- **Hong-Wen Deng** (Tulane University Medical School, External), NIH, "Comprehensive metabolomics study of osteoporosis". *Status update: **Awarded**, Project started since September 1st, 2022*; includes 10% effort for Core Director.

- **Qi Zhao** (Preventive Medicine, COM), NIH, "Prenatal longitudinal Metabolomics Profiling and Child Obesity Risk in a Biracial Birth Cohort". *Status update: **Awarded:** Project will be started on January 1st, 2023*; includes 10% effort for Core Director.

- **Jianxiong Jiang** (Pharmaceutical Sciences, COP), NIH, "EP2 Antagonists for Ischemic Stroke". ***Pending review*** (Resubmission, latest IF, 38); includes 15% effort for Core Director.

V. BUSINESS DEVELOPMENT

A. Market Assessment

The MedChem Core is defined as an institutional core based on its service to faculty in two colleges and multiple departments within UTHSC. The potential customers for our user base include UTHSC, other UT campuses, the University of Memphis, the VA, LeBonheur Hospital, and other commercial and academic partners in the Memphis metropolitan area. During its first five fiscal years of operations (FY18-FY22), the core has provided services to 34 UTHSC investigators, four external investigators, two

pharmaceutical companies (GTx and Kodikaz) and a Korean Institute, Pusan National University. Based on Dr. Liu's prior success at Xavier University of Louisiana directing a similar core, it is also likely that, over time, more external users will begin to use our core at UTHSC.

Development of New Core Services

In FY20-FY21, the core established a mature small-molecule quantitative analysis platform based on LC-MS/MS techniques. These services were developed to serve researchers who could not have their needs met through instrumentation housed in the Proteomics and Metabolomics Core (PMC), which also includes the Metabolic Phenotyping Mass Spectrometry (MPMS) Unit. The MedChem Core purchased HPLC/UPLC columns (including an analytical chiral column) and essential small equipment (<$3,000), such as an Eppendorf micro centrifuge, a 24-well evaporator manifold, and a Buchi V-300 vacuum pump. In FY21, the core also purchased a -80 degree freezer to stock cell and plasma samples provided by investigators for analysis.

Small Molecule Quantitative Analysis Service Milestones

1. In FY19, the core performed the first metabolite analysis case to detect one metabolite in cell suspensions. (Dr. Ying Kong, COM)
2. In FY20, the core completed quantitation of three metabolites in various yeast cells. (Dr. Glen Palmer, COP)
3. In late FY20, the core started a long-term project with Dr. Qi Zhao (COM) to analyze 30 metabolites in frozen human plasma, which will provide an estimated >$10,000 in core recoveries per year during FY21-24.
4. In FY21, the core finished a purity analysis project on a drug candidate in aqueous formulation. (Leonard Lothstein, Pathology, COM)
5. In FY21, the core completed the stability analysis of FGF-23 antagonists. (Zhousheng Xiao, Medicine, COM)
6. In FY21, the core performed a pharmacokinetic (PK) study of a drug candidate. (Tauheed Ishrat, Anatomy and Neurobiology, COM)
7. In FY22, the core completed the stability assay service for 9 antifungal drugs. (Dr. Glen Palmer, COP)

Thus, the core is now capable of providing a complete LC-MS/MS-based quantitative analysis platform, including small-molecule quantitation, purity and stability analysis, and pharmacokinetic analysis.

B. Competitive Analysis

The Medicinal Chemistry Core is essential to the campus to support drug discovery efforts and all basic, pre-clinical, clinical and translational research that impacts human disease and treatment. The core plays a key role in providing the chemistry platform to support faculty members' external grant submissions. In the first five FY of operation, the core has assisted UTHSC investigators with multiple grant submissions, resulting in four awarded NIH RO1 grants and one awarded NIH U19 grant. The core is also critical for the successful hiring of faculty interested in precision medicine and translational medicine. The MedChem Core offers value-added services that include the scientific expertise and breadth of training of the director, quick turnaround time, and state-of-the-art instrumentation that most core facilities in the United States have not yet adopted.

C. Marketing Plans to Obtain New Business

A primary focus of the Medicinal Chemistry Core in FY23 will be to expand the advertisement of core services to the UTHSC campus, throughout the Memphis Medical Center and throughout the University of Tennessee system. The core director has presented in the Hot Topics in Research seminar series (October 26, 2021) as local advertisement on the campus. The core will also participate in the annual Office of Research Research Resource Fair, once COVID-19 restrictions are lifted, and in special technology seminars focused on advances on drug discovery and development. These activities will be supported by updating the core website by the Office of Research to include publications and grants supported by the core, and the new metabolite service. To maintain expertise and to remain current in evolving medicinal chemistry technologies, the director will attend regional and national meetings, such as conferences sponsored by the American Chemical Society and the American Association for Cancer Research. Attendance of those meetings will also be a venue for advertisement of the medicinal chemistry core at the regional/national levels since the core facility will be advertised in all posters or oral presentations made by the director. The MedChem core will also be advertised at annual meetings of the Southeastern Association of Shared Resources (SEASR) since UTHSC is a recurring institutional sponsor of this meeting.

D. Forecasted Volumes for New Business

The subsidy before state appropriation in FY22 is $56,398, which is 6% lower than the subsidy in FY21 ($60,014). Based upon the current core performance year to date as posted in iLab (Q1, FY23), the cdore predicts an approximate 50% increase in revenues in FY23 over FY22, suggesting that the net subsidy will decrease again in FY23.

VI. Actual Budget – FY22: (July 1, 2021 to June 30, 2022)
MEDCHEM – FY2022 Core Activities

FY2022	DEBITS	CREDITS
Salaries*	60,491	
Supplies	11,452	
Service Contracts	0	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***71,943***	
FY22 Internal Recoveries		15,098
FY22 External Recoveries		447
TOTAL CREDITS		***15,545***
Income / (Subsidy)	(56,398)	
State Appropriation	6,941	
Net Income / (Subsidy)	**(49,457)**	

*16.67% of Dr. Jiawang Liu's salary was paid from Dr. Darryl Quarles' USPHS Grant DK-121132, beginning 07/01/2021. 10% of Dr. Liu's salary was paid from Dr. Qi Zhao's grants: 1) USPHS AG-061917 Grant, 10% effort, beginning 07/01/2021 and 2) USPHS AG-068232, 5% effort, beginning 09/30/2021.

Subsidy, % before state appropriation: 78%
Subsidy, % after state appropriation: 69%%

Molecular Resource Center of Excellence (MRC) Institutional Research Core Facility Analysis Report- FY22

Written by William Taylor, PhD; Zoe Brookover; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?

The MRC core designation as an institutional core is appropriate since it served 71 total users (65 internal and six external) across 16 departments and four colleges. The external users included six users across three unique academic institutions (Rhodes College, University of Memphis, University of Toledo).

2. Does the core pass the multi-departmental, multi-investigator litmus test?

Yes. In FY22, this core processed 9,106 service units for four colleges (COM, COP, CON, and COD). The MRC also served nine external users from six external academic centers, and one commercial entity. The internal departments with the largest number of unique users were Pediatrics (eight users), Pharmacology (eight users), and Genetics, Genomics, and Informatics (eight users), and rounding out the top five were Anatomy and Neurobiology (seven users) and Medicine (seven users). The top five users accounted for 47.87% of total core service revenues for work completed in FY22. These investigators were: 1) Robert Williams (CGI, COM, 13.32%), 2) Enkhsiakihan Purevjav (Pediatrics, COM, 12.54%), 3) Ramesh Narayanan (Medicine, COM, 7.76%), 4) Hao Chen (Pharmacology, COM, 7.42%) and 5) Gangaraju Raja (Ophthalmology, COM, 6.83%). The remaining core users accounted for the other 52.13%.

3. Is there sufficient intra- and inter-departmental use and if not, why?

Yes. There were 71 unique internal users who were served across 16 departments and four colleges at UTHSC.

4. Can the services for the core be outsourced more economically?

No. Moreover, few academic cores continue to offer Affymetrix microarray services, which are still processed in high-volume at the MRC. The MRC continues to perform NGS services locally for investigators, primarily those investigators with time constraints, or who have data sharing privacy concerns. Looking forward, as Q4 of FY22 closed, we entered into an agreement to trade the NextSeq500 instrument for a NextSeq2000 instrument as of July of 222. The changes in instrumentation, which greatly increases throughput will decrease the pricing of NGS services in FY23, which will make the MRC competitive with external vendors who offer sequencing services.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g., grants funded through investigator use, publications, etc.)?

Yes. In FY22, core activities led to 109 PubMed-indexed publications. Seventy extramural grants and contract awards were supported by the MRC in FY22. In addition, Dr. Taylor provided expert consultation for over 75 proposed projects. Dr. Taylor and the MRC staff also provided hands-on training in molecular technologies to >20 new core users, primarily new students, residents and/or postdocs. Additionally, the MRC provided support letters for eight investigators (Drs. Shen, Laribee, Iskunykh, Gangaraju, Chizhikov, Liu-Smith, Maxwell, and Starland-Davenport) for a total of 17 grant proposals.

6. Is the core currently self-sufficient, or is it subsidized by the institution?

Yes, the core is currently self-sufficient. In FY22 the core was subsidized by the THEC appropriation as a state-funded Center of Excellence. FY22 ended with a net income of $8,972, to be rolled over to the FY23 budget.

Accomplishments this past year:
• The MRC director provided >75 experimental design consultations for clients.
• The MRC core supported 193 publications, numerous abstract presentations and 71 extramural and intramural grant awards.
• The MRC continued its educational mission of providing hands-on training to laboratory personnel.

MRC – FY2022 Core Analysis

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues	264,401	267,645	153,950	167,409	204,424
Expenses	853,184	850,757	801,773	854,536	844,129
Income (Subsidy)	(588,783)	(583,112)	(647,823)	(687,127)	(639,705)
Other Costs*	0	0	0	0	0
Income (Subsidy)	(588,783)	(583,112)	(647,823)	(687,127)	(639,705)
THEC Appropriation*	620,121	632,516	696,094	696,098	673,793
Net Income (Subsidy)	31,338	49,404	48,271	8,971	34,088
Subsidy, % before THEC Appropriation	69%	69%	81%	80%	76%
Subsidy, % after THEC Appropriation	--	--	--	--	--

*Row includes any THEC funding rollover from prior FY appropriations. The THEC carryover for FY22 to FY23 was $8,972.

7. Suggested outcomes:

It is recommended that the MRC continue as an institutional core.

Molecular Resource Center of Excellence (MRC) Core
Summary of Institutional Core Activities for FY22
(July 1, 2021- June 30, 2022)

Written by William Taylor, PhD, Natalie Smith, MS, and Tiffany Seagroves, PhD

I. A. PUBLICATIONS (Full-length published articles: Journal publication dates: July 1, 2021 to June 30, 2022; UTHSC investigators invoiced are bolded; core director is underlined).

Ackermann M, Anders HJ, Bilyy R, Bowlin GL, Daniel C, De Lorenzo R, EgebladM, Henneck T, Hidalgo A, Hoffmann M, Hohberger B, Kanthi Y, Kaplan MJ, KnightJS, Knopf J, Kolaczkowska E, Kubes P, Leppkes M, Mahajan A, Manfredi AA,Maueröder C, Maugeri N, Mitroulis I, Muñoz LE, Narasaraju T, Naschberger E,Neeli I, Ng LG, **Radic MZ**, Ritis K, Rovere-Querini P, Schapher M, Schauer C,Simon HU, Singh J, Skendros P, Stark K, Stürzl M, van der Vlag J, VandenabeeleP, Vitkov L, von Köckritz-Blickwede M, Yanginlar C, Yousefi S, Zarbock A, SchettG, Herrmann M. Patients with COVID-19: in the dark-NETs of neutrophils. Cell Death Differ. 2021 Nov;28(11):3125-3139. doi: 10.1038/s41418-021-00805-z. Epub2021 May 24. PMID: 34031543; PMCID: PMC8142290.

Williams EG, Pfister N, Roy S, Statzer C, Haverty J, Ingels J, Bohl C, HasanM, Čuklina J, Bühlmann P, Zamboni N, **Lu L**, Ewald CY, **Williams RW**, Aebersold R. Multiomic profiling of the liver across diets and age in a diverse mouse population. Cell Syst. 2022 Jan 19;13(1):43-57.e6. doi:10.1016/j.cels.2021.09.005. Epub 2021 Oct 18. PMID: 34666007; PMCID: PMC8776606.

Conde-Dusman MJ, Dey PN, Elía-Zudaire Ó, Rabaneda LG, García-Lira C, Grand T,Briz V, Velasco ER, Andero R, Niñerola S, Barco A, Paoletti P, Wesseling JF, Gardoni F, **Tavalin SJ**, Perez-Otaño I. Control of protein synthesis and memory by GluN3A-NMDA receptors through inhibition of GIT1/mTORC1 assembly. Elife. 2021Nov 17;10:e71575. doi: 10.7554/eLife.71575. PMID: 34787081; PMCID: PMC8598234.

Liao FF, Lin G, Chen X, Chen L, Zheng W, Raghow R, Zhou FM, Shih AY, Tan XL. Endothelial Nitric Oxide Synthase-Deficient Mice: A Model of Spontaneous Cerebral Small-Vessel Disease. Am J Pathol. 2021 Nov;191(11):1932-1945. doi:10.1016/j.ajpath.2021.02.022. Epub 2021 Mar 10. PMID: 33711310; PMCID:PMC8647425.

Kumari R, Irudayam MJ, Al Abdallah Q, Jones TL, Mims TS, Puchowicz MA, **Pierre JF**, Brown CW. SMAD2 and SMAD3 differentially regulate adiposity and the growth of subcutaneous white adipose tissue. FASEB J. 2021 Dec;35(12):e22018.doi: 10.1096/fj.202101244R. PMID: 34731499.

Pierre JF, Phillips GJ, Chandra LC, Rendina DN, Thomas-Gosain NF, Lubach GR, Lyte M, Coe CL, **Gosain A**. Lyticase Facilitates Mycobiome Resolution Without Disrupting Microbiome Fidelity in Primates. J Surg Res. 2021 Nov;267:336-341.doi: 10.1016/j.jss.2021.06.023. Epub 2021 Jun 26. PMID: 34186310; PMCID:PMC8678161.

Ren Z, Liu Z, Ma S, **Yue J**, Yang J, Wang R, Gao Y, Guo Y. Expression and clinical significance of UBE2V1 in cervical cancer. Biochem Biophys Rep. 2021Aug 18;28:101108. doi: 10.1016/j.bbrep.2021.101108. PMID: 34466666; PMCID:PMC8385167.

Perkins RS, Suthon S, **Miranda-Carboni GA**, **Krum SA**. WNT5B in cellular signaling pathways. Semin Cell Dev Biol. 2022 May;125:11-16. doi:10.1016/j.semcdb.2021.09.019. Epub 2021 Oct 9. PMID: 34635443.

Sumida K, Han Z, Chiu CY, Mims TS, Bajwa A, Demmer RT, Datta S, **Kovesdy CP**, **Pierre JF**. Circulating Microbiota in Cardiometabolic Disease. Front Cell Infect Microbiol. 2022 May 3;12:892232. doi: 10.3389/fcimb.2022.892232. PMID: 35592652;PMCID: PMC9110890.

D'Addio F, Maestroni A, Assi E, Ben Nasr M, Amabile G, Usuelli V, LoretelliC, Bertuzzi F, Antonioli B, Cardarelli F, El Essawy B, Solini A, **Gerling IC**, Bianchi C, Becchi G, Mazzucchelli S, Corradi D, Fadini GP, Foschi D, Markmann JF, Orsi E, Škrha J Jr, Camboni MG, Abdi R, James Shapiro AM, Folli F, Ludvigsson J, Del Prato S, Zuccotti G, Fiorina P. The IGFBP3/TMEM219 pathway regulates beta cell homeostasis. Nat Commun. 2022 Feb 3;13(1):684. doi:10.1038/s41467-022-28360-2. PMID: 35115561; PMCID: PMC8813914.

Skaar DA, Dietze EC, Alva-Ornelas JA, Ann D, Schones DE, Hyslop T, SistrunkC, Zalles C, Ambrose A, Kennedy K, Idassi O, **Miranda Carboni G**, Gould MN, Jirtle RL, Seewaldt VL. Epigenetic Dysregulation of KCNK9 Imprinting and Triple-Negative Breast Cancer. Cancers (Basel). 2021 Nov 30;13(23):6031. doi:10.3390/cancers13236031. PMID: 34885139; PMCID: PMC8656495.

Siegel EM, Ajidahun A, Berglund A, Guerrero W, Eschrich S, Putney RM, Magliocco A, Riggs B, Winter K, Simko JP, Ajani JA, Guha C, Okawara GS, AbdallaI, Becker MJ, Pizzolato JF, Crane CH, Brown KD, **Shibata D**. Genome-wide host methylation profiling of anal and cervical carcinoma. PLoS One. 2021 Dec9;16(12):e0260857. doi: 10.1371/journal.pone.0260857. PMID: 34882728; PMCID:PMC8659695.

Trotter C, **Kim H**, Farage G, Prins P, **Williams RW**, Broman KW, Sen Ś. Speeding up eQTL scans in the BXD population using GPUs. G3 (Bethesda). 2021 Dec8;11(12):jkab254. doi: 10.1093/g3journal/jkab254. PMID: 34499130; PMCID:PMC8664437.

Sharp BM, Fan X, Redei EE, **Mulligan MK**, **Chen H**. Sex and heredity are determinants of drug intake in a novel model of rat oral oxycodone self-administration. Genes Brain Behav. 2021 Nov;20(8):e12770. doi:10.1111/gbb.12770. Epub 2021 Sep 16. PMID: 34459088; PMCID: PMC8815756.

Xu F, Gao J, Orgil BO, Bajpai AK, Gu Q, Purevjav E, Davenport AS, **Li K**, **Towbin JA**, Black DD, **Pierre JF**, **Lu L**. Ace2 and Tmprss2 Expressions Are Regulated by Dhx32 and Influence the Gastrointestinal Symptoms Caused by SARS-CoV-2. J Pers Med. 2021 Nov 16;11(11):1212. doi: 10.3390/jpm11111212.PMID: 34834564; PMCID: PMC8621576.

DeJarnette C, Meyer CJ, Jenner AR, Butts A, Peters T, Cheramie MN, Phelps GA, Vita NA, Loudon-Hossler VC, Lee RE, **Palmer GE**. Identification of Inhibitors of Fungal Fatty Acid Biosynthesis. ACS Infect Dis. 2021 Dec 10;7(12):3210-3223.doi: 10.1021/acsinfecdis.1c00404. Epub 2021 Nov 17. PMID: 34786940; PMCID:PMC8670506.

Nagy-Szakal D, Couto-Rodriguez M, Wells HL, Barrows JE, Debieu M, Butcher K, Chen S, Berki A, Hager C, Boorstein RJ, Taylor MK, **Jonsson CB**, Mason CE, O'Hara NB. Targeted Hybridization Capture of SARS-CoV-2 and Metagenomics Enables Genetic Variant Discovery and Nasal Microbiome Insights. Microbiol Spectr. 2021Oct 31;9(2):e0019721. doi: 10.1128/Spectrum.00197-21. Epub 2021 Sep 1. PMID:34468193; PMCID: PMC8557865.

MacKay CE, Floen M, Leo MD, Hasan R, Garrud TAC, Fernández-Peña C, Singh P, **Malik KU**, **Jaggar JH**. A plasma membrane-localized polycystin-1/polycystin-2complex in endothelial cells

elicits vasodilation. Elife. 2022 Mar 1;11:e74765.doi: 10.7554/eLife.74765. PMID: 35229718; PMCID: PMC8933003.

Xue Y, Yang D, Vogel P, Stabenow J, Zalduondo L, Kong Y, Ravi Y, Sai-Sudhakar CB, Parvathareddy J, Hayes E, Taylor S, **Fitzpatrick E**, **Jonsson CB**. Cardiopulmonary Injury in the Syrian Hamster Model of COVID-19. Viruses. 2022Jun 27;14(7):1403. doi: 10.3390/v14071403. PMID: 35891384; PMCID: PMC9316644.

Torres-Rojas C, Zhao W, Zhuang D, O'Callaghan JP, **Lu L**, **Mulligan MK**, **Williams RW**, **Jones BC**. Paraquat Toxicogenetics: Strain-Related Reduction of Tyrosine Hydroxylase Staining in Substantia Nigra in Mice. Front Toxicol.2021 Nov 11;3:722518. doi: 10.3389/ftox.2021.722518. PMID: 35295113; PMCID:PMC8915807.

Earley CJ, **Jones BC**, Ferré S. Brain-iron deficiency models of restless legs syndrome. Exp Neurol. 2022 Oct;356:114158. doi: 10.1016/j.expneurol.2022.114158.Epub 2022 Jun 30. PMID: 35779614; PMCID: PMC9357217.

Rybak JM, Sharma C, Doorley LA, Barker KS, **Palmer GE**, Rogers PD. Delineation of the Direct Contribution of Candida auris ERG11 Mutations to Clinical Triazole Resistance. Microbiol Spectr. 2021 Dec 22;9(3):e0158521. doi:10.1128/Spectrum.01585-21. Epub 2021 Dec 8. PMID: 34878305; PMCID: PMC8653815.

Bansal S, **Jonsson CB**, Taylor SL, Figueroa JM, Dugour AV, Palacios C, Vega JC. Iota-carrageenan and xylitol inhibit SARS-CoV-2 in Vero cell culture. PLoS One. 2021 Nov 19;16(11):e0259943. doi: 10.1371/journal.pone.0259943. PMID:34797868; PMCID: PMC8604354.

Samak G, Rao R, **Rao R**. Lactobacillus casei and Epidermal Growth Factor Prevent Osmotic Stress-Induced Tight Junction Disruption in Caco-2 Cell Monolayers. Cells. 2021 Dec 18;10(12):3578. doi: 10.3390/cells10123578. PMID:34944085; PMCID: PMC8700399.

Mitachi K, Mingle D, Effah W, Sánchez-Ruiz A, Hevener KE, **Narayanan R**, Clemons WM Jr, Sarabia F, Kurosu M. Concise Synthesis of Tunicamycin V and Discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID:35594368; PMCID: PMC9329268.

Neilson DE, Zech M, Hufnagel RB, Slone J, Wang X, Homan S, Gutzwiller LM, Leslie EJ, Leslie ND, **Xiao J**, Hedera P, LeDoux MS, Gebelein B, Wilbert F, Eckenweiler M, Winkelmann J, Gilbert DL, Huang T. A Novel Variant of ATP5MC3Associated with Both Dystonia and Spastic Paraplegia. Mov Disord. 2022Feb;37(2):375-383. doi: 10.1002/mds.28821. Epub 2021 Oct 11. PMID: 34636445;PMCID: PMC8840961.

Kneller DW, Li H, Phillips G, Weiss KL, Zhang Q, Arnould MA, **Jonsson CB**, Surendranathan S, Parvathareddy J, Blakeley MP, Coates L, Louis JM, Bonnesen PV, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors ofSARS-CoV-2 main protease. Nat Commun. 2022 Apr 27;13(1):2268. doi:10.1038/s41467-022-29915-z. PMID: 35477935; PMCID: PMC9046211.

de Jong TV, **Chen H**, Brashear WA, Kochan KJ, Hillhouse AE, Zhu Y, Dhande IS, Hudson EA, Sumlut MH, Smith ML, Kalbfleisch TS, Doris PA. mRatBN7.2: familiar and unfamiliar features of a new rat genome reference assembly. Physiol Genomics. 2022 Jul 1;54(7):251-260. doi: 10.1152/physiolgenomics.00017.2022.Epub 2022 May 11. PMID: 35543507; PMCID: PMC9236863.

Gunturkun MH, Flashner E, Wang T, **Mulligan MK**, **Williams RW**, Prins P, **Chen H**. GeneCup: mining PubMed and GWAS catalog for gene-keyword relationships. G3(Bethesda). 2022 May 6;12(5):jkac059. doi: 10.1093/g3journal/jkac059. PMID:35285473; PMCID: PMC9073678.

Shetty A, Kundu S, Vernel-Pauillac F, Ratet G, Werts C, **Gomes-Solecki M**. Transient Presence of Live Leptospira interrogans in Murine Testes. Microbiol Spectr. 2022 Jun 29;10(3):e0277521. doi: 10.1128/spectrum.02775-21. Epub 2022Apr 21. PMID: 35446113; PMCID: PMC9241917.

Albadari N, Deng S, **Chen H**, Zhao G, **Yue J**, Zhang S, Miller DD, Wu Z, Li W. Synthesis and biological evaluation of selective survivin inhibitors derived from the MX-106 hydroxyquinoline scaffold. Eur J Med Chem. 2021 Nov15;224:113719. doi: 10.1016/j.ejmech.2021.113719. Epub 2021 Jul 30. PMID:34371464; PMCID: PMC8511083.

Gu Q, Xu F, Orgil BO, Khuchua Z, Munkhsaikhan U, Johnson JN, Alberson NR, **Pierre JF**, Black DD, Dong D, Brennan JA, Cathey BM, Efimov IR, **Towbin JA**, Purevjav E, **Lu L**. Systems genetics analysis defines importance of TMEM43/LUMA for cardiac- and metabolic-related pathways. Physiol Genomics. 2022 Jan 1;54(1):22-35. doi: 10.1152/physiolgenomics.00066.2021. Epub2021 Nov 12. PMID: 34766515; PMCID: PMC8721901.

Bhattacharya S, Yin J, Yang C, Wang Y, Sims M, **Pfeffer LM**, Chaum E. STAT3 suppresses the AMPKα/ULK1-dependent induction of autophagy in glioblastoma cells. J Cell Mol Med. 2022 Jul;26(14):3873-3890. doi: 10.1111/jcmm.17421. Epub2022 Jun 6. PMID: 35670018; PMCID: PMC9279602.

Goldberg LR, Yao EJ, Kelliher JC, Reed ER, Wu Cox J, Parks C, Kirkpatrick SL, Beierle JA, Chen MM, Johnson WE, Homanics GE, **Williams RW**, Bryant CD, **Mulligan MK**. A quantitative trait variant in Gabra2 underlies increased methamphetamine stimulant sensitivity. Genes Brain Behav. 2021 Nov;20(8):e12774.doi: 10.1111/gbb.12774. Epub 2021 Oct 22. PMID: 34677900; PMCID: PMC9083095.

Dattwyler RJ, **Gomes-Solecki M**. The year that shaped the outcome of the Osp Avaccine for human Lyme disease. NPJ Vaccines. 2022 Jan 27;7(1):10. doi:10.1038/s41541-022-00429-5. PMID: 35087055; PMCID: PMC8795424.

Krutilina RI, Playa H, Brooks DL, Schwab LP, Parke DN, Oluwalana D, Layman DR, Fan M, Johnson DL, **Yue J**, Smallwood H, **Seagroves TN**. HIF-Dependent CKB Expression Promotes Breast Cancer Metastasis, Whereas Cyclocreatine Therapy Impairs Cellular Invasion and Improves Chemotherapy Efficacy. Cancers (Basel).2021 Dec 22;14(1):27. doi: 10.3390/cancers14010027. PMID: 35008190; PMCID:PMC8749968.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y, Vogel P, Channappanavar R, **Jonsson CB**, Smith AM. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infections During SARS-CoV-2.Front Immunol. 2022 May 12;13:894534. doi: 10.3389/fimmu.2022.894534. PMID:35634338; PMCID: PMC9134015.

Zheng T, Huang W, Yu H, Hu BH, Song P, McCarty CM, **Lu L**, Jaster J, Jin G, Zhang Y, Zheng QY. gom1 Mutant Mice as a Model of Otitis Media. J Assoc Res Otolaryngol. 2022 Apr;23(2):213-223. doi: 10.1007/s10162-022-00838-2. Epub 2022Feb 3. PMID: 35118601; PMCID: PMC8964886.

Meena AS, Shukla PK, Bell B, Giorgianni F, Caires R, Fernández-Peña C, Beranova S, Aihara E, Montrose MH, Chaib M, **Makowski L**, Neeli I, **Radic MZ**, Vásquez V, **Jaggar JH**, **Cordero-**

Morales JF, **Rao R**. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID:PMC9250449.

Victor AK, Donaldson M, Johnson D, Miller W, **Reiter LT**. Molecular Changes in Prader-Willi Syndrome Neurons Reveals Clues About Increased Autism Susceptibility. Front Mol Neurosci. 2021 Oct 29;14:747855. doi:10.3389/fnmol.2021.747855. PMID: 34776864; PMCID: PMC8586424.

Luna-Tapia A, Parker JE, Kelly SL, **Palmer GE**. Species-Specific Differences in C-5 Sterol Desaturase Function Influence the Outcome of Azole Antifungal Exposure. Antimicrob Agents Chemother. 2021 Nov 17;65(12):e0104421. doi:10.1128/AAC.01044-21. Epub 2021 Sep 13. PMID: 34516249; PMCID: PMC8597749.

Shukla PK, Meena AS, **Pierre JF**, **Rao R**. Central role of intestinal epithelial glucocorticoid receptor in alcohol- and corticosterone-induced gut permeability and systemic response. FASEB J. 2022 Jan;36(1):e22061. doi:10.1096/fj.202101424R. PMID: 34861075; PMCID: PMC8647846.

Alleboina S, Aljouda N, Miller M, **Freeman KW**. Therapeutically targeting oncogenic CRCs facilitates induced differentiation of NB by RA and the BET bromodomain inhibitor. Mol Ther Oncolytics. 2021 Sep 25;23:181-191. doi:10.1016/j.omto.2021.09.004. PMID: 34729395; PMCID: PMC8526497.

Trebska-McGowan K, Chaib M, Alvarez MA, Kansal R, Pingili AK, **Shibata D**, **Makowski L**, Glazer ES. TGF-β Alters the Proportion of Infiltrating Immune Cells in a Pancreatic Ductal Adenocarcinoma. J Gastrointest Surg. 2022Jan;26(1):113-121. doi: 10.1007/s11605-021-05087-x. Epub 2021 Jul 14. PMID:34260016.

Berglund A, Muenyi C, Siegel EM, Ajidahun A, Eschrich SA, Wong D, Hendrick LE, Putney RM, Kim S, Hayes DN, **Shibata D**. Characterization of Epigenomic Alterations in HPV16+ Head and Neck Squamous Cell Carcinomas. Cancer Epidemiol Biomarkers Prev. 2022 Apr 1;31(4):858-869. doi: 10.1158/1055-9965.EPI-21-0922.PMID: 35064062; PMCID: PMC8983563.

Wang X, Bajpai AK, Gu Q, Centeno A, Starlard-Davenport A, Prins P, Xu F, **Lu L**. A systems genetics approach delineates the role of Bcl2 in leukemia pathogenesis. Leuk Res. 2022 Mar;114:106804. doi: 10.1016/j.leukres.2022.106804.Epub 2022 Feb 9. PMID: 35182904; PMCID: PMC9272521.

Yoon TW, **Fitzpatrick EA**, Snyder JD, Lee S, Kim YI, Zacheaus C, **Yi AK**. Contribution of Protein Kinase D1 on Acute Pulmonary Inflammation and Hypersensitivity Pneumonitis Induced by Saccharopolyspora rectivirgula. Immunohorizons. 2022 Mar 10;6(3):224-242. doi: 10.4049/immunohorizons.2200017.PMID: 35273098.

Musicante M, **Kim HH**, Chen Y, **Liao F**, Bhattacharya SK, **Lu L**, Sun Y. Regulation of endothelial nitric oxide synthase in cardiac remodeling. Int J Cardiol. 2022 Oct 1;364:96-101. doi: 10.1016/j.ijcard.2022.05.013. Epub 2022 May30. PMID: 35654172.

Camors EM, Roth AH, Alef JR, Sullivan RD, Johnson JN, Purevjav E, **Towbin JA**. Progressive Reduction in Right Ventricular Contractile Function Attributable to Altered Actin Expression in an Aging Mouse Model of Arrhythmogenic Cardiomyopathy. Circulation. 2022 May 24;145(21):1609-1624. doi:10.1161/CIRCULATIONAHA.120.049261. Epub 2022 Apr 19. PMID: 35437032; PMCID:PMC9133220.

Shukla PK, Meena AS, **Rao R**. Prevention and mitigation of alcohol-induced neuroinflammation by Lactobacillus plantarum by an EGF receptor-dependent mechanism. Nutr Neurosci. 2022 Apr;25(4):871-883. doi:10.1080/1028415X.2020.1819105. Epub 2020 Sep 18. PMID: 32945721; PMCID:PMC7969470.

Brown Lobbins ML, Slominski AT, **Hasty KA**, Zhang S, Miller DD, Li W, Kim TK, Janjetovic Z, Tuckey RC, Scott IO, Myers LK, Postlethwaite AE. Modulation by17,20S(OH)2pD of Fibrosis-Related Mediators in Dermal Fibroblast Lines from Healthy Donors and from Patients with Systemic Sclerosis. Int J MolSci. 2021 Dec 29;23(1):367. doi: 10.3390/ijms23010367. PMID: 35008794; PMCID:PMC8745512.

Suthon S, Lin J, Perkins RS, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**. Estrogen receptor alpha and NFATc1 bind to a bone mineral density-associated SNP to repress WNT5B in osteoblasts. Am J Hum Genet. 2022 Jan 6;109(1):97-115. doi:10.1016/j.ajhg.2021.11.018. Epub 2021 Dec 13. PMID: 34906330; PMCID: PMC8764205.

Sasani TA, Ashbrook DG, Beichman AC, **Lu L**, Palmer AA, **Williams RW**, Pritchard JK, Harris K. A natural mutator allele shapes mutation spectrum variation in mice. Nature. 2022 May;605(7910):497-502. doi:10.1038/s41586-022-04701-5. Epub 2022 May 11. PMID: 35545679; PMCID: PMC9272728.

Banerjee S, Yadav S, Banerjee S, Fakayode SO, Parvathareddy J, Reichard W, Surendranathan S, Mahmud F, Whatcott R, Thammathong J, Meibohm B, Miller DD, **Jonsson CB**, Dubey KD. Drug Repurposing to Identify Nilotinib as a PotentialSARS-CoV-2 Main Protease Inhibitor: Insights from a Computational and InVitro Study. J Chem Inf Model. 2021 Nov 22;61(11):5469-5483. doi:10.1021/acs.jcim.1c00524. Epub 2021 Oct 20. PMID: 34666487; PMCID: PMC8547516.

Temiz-Resitoglu M, Guden DS, Senol SP, Vezir O, Sucu N, Kibar D, Yılmaz SN, Tunctan B, **Malik KU**, Sahan-Firat S. Pharmacological Inhibition of Mammalian Target of Rapamycin Attenuates Deoxycorticosterone Acetate Salt-Induced Hypertension and Related Pathophysiology: Regulation of Oxidative Stress, Inflammation, and Cardiovascular Hypertrophy in Male Rats. J Cardiovasc Pharmacol. 2022 Mar 1;79(3):355-367. doi: 10.1097/FJC.0000000000001187. PMID:34840266.

Krogvold L, Leete P, Mynarek IM, Russell MA, **Gerling IC**, Lenchik NI, Mathews C, Richardson SJ, Morgan NG, Dahl-Jørgensen K. Detection of Antiviral Tissue Responses and Increased Cell Stress in the Pancreatic Islets of Newly Diagnosed Type 1 Diabetes Patients: Results From the DiViD Study. Front Endocrinol (Lausanne). 2022 Jul 26;13:881997. doi: 10.3389/fendo.2022.881997.PMID: 35957810; PMCID: PMC9360491.

Kneller D, Li H, Phillips G, Weiss K, Zhang Q, Arnould M, **Jonsson C**, Surendranathan S, Parvathareddy J, Blakeley M, Coates L, Louis J, Bonnesen P, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors ofSARS-CoV-2 main protease: room-temperature X-ray and neutron crystallography, binding thermodynamics, and antiviral activity. Res Sq [Preprint]. 2022 Feb11:rs.3.rs-1318037. doi: 10.21203/rs.3.rs-1318037/v1. Update in: Nat Commun.2022 Apr 27;13(1):2268. PMID: 35169792; PMCID: PMC8845512.

Munkhsaikhan U, Kwon Y, Sahyoun AM, Ait-Aissa K, Kassan A, **Kassan M**. The microsomal triglyceride transfer protein inhibitor lomitapide improves vascular function in mice with obesity. Obesity (Silver Spring). 2022 Apr;30(4):893-901.doi: 10.1002/oby.23389. Epub 2022 Mar 6. PMID: 35253407; PMCID: PMC8957593.

Taylor AP, Lee AS, Goedecke PJ, Tolley EA, Joyner AL, **Heck DH**. Conditional loss of Engrailed1/2 in Atoh1-derived excitatory cerebellar nuclear neurons impairs eupneic respiration in mice. Genes Brain Behav. 2022 Feb;21(2):e12788.doi: 10.1111/gbb.12788. Epub 2022 Jan 19. PMID: 35044072; PMCID: PMC8852233.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, **Yue J**, Benyó Z, **Tigyi GJ**. Prometastatic Effect of ATX Derived from Alveolar Type II Pneumocytes andB16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi:10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.

Gropler MRF, Lipshultz SE, Wilkinson JD, **Towbin JA**, Colan SD, Canter CE, Lavine KJ, Simpson KE. Pediatric and adult dilated cardiomyopathy are distinguished by distinct biomarker profiles. Pediatr Res. 2022Jul;92(1):206-215. doi: 10.1038/s41390-021-01698-x. Epub 2021 Aug 17. PMID:34404929.

Kneller DW, Li H, Galanie S, Phillips G, Labbé A, Weiss KL, Zhang Q, Arnould MA, Clyde A, Ma H, Ramanathan A, **Jonsson CB**, Head MS, Coates L, LouisJM, Bonnesen PV, Kovalevsky A. Structural, Electronic, and Electrostatic Determinants for Inhibitor Binding to Subsites S1 and S2 in SARS-CoV-2 Main Protease. J Med Chem. 2021 Dec 9;64(23):17366-17383. doi:10.1021/acs.jmedchem.1c01475. Epub 2021 Oct 27. PMID: 34705466; PMCID:PMC8565456.

Ahmed HA, Ismael S, Salman M, Devlin P, McDonald MP, **Liao FF**, Ishrat T. Direct AT2R Stimulation Slows Post-stroke Cognitive Decline in the 5XFADAlzheimer's Disease Mice. Mol Neurobiol. 2022 Jul;59(7):4124-4140. doi:10.1007/s12035-022-02839-x. Epub 2022 Apr 29. PMID: 35486224.

Corradi V, **Bukiya AN**, Miranda WE, Cui M, Plant LD, Logothetis DE, TielemanDP, Noskov SY, Rosenhouse-Dantsker A. A molecular switch controls the impact of cholesterol on a Kir channel. Proc Natl Acad Sci U S A. 2022 Mar29;119(13):e2109431119. doi: 10.1073/pnas.2109431119. Epub 2022 Mar 25. PMID:35333652; PMCID: PMC9060494.

Merigeon EY, Yang D, Ihms EA, Bassit LC, **Fitzpatrick EA**, **Jonsson CB**, Schinazi RF, Block DS, Olsen HS. An ACE2-IgG4 Fc Fusion Protein Demonstrates Strong Binding to All Tested SARS-CoV-2 Variants and Reduced Lung Inflammation in Animal Models of SARS-CoV-2 and Influenza. Pathog Immun. 2022 Aug23;7(1):104-121. doi: 10.20411/pai.v7i1.491. PMID: 36072571; PMCID: PMC9438944.

Suthon S, Perkins RS, Lin J, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**.GATA4 and estrogen receptor alpha bind at SNPs rs9921222 and rs10794639 to regulate AXIN1 expression in osteoblasts. Hum Genet. 2022 Jun 9. doi:10.1007/s00439-022-02463-8. Epub ahead of print. PMID: 35678873.

Kim S, Kim YE, Song I, Ujihara Y, Kim N, Jiang YH, Yin HH, Lee TH, **Kim IH**. Neural circuit pathology driven by Shank3 mutation disrupts social behaviors. Cell Rep. 2022 Jun 7;39(10):110906. doi: 10.1016/j.celrep.2022.110906. PMID:35675770; PMCID: PMC9210496.

Dietrich P, Alli S, **Mulligan MK**, Cox R, Ashbrook DG, **Williams RW**, Dragatsis I. Identification of cyclin D1 as a major modulator of 3-nitropropionic acid-induced striatal neurodegeneration. Neurobiol Dis. 2022 Jan;162:105581. doi:10.1016/j.nbd.2021.105581. Epub 2021 Dec 3. PMID: 34871739; PMCID: PMC8717869.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, **Yue J**, **Zhang W**. Adipose-Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal

Transition Through Activating the TGF-β Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276;PMCID: PMC8727693.

Rana M, Kansal R, Chaib M, Teng B, Morrrison M, Hayes DN, Stanfill AG, **Shibata D**, Carson JA, **Makowski L**, Glazer ES. The pancreatic cancer immune tumor microenvironment is negatively remodeled by gemcitabine while TGF-β receptor plus dual checkpoint inhibition maintains antitumor immune cells. Mol Carcinog.2022 Jun;61(6):549-557. doi: 10.1002/mc.23401. Epub 2022 Mar 23. PMID: 35319799.

Di L, Akther S, Bezrucenkovas E, Ivanova L, Sulkow B, Wu B, Mneimneh S, **Gomes-Solecki M**, Qiu WG. Maximum antigen diversification in a lyme bacterial population and evolutionary strategies to overcome pathogen diversity. ISME J.2022 Feb;16(2):447-464. doi: 10.1038/s41396-021-01089-4. Epub 2021 Aug 19. PMID:34413477; PMCID: PMC8376116.

Ryan MC, Kim E, Cao X, Reichard W, Ogorek TJ, Das P, **Jonsson CB**, Baudry J,Chung D, Golden JE. Piperazinobenzodiazepinones: New Encephalitic Alphavirus Inhibitors via Ring Expansion of 2-Dichloromethylquinazolinones. ACS Med Chem Lett. 2022 Mar 14;13(4):546-553. doi: 10.1021/acsmedchemlett.1c00539. PMID:35450382; PMCID: PMC9014857.

McAfee SS, Liu Y, Sillitoe RV, **Heck DH**. Cerebellar Coordination of Neuronal Communication in Cerebral Cortex. Front Syst Neurosci. 2022 Jan 11;15:781527.doi: 10.3389/fnsys.2021.781527. PMID: 35087384; PMCID: PMC8787113.

Hu X, Zhang J, Zhang Y, Jiao F, Wang J, **Chen H**, Ouyang L, Wang Y. Dual-target inhibitors of poly (ADP-ribose) polymerase-1 for cancer therapy: Advances, challenges, and opportunities. Eur J Med Chem. 2022 Feb 15;230:114094.doi: 10.1016/j.ejmech.2021.114094. Epub 2021 Dec 30. PMID: 34998039.

Xiao Y, Song X, Wang T, Meng X, Feng Q, **Li K**, Kang YJ. Copper Preserves Vasculature Structure and Function by Protecting Endothelial Cells from Apoptosis in Ischemic Myocardium. J Cardiovasc Transl Res. 2021Dec;14(6):1146-1155. doi: 10.1007/s12265-021-10128-6. Epub 2021 May 17. PMID:33999373.

Poje JE, Azevedo JF, Nair N, Mahachi K, Frank LE, Sherpa P, Krizek RS, Baccam T, **Gomes-Solecki M**, Petersen CA. Borrelia burgdorferi (Spirochaetales:Spirochaetaceae) Infection Prevalence and Host Associations of Ticks Found on Peromyscus spp. in Maryland. J Med Entomol. 2022 Mar 16;59(2):752-757. doi:10.1093/jme/tjab206. PMID: 34971369; PMCID: PMC8924970.

Mozhui K, Lu AT, Li CZ, Haghani A, Sandoval-Sierra JV, Wu Y, **Williams RW**, Horvath S. Genetic loci and metabolic states associated with murine epigenetic aging. Elife. 2022 Apr 7;11:e75244. doi: 10.7554/eLife.75244. PMID: 35389339;PMCID: PMC9049972.

North KC, Zhang M, Singh AK, Zaytseva D, Slayden AV, **Bukiya AN**, **Dopico AM**. Cholesterol Inhibition of Slo1 Channels Is Calcium-Dependent and Can Be Mediated by Either High-Affinity Calcium-Sensing Site in the Slo1 Cytosolic Tail. Mol Pharmacol. 2022 Mar;101(3):132-143. doi: 10.1124/molpharm.121.000392. Epub 2021Dec 30. PMID: 34969832; PMCID: PMC8969144.

He Y, Yang C, Wang Y, Sacher JR, Sims MM, **Pfeffer LM**, Miller DD. Novel structural-related analogs of PFI-3 (SRAPs) that target the BRG1 catalytic subunit of the SWI/SNF complex increase the activity of temozolomide in glioblastoma cells. Bioorg Med Chem. 2022 Jan 1;53:116533. doi:10.1016/j.bmc.2021.116533. Epub 2021 Nov 27. PMID: 34863065.

Collyer J, Xu F, Munkhsaikhan U, Alberson NF, Orgil BO, **Zhang W**, Czosek RJ, **Lu L**, Jefferies JL, **Towbin JA**, Purevjav E. Combining whole exome sequencing within silico analysis and

clinical data to identify candidate variants in pediatric left ventricular noncompaction. Int J Cardiol. 2022 Jan 15;347:29-37. doi:10.1016/j.ijcard.2021.11.001. Epub 2021 Nov 6. PMID: 34752814.

Välikangas T, Lietzén N, Jaakkola MK, Krogvold L, Eike MC, Kallionpää H, Tuomela S, Mathews C, **Gerling IC**, Oikarinen S, Hyöty H, Dahl-Jorgensen K, Elo LL, Lahesmaa R. Pancreas Whole Tissue Transcriptomics Highlights the Role of the Exocrine Pancreas in Patients With Recently Diagnosed Type 1 Diabetes. Front Endocrinol (Lausanne). 2022 Apr 13;13:861985. doi: 10.3389/fendo.2022.861985.PMID: 35498413; PMCID: PMC9044038.

Huo X, **Zhang W**, Zhao G, Chen Z, Dong P, Watari H, **Narayanan R**, Tillmanns TD, **Pfeffer LM**, **Yue J**. FAK PROTAC Inhibits Ovarian Tumor Growth and Metastasis by Disrupting Kinase Dependent and Independent Pathways. Front Oncol. 2022 Apr28;12:851065. doi: 10.3389/fonc.2022.851065. PMID: 35574330; PMCID: PMC9095959.

Slayden AV, Dyer CL, Ma D, Li W, **Bukiya AN**, Parrill AL, **Dopico AM**. Discovery of agonist-antagonist pairs for the modulation of Ca [2]+and voltage-gated K+ channels of large conductance that contain beta1subunits. Bioorg Med Chem. 2022 Aug 15;68:116876. doi:10.1016/j.bmc.2022.116876. Epub 2022 Jun 13. PMID: 35716586.

Hitzemann R, Bergeson SE, Berman AE, Bubier JA, Chesler EJ, Finn DA, Hein M, Hoffman P, Holmes A, Kisby BR, Lockwood D, Lodowski KH, McManus M, Owen JA, Ozburn AR, Panthagani P, Ponomarev I, Saba L, Tabakoff B, Walchale A, **Williams RW**, Phillips TJ. Sex Differences in the Brain Transcriptome Related to Alcohol Effects and Alcohol Use Disorder. Biol Psychiatry. 2022 Jan 1;91(1):43-52. doi:10.1016/j.biopsych.2021.04.016. Epub 2021 May 1. PMID: 34274109; PMCID:PMC8558111.

Wang D, Wang R, **Li K**. Impaired Antiviral Responses to Extracellular Double-Stranded RNA and Cytosolic DNA, but Not to Interferon-α Stimulation, in TRIM56-Deficient Cells. Viruses. 2022 Jan 5;14(1):89. doi: 10.3390/v14010089.PMID: 35062293; PMCID: PMC8777648.

Regan J, DeJarnette C, Luna-Tapia A, Parker JE, Reitler P, Barnett S, Tucker KM, Kelly SL, **Palmer GE**. Titration of C-5 Sterol Desaturase Activity Reveals Its Relationship to Candida albicans Virulence and Antifungal Susceptibility Is Dependent upon Host Immune Status. mBio. 2022 Apr26;13(2):e0011522. doi: 10.1128/mbio.00115-22. Epub 2022 Apr 5. PMID: 35380453;PMCID: PMC9040724.

Kassan A, Ait-Aissa K, **Kassan M**. Gut Microbiota Regulates the Sympathetic Nerve Activity and Peripheral Serotonin Through Hypothalamic MicroRNA-204 in Order to Increase the Browning of White Adipose Tissue in Obesity. Cureus. 2022Feb 4;14(2):e21913. doi: 10.7759/cureus.21913. PMID: 35155042; PMCID:PMC8820388.

Hollingsworth TJ, Wang X, White WA, Simpson RN, **Jablonski MM**. Chronic Proinflammatory Signaling Accelerates the Rate of Degeneration in a Spontaneous Polygenic Model of Inherited Retinal Dystrophy. Front Pharmacol. 2022 Mar21;13:839424. doi: 10.3389/fphar.2022.839424. PMID: 35387333; PMCID: PMC8978607.

Fortes-Gabriel E, Guedes MS, Shetty A, Gomes CK, Carreira T, Vieira ML, Esteves L, Mota-Vieira L, **Gomes-Solecki M**. Enzyme immunoassays (EIA) for serodiagnosis of human leptospirosis: specific IgG3/IgG1 isotyping may further inform diagnosis of acute disease. PLoS Negl Trop Dis. 2022 Feb23;16(2):e0010241. doi: 10.1371/journal.pntd.0010241. PMID: 35196321; PMCID:PMC8901056.

Wang Y, Yang C, Sims MM, Sacher JR, Raje M, Deokar H, Yue P, Turkson J, Buolamwini JK, **Pfeffer LM**. SS-4 is a highly selective small molecule inhibitor of STAT3 tyrosine phosphorylation that potently inhibits GBM tumorigenesis invitro and in vivo. Cancer Lett. 2022 May 1;533:215614. doi:10.1016/j.canlet.2022.215614. Epub 2022 Mar 1. PMID: 35245627.

Duttke SH, Montilla-Perez P, Chang MW, Li H, **Chen H**, Carrette LLG, deGuglielmo G, George O, Palmer AA, Benner C, Telese F. Glucocorticoid Receptor-Regulated Enhancers Play a Central Role in the Gene Regulatory Networks Underlying Drug Addiction. Front Neurosci. 2022 May 16;16:858427. doi:10.3389/fnins.2022.858427. PMID: 35651629; PMCID: PMC9149415.

Gunturkun MH, Wang T, Chitre AS, Garcia Martinez A, Holl K, St Pierre C, Bimschleger H, Gao J, Cheng R, Polesskaya O, Solberg Woods LC, Palmer AA, **Chen H**. Genome-Wide Association Study on Three Behaviors Tested in an Open Field in Heterogeneous Stock Rats Identifies Multiple Loci Implicated in Psychiatric Disorders. Front Psychiatry. 2022 Feb 14;13:790566. doi:10.3389/fpsyt.2022.790566. PMID: 35237186; PMCID: PMC8882588.

Pauleck S, Gigic B, Cawthon RM, Ose J, Peoples AR, Warby CA, Sinnott JA, Lin T, Boehm J, Schrotz-King P, Li CI, **Shibata D**, Siegel EM, Figueiredo JC, Toriola AT, Schneider M, Ulrich AB, Hoffmeister A, Ulrich CM, Hardikar S. Association of circulating leukocyte telomere length with survival in patients with colorectal cancer. J Geriatr Oncol. 2022 May;13(4):480-485. doi:10.1016/j.jgo.2021.12.008. Epub 2022 Jan 5. PMID: 34998722; PMCID: PMC9197691.

169. Thomas MH, Gui Y, Garcia P, Karout M, Gomez Ramos B, Jaeger C, Michelucci A, Gaigneaux A, Kollmus H, Centeno A, Schughart K, Balling R, Mittelbronn M, Nadeau JH, Sauter T, **Williams RW**, Sinkkonen L, Buttini M. Quantitative traitl ocus mapping identifies a locus linked to striatal dopamine and points to collagen IV alpha-6 chain as a novel regulator of striatal axonal branching in mice. Genes Brain Behav. 2021 Nov;20(8):e12769. doi: 10.1111/gbb.12769. Epub2021 Sep 28. PMID: 34453370.

Chaib M, Sipe LM, Yarbro JR, Bohm MS, Counts BR, Tanveer U, Pingili AK, Daria D, Marion TN, Carson JA, Thomas PG, **Makowski L**. PKC agonism restricts innate immune suppression, promotes antigen cross-presentation and synergizes with agonistic CD40 antibody therapy to activate CD8+ T cells in breast cancer. Cancer Lett. 2022 Apr 10;531:98-108. doi:10.1016/j.canlet.2022.01.017. Epub 2022 Jan 21. PMID: 35074498.

Senko AN, Overall RW, Silhavy J, Mlejnek P, Malínská H, Hüttl M, Marková I, Fabel KS, **Lu L**, Stuchlik A, **Williams RW**, Pravenec M, Kempermann G. Systems genetics in the rat HXB/BXH family identifies Tti2 as a pleiotropic quantitative trait gene for adult hippocampal neurogenesis and serum glucose. PLoS Genet.2022 Apr 4;18(4):e1009638. doi: 10.1371/journal.pgen.1009638. PMID: 35377872;PMCID: PMC9060359.

Dong P, Wang F, Taheri M, Xiong Y, Ihira K, Kobayashi N, Konno Y, **Yue J**, Watari H. Long Non-Coding RNA TMPO-AS1 Promotes GLUT1-Mediated Glycolysis and Paclitaxel Resistance in Endometrial Cancer Cells by Interacting With miR-140and miR-143. Front Oncol. 2022 May 27;12:912935. doi: 10.3389/fonc.2022.912935.PMID: 35712514; PMCID: PMC9195630.

Koffman EE, Kruse CM, Singh K, Naghavi FS, Curtis MA, Egbo J, Houdi M, LinB, Lu H, Debiec J, **Du J**. Acid-sensing ion channel 1a regulates the specificity of reconsolidation of conditioned threat responses. JCI Insight. 2022 Feb22;7(4):e155341. doi: 10.1172/jci.insight.155341. PMID: 35025766; PMCID:PMC8876458.

Deng T, Li J, Liu J, Xu F, Liu X, Mi J, Bergquist J, Wang H, Yang C, **Lu L**, Song X, Yao C, Tian G, Zheng QY. Hippocampal Transcriptome-Wide Association Study Reveals Correlations Between Impaired Glutamatergic Synapse Pathway and Age-Related Hearing Loss in BXD-

Recombinant Inbred Mice. Front Neurosci. 2021Nov 17;15:745668. doi: 10.3389/fnins.2021.745668. PMID: 34867157; PMCID:PMC8636065.

Regan J, **Palmer GE**. Identifying Specific Small Molecule-Protein Interactions Using Target Abundance-Based Fitness Screening (TAFiS). Methods Mol Biol. 2022;2542:115-126. doi: 10.1007/978-1-0716-2549-1_8. PMID: 36008660.

Dong P, Wang F, Chang L, **Yue J**. Editorial: Non-Coding RNAs in Gastrointestinal and Gynecological Cancers: New Insights Into the Mechanisms of Cancer Therapeutic Resistance. Front Cell Dev Biol. 2022 May 13;10:893868. doi:10.3389/fcell.2022.893868. PMID: 35646928; PMCID: PMC9136281.

Song CY, Singh P, Motiwala M, Shin JS, Lew J, Dutta SR, Gonzalez FJ, Bonventre JV, **Malik KU**. 2-Methoxyestradiol Ameliorates Angiotensin II-Induced Hypertension by Inhibiting Cytosolic Phospholipase A2α Activity in Female Mice. Hypertension. 2021 Nov;78(5):1368-1381. doi:10.1161/HYPERTENSIONAHA.121.18181. Epub 2021 Oct 11. PMID: 34628937; PMCID:PMC8516072.

Whittington KB, Prislovsky A, Beaty J, Albritton L, **Radic M**, Rosloniec EF.CD8+ T Cells Expressing an HLA-DR1 Chimeric Antigen Receptor Target Autoimmune CD4+ T Cells in an Antigen-Specific Manner and Inhibit the Development of Autoimmune Arthritis. J Immunol. 2022 Jan 1;208(1):16-26. doi:10.4049/jimmunol.2100643. Epub 2021 Nov 24. PMID: 34819392; PMCID: PMC8702470.

Seagroves TN, Bagarozzi D, Bagchi P, Boukli NM, Browner N, Colton-Lee F, Constable S, Dahlman KB, Griffiths L, Mesa TE, Somasundaram T. The Eighth Annual Meeting of the Southeastern Association of Shared Resources (SEASR), Atlanta, GA, June 10-11, 2021. J Biomol Tech. 2021 Dec 15;32(4):3fc1f5fe.ea38010c. doi:10.7171/3fc1f5fe.ea38010c. PMID: 35837271; PMCID: PMC9258611.

Adhikari P, Shukla PK, Alharthi F, **Rao R**, Pradhan P. Photonic technique to study the effects of probiotics on chronic alcoholic brain cells by quantifying their molecular specific structural alterations via confocal imaging. J Biophotonics. 2022 Mar;15(3):e202100247. doi: 10.1002/jbio.202100247. Epub 2021Dec 2. PMID: 34786860.

Ye X, Pan T, Wang D, Fang L, Ma J, Zhu X, Shi Y, Zhang K, Zheng H, **Chen H**, **Li K**, Xiao S. Corrigendum: Foot-and-Mouth Disease Virus Counteracts on Internal Ribosome Entry Site Suppression by G3BP1 and Inhibits G3BP1-Mediated Stress Granule Assembly via Post-Translational Mechanisms. Front Immunol. 2021Nov 4;12:702530. doi: 10.3389/fimmu.2021.702530. Erratum for: Front Immunol.2018 May 25;9:1142. PMID: 34804006; PMCID: PMC8600380.

Taylor MK, Williams EP, Wongsurawat T, Jenjaroenpun P, Nookaew I, **Jonsson CB**. Corrigendum: Amplicon-Based, Next-Generation Sequencing Approaches to Characterize Single Nucleotide Polymorphisms of Orthohantavirus Species. Front Cell Infect Microbiol. 2022 Jan 24;11:804914. doi: 10.3389/fcimb.2021.804914.Erratum for: Front Cell Infect Microbiol. 2020 Oct 14;10:565591. PMID: 35141171;PMCID: PMC8819723.

Gosain A, Goldstein AM. Invited commentary on Ahmad et al.: Routine botulinum toxin injection one month after a Swenson pull-through does not change the incidence of Hirschsprung associated enterocolitis. J Pediatr Surg. 2022Aug;57(8):1458-1459. doi: 10.1016/j.jpedsurg.2021.12.021. Epub 2021 Dec 25.PMID: 34980468.

Chen K, Zhang B, **Sun Z**. MicroRNA 379 Regulates Klotho Deficiency-Induced Cardiomyocyte Apoptosis Via Repression of Smurf1. Hypertension. 2021 Aug;78(2):342-352. doi: 10.1161/HYPERTENSIONAHA.120.16888. Epub 2021 Jun 14.. PMID:34120450

B. Top five users (based on $204,424, the value of completed services for FY22)

User:	Invoiced	% of Total
Robert Williams	$27,085	13.32
Enkhsiakhan Purevjav	$25,509	12.54
Ramesh Narayanan	$15,781	7.76
Hao Chen	$15,089	7.42
Gangaraju Raja	$13,880	6.83

II. PRESENTATIONS GIVEN TO PROMOTE CORE USAGE AND LETTERS OF SUPPORT

The MRC conducted laboratory tours and information sessions for 12 prospective faculty from Clinical Pharmacy, Comparative Medicine, Physiology, Dentistry, and Pharmacology. The director also had >75 consultations with clients during this time. Additionally, the MRC provided 17 support letters for investigators (Drs. Shen, Laribee, Iskunykh, Gangaraju, Chizhikov, Liu-Smith, Maxwell, and Starland-Davenport).

III. SUMMARY OF ACTIVITIES

A. FY22 Personnel

Executive Director: Tiffany Seagroves (6.59% effort)
Director: William Taylor (100% effort)
Research Specialist: Lorne Rose (100% effort) -Retired Jan 2022
Research Specialist Zoe Brookover (100% effort) Starting Jan 2022
Assistant Director (Core Business): Natalie Smith (50% effort)

B. FY22 Internal Advisory Board (IAB)

Hao Chen (Pharmacology, COM)
Lu Lu (Genetics, Genomics and Informatics, COM)
Lawrence Reiter (Neurology, COM)
Ramesh Narayanan (Medicine, COM), *IAB CHAIR*

C. Major Equipment (>$5,000)

Equipment	MRC Cost	Funding source; Year purchased
Ion Torrent Proton sequencer and server	$87,149	MRC/CITG cost-share, $174,2982013
Ion Torrent PGM sequencer	$49,635	MRC/CITG cost-share, $99,2702013
Affymetrix Scanner	$41,483	MRC/CITG cost-share $80,0002010
Fluidigm BioMark qPCR system	$41,484	MRC/ARRA funds/VCR, cost-share, $203,1492010
ABI 3130XL Genetic Analyzer	$131,483	MRC2001
Nanodrop Spectrophotometer	$7,153	MRC, 2003
Zeiss Axiphot Microscope	$43,631	Gift1993
Genepix 4000B Microarray Scanner	$55,265	MRC2001

Qiacube Robot	$14,900	MRC2007
LightCycler 480 qPCR instruments (2)	$39,900	MRC2007
Agilent Bioanalyzer (2)	$20,717	MRC/CITG2002
Light Cycler 480 384-well block	$7,500	MRC2014
Nanodrop 8 sample Spectrophotometer	$20,000	MRC2007
Spectramax M2e Microplate Reader	$41,123	MRC2007
Eppendorf EPmotion Robot	$35,500	MRC2009
Dell Precision T7500 workstation for Partek Software	$10,570	MRC2011
SWT Dual Xeon Server for Partek Flow Software	$8,359	MRC2014
Illumina NextSeq500	$202,000	VC Research2016
Hamilton Robotics Starlet robot	$100,000	VC Research2017

D. Service Contracts FY22

Specialty Underwriters:	**Cost:**
Ion One Touch 2.0 System (2 units)	$4,587
Ion Proton sequencer	$17,202
SpectraMax M2E plate reader	$3,868
Qiagen Qiacube	$1,589
Roche LightCycler 480 (2 units)	$8,148
SU total:	**$40,173**

Life Tech/Affymetrix (OEM):	**Cost:**
Microarray scanner	$35,900.04

Illumina (OEM):	
NextSeq500	$19,125

Hamilton Robotics (OEM):	
Starlet Liquid handling robot	$10,472

Agilent Technologies	$48,372

Total, Service Contracts:	**$154,042.04**

E. Advertisement of Core

MRC participated in tours provided during national postdoc week, provided tours for prospective and current faculty, and sponsored several seminars from vendors. The director also teaches a lecture in and provides a core tour for two courses, Genetic Epidemiology and Pathology 804 (approaches to biological research).

F. Usage Volumes

FY22 Services:

Affymetrix Microarrays: 45 chips, 3 UTHSC investigators

Next generation sequencing (Proton/PGM) sequencing Runs: 1 run for 1 external investigator
Agilent Bioanalyzer: 262 chips for 30 UTHSC investigators and 1 external investigator
Next Generation sequencing Illumina (NextSeq) sequencing: 6 runs for 2 internal investigators; plus 54 libraries for 2 investigators
Novagene Illumina sequencing; 27 runs for 5 investigators
GeneWiz/Azenta sequencing: 2527 samples for 22 investigators
Covaris Sonicator: 158 samples for 5 investigators
LC480 qPCR instruments: 290 runs for 16 UTHSC investigators
Transnetyx: 3,088 samples for 15 UTHSC investigators
Qbit fluorometer: 254 samples for 11 investigators
Qiacube robot: 707 runs for 8 investigators

Use of equipment available at no recharge:
Zeiss Axiphot microscope: 17 samples for 1 investigator
SpectraMax plate Reader: 40 plates for 5 internal investigators
Eppendorf EP motion robot: 0 runs for 0 UTHSC investigators
Covaris Sonicator: 37 runs for 3 UTHSC investigators

Affymetrix Microarrays

Year	Usage
FY22	45
FY 21	185
FY20	146

Next-Generation Sequencing, library preps

Year	Usage
FY22	35
FY21	54
FY20	5

Next-Generation Sequencing, runs

Year	Proton PGM or NextSeq
FY 22	7
FY21	6
FY 20	36

Agilent Bioanalyzer, samples

Year	Usage
FY 22	262
FY21	184
FY20	174

Sanger sequencing (ABI 3130XL), samples

Year	Usage
FY 22	discontinued
FY21	1,058
FY20	5,747

GeneWiz/Azenta dropbox (External Sanger sequencing vendor), samples

Year	Usage
FY22	2,527
FY21	919
FY20	525

QiaCube automated nucleic acid preparation, samples

Year	Usage
FY22	707
FY21	556
FY20	276

Roche LC480 quantitative PCR, runs

Year	Usage
FY22	290
FY21	337
FY20	299

Transnetyx genotyping, samples

Year	Usage
FY22	3088
FY21	3,649
FY20	3,992

Total MRC Recoveries, All Services*

FY period:	Total Credits:
FY22	$204,424
FY21	$167,408
FY20	$160,241
FY19	$247,732
FY18	$264,401
FY17	$429,816

H. FY22 service fee structure

Affymetrix Arrays			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Affymetrix Human Gene ST 2.0	$368.97	$448.67	$560.84
Clariom S	$220.97	$258.00	$322.50
Clariom D	$348.97	$411.60	$514.50
Affymetrix miRNA 4.0	$404.97	$493.16	$616.46
Agilent			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Agilent DNA High Sensitivity chip	$59.55	$69.38	$86.73
Agilent RNA Nano Chip	$39.30	$45.90	$57.37
Agilent DNA 1000 Chip	$39.30	$45.90	$57.37
Agilent RNA Pico Chip	$45.77	$52.45	$65.56
Agilent RNA small RNA Chip	$56.28	$65.56	$81.96
Agilent DNA 7500 Chip	$39.38	$45.90	$57.37
Next Gen Sequencing			
Product	**Internal Cost**	**External, Academic**	**Commercial**
CHIP-seq libraries	$117.42	$74.40	$93.00
Covaris Tubes	$5.15	$6.00	$8.00
DNA Libraries	$117.42	$74.40	$93.00
Fragment Library	$117.42	$74.40	$93.00

Ion Torrent P1 chips	$700.40	$840.48	$1050.60
Ion Torrent PGM 314 Chip	$360.50	$432.60	$540.75
Lexogen RNA-Seq Libraries	$159.65	$191.58	$239.48
RNA seq Libraries	$159.65	$98.40	$123
Nextera DNA Libraries	$117.42	$84	$105

Eppendorf Robot			
Product	**Internal Cost**	**External, Academic**	**Commercial**
EpMotion reservoir 30ml	$5.25	$6.30	$7.88
Eppendorf 96 deep well plates	$4.00	$4.80	$6.00
Eppendorf epTips Motion 1-50, sterile	$7.25	$8.70	$10.88
Fluidigm			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Fluidigm qdPCR37k digital PCR chip	$110.00	$132.00	$165.00
Fluidigm 48x48 Genotyping	$299.00	$358.80	$448.50
Fluidigm 48 x 48 Gene Expression	$299.00	$358.80	$448.50
Fluidigm 96 sample gene expression chip	$608.00	$729.60	$912
LC480 RT-PCR			
Product	**Internal Cost**	**External, Academic**	**Commercial**
LC480 384-well plate	$6.00	$7.20	$9.00
LC480 96-well plates	$5.00	$6.00	$7.50
LC480 RT-PCR machine Time	$10.93	$12.76	$16.39
LC480 SyBr Green Master Mix	$49.50	$59.40	$74.25
LC480 TaqMan Master Mix	$44.00	$52.80	$66.00
LC480 Transcriptor First Strand Kit	$185.00	$207.60	$259.50
LC480 UPL probe	$8.24	$9.89	$12.36

Qiacube			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Qiacube, DNA	$7.43	$8.91	$11.14
Qiacube, RNA w/o kit	$10.73	$12.36	$15.45

Sanger Sequencing Genewiz/Azenta			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Sequencing	$4.00	$5.08	$6.36
Sequencing, complex/difficult samples	$10.00	$12.00	$15.00
Miscellaneous			
Product	**Internal Cost**	**External, Academic**	**Commercial**
Qubit, Per sample	$1.00	$2.40	$3.00

IV. GRANTS AND CONTRACTS SUPPORTED BY THE CORE, FY22

Boughter, John
USPHS NIH Grant DC016833, Spatial taste coding in mouse gustatory cortex

Bukiya, Anna
USPHS NIH Grant AA-028380, Fatty acid and alcohol modulation of cerebral artery diameter

Chen, Hao
USPHS NIH Grant DA-048017, Reduced complexity mapping of oxycodone self-administration and stress responsiveness in rats

USPHS NIH Grant DA-047638, System genetics of menthol and nicotine addiction

UCSD Subcontract to USPHS NIH Grant DA-037844, Integrated GWAS of Complex Behavioral and Gene Expression Traits in Outbred Rats

Chizhikov, Viktor
USPHS NIH Grant NS-093009, Mesenchymal-neuroepithelial interactions in the developing telencephalon.

Collier, Daniel
USPHS NIH Grant HL-133451, Trauma Induced Endothelial Cell Ca2+ Signaling

Cordero-Morales, Julio
USPHS NIH Grant GM 125629, The Role of Bioactive Lipids in Transient Receptor Potential Channels Gating

USPHS NIH Grant NS-117873, Spectroscopic analyses of TRPV1 during gating

Dopico, Alejandro
USPHS NIH Grant HL-147315, Regulation of arterial diameter through specific sensing of endogenous steroids and novel nonsteroidal analogs by BK channel subunits.

USPHS NIH Grant HL-148941, Cholesterol regulation of smooth muscle BK channel proteins and consequent control of cerebral artery diameter

Du, Jianyang
USPHS NIH Grant MH-113986, CO2 inhalation enhances the lability of fear memory.

Fletcher, Max
USPHS NIH Grant DC-013779, Cholinergic modulation of olfactory bulb glomerular sensitivity

Fortwendel, Jarrod
USPHS NIH Grant AI-143197, Non-cyp51A-mutation Mediated Triazole Resistance in Aspergillus fumigatus

USPHS NIH Grant AI-158442, Unlocking the cidal activity of echinocandins against Aspergillus fumigatus

Freeman, Kevin
USPHS NIH Grant CA-216394, Dissecting the contribution of the transcriptional regulators of SNS fate to neuroblastoma oncogenesis

Army Grant W81XWH-18-1-0477, Investigating the downstream oncogenic consequences and therapeutic susceptibilities caused by loss of ARID1A in neuroblastoma.

Gomes-Solecki, Maria
University of Iowa Subcontract to USPHS NIH Grant AI-39267, Field trial and modeling of transmission-blocking vaccine to prevent Lyme disease

Gosain, Ankush
USPHS NIH Grant DK-125047, Dysbiosis in Hirschsprung Associated Enterocolitis Pathogenesis

Northwestern University Subcontract to USPHS NIH Grant HD-099344, Clinical Trial of ENhancing Recovery in CHildren Undergoing Surgery - ENRICH-US

Gu, Weikuan
Tiantan Hospital Agreement, Center of Integrating Genomics and Bioinformatics for International Study of Stroke (CIGB-ISS)

Heck, Detlef
USPHS NIH Grant MH-112143, Neuronal mechanisms of cerebellar cognitive function

Sloan Kettering Subcontract to USPHS NIH Grant MH-085726, Engrailed genes and cerebellum morphology, spatial gene expression and circuitry Amendment 4

Hevener, Kirk
Army Grant W81XWH2010296, Development and evaluation of inhibitors of the C. difficile enzyme, FabK, as microbiome-sparing antibacterials

Jablonski, Monica
USPHS NIH Grant EY-029950, Novel Extended Release Glaucoma Therapy for Once Daily Dosing

Jaggar, Jonathan
USPHS NIH Grant HL-133256, Blood pressure regulation by smooth muscle cell ion channels

USPHS NIH Grant HL-137745, Endothelial cell potassium channels

USPHS NIH Grant HL-155180, PKD proteins in endothelial cells

USPHS NIH Grant HL-158846, SK3 channel trafficking in endothelial cells

Johnson, Rajasingh
USPHS NIH Grant HL-141345, scaRNA Modified Induced Pluripotent Stem Cell-Derived Cardiomyocytes or Exosomes Therapy for Chronic Ischemic Cardiomyopathy Patients

Jones, Byron
USPHS NIH Grant ES-031656, Genetics of epigenetic response to high circulating glucocorticoids and organophosphorus compounds

Jonsson, Colleen
USPHS NIH Grant AI-142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

Kassan, Modar
USPHS NIH Grant Hl-150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Khan, Mohammad Moshahid
USPHS NIH Grant NS-114616, Examining Progression of a Neurodegenerative Disorder

Kim, Il Hwan
USPHS NIH Grant MH-117429, Genes, Neural Circuits and Behavior

Laribee, Ronald
USPHS NIH Grant CA-233028, Endolysosomal-nuclear communication mediated through V-ATPase and NHE9 dependent epigenetic signaling

Liao, Francesca-Fan
USPHS NIH Grant AG-058467, Novel mechanistic link between metabolic changes and dementia potential role of miRNA21

Lu, Lu
Binzhou Medical University contract, Systems genetics study of hearing loss

Makowski, Liza
USPHS NIH Grant CA-253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

Mary Kay Ash Foundation, PKC agonism reprograms innate immune suppression in TNBC

Malik, Kafait
USPHS NIH Grant HL-019134, Angiotensins, Prostaglandins, Adrenergic Interactions

Mancarella, Salvatore
USPHS NIH Grant HL-153638, Defining the roles of Orai3 channel in cardiomyocytes and cardiomyopathy.

Miranda, Susan
MRC-Musculoskeletal-Canale foundation

Kappa Delta Foundation, Kappa Delta Foundation 2021 award

Kappa Delta FDN Agrmt, Kappa Delta Foundation 2022 award

Narayanan, Ramesh
USPHS NIH Grant CA-229164, Novel Degraders of the Androgen Receptor (AR) and AR Splice Variants (AR-SVs)

Army Grant W81XWH- 21-1-0055, Androgen Receptor-Targeted Treatment for Therapeutically Challenging Breast Cancer

Nowak Jr, Thaddeus S
USPHS NIH Grant NS-113957, Genetics of stroke vulnerability in C57BL/6 mouse substrains

Palmer, Glen
USPHS NIH Grant AI-156611, Examining the importance of folate biosynthetic enzymes in infectious fungi

USPHS NIH Grant AI-127607, Broad spectrum antifungals targeting fatty acid biosynthesis

USPHS NIH Grant AI-152067, Antifungal antagonism as a cause of treatment failure for invasive mycoses

Peters, Brian
USPHS NIH Grant AI-153768, Lipid emulsion composition as a determinant of fungal biofilm formation and incidence of candidemia

Pfeffer, Lawrence M
William & Ella Owens Foundation, Characterizing a novel STAT3 inhibitor to treat glioblastoma

Pierre, Joseph
USPHS NIH Grant AI-163503, Modeling Host-Fungal Interactions in Hirschsprung-Associated Enterocolitis

Quarles, Leigh Darryl
USPHS NIH Grant DK-121132, Optimization of Novel Small Molecules to Antagonize FGF-23

USPHS NIh Grant DK-120567, Genetic and Environmental Determinants of GPRC6A Regulation of Energy Metabolism Using Genetically Engineered Mice and Systems Biology.

Rao, Radhakrishna
USPHS NIH Grant DK-055532, Intestinal Mucosal Protection by Epidermal Growth Factor

Reiter, Lawrence
USPHS NIH Grant NS-115776, The role of UBE3A in gliopathic seizures.

Foundation for Prader-Willi Research, Assessment of epigenetic driven circadian rhythm defects in neurons from individuals with PWS

Foundation for Prader-Willi Research, Analysis of Delayed Neural Development in PWS DPSC Derived Neurons

Sakata, Kazuko
USPHS Grant NS-101703, Heat shock factor HSF1 regulation of promoter-specific BDNF transcription

Seagroves, Tiffany
Army Grant W81X-WH-21-0019, Discovery of Orally Bioavailable Tubulin Inhibitors to Overcome Taxane Resistance in Metastatic Breast Cancer

Sharp, Burt
USPHS NIH Grant DA-053672, Genetics of oxycodone intake in a hybrid rat diversity panel

Tavalin, Steven J
USPHS NIH Grant AG-065813, Amyloid precursor protein control of NMDA receptor signaling

Tigyi, Gabor
USPHS NIH Grant CA-092160, Anticancer Strategies Targeting the Autotaxin-LPA Receptor Axis

Towbin, Jeffrey Allen
USPHS NIH Grant HL-151438, Discovery of modifier genes in cardiomyopathy

Williams, Robert
USPHS NIH Grant AG-070913, Imaging Genetics of Brain Structure and Cognitive Aging in Murine Models of Alzheimer's Disease

USPHS NIH Grant DA-044223, NIDA Core

Xiao, Jianfeng
USPHS NIH Grant NS-119967, Identification and characterization of the gene associated with the spontaneous autosomal recessive Spinning mice

Yi, Ae-Kyung
USPHS NIH Grant AR-069010, Inhibitory Receptors and Autoimmune Arthritis

V. Budget-
MRC – FY2022 Core Activities

FY2022	DEBITS	CREDITS
Salaries	387,309	
Supplies	119,505	
Service Contracts	206,618	
Equipment (> $5,000)	66,034	
Other Expenses	64,663	
TOTAL EXPENSES	***844,129***	
FY21 Internal Recoveries		200,308
FY21 External Recoveries		4,116
TOTAL CREDITS*		***204,424***
Income / (Subsidy)	(639,705)	
THEC Appropriation	664,821	
Carryover THEC Appropriation	**8,972**	
Net Income / (Subsidy)	**34,088**	

*Other expenses consist of the following categories: Media/Communications, Travel, Maintenance/Repairs, Memberships, Copier Rental, and Registration fees.

Subsidy, % after THEC Appropriation N/A

VI. BUSINESS DEVELOPMENT

A. Market Assessment

The MRC provides state of the art molecular and genomics resources and facilities for users on the UTHSC campus, external academic institutions, and commercial vendors. The core is staffed to provide expertise to aid investigators from start to finish in answering their research questions. The typical experiment flows from experimental design to the isolation of nucleic acids to next-generation sequencing, ending with downstream data analyses through referral to the Molecular Bioinformatics Core. Additional services include robotic DNA/RNA isolation, microarrays offered by Affymetrix, real time qPCR, Sanger sequencing of plasmids and PCR products, and all forms of next-generation sequencing (NGS) services. NGS services include whole genome, whole exome, whole transcriptome, ChIP-seq, targeted sequencing and de novo genome assembly, among other applications. For all services, the MRC director and staff are available locally and on demand to answer questions and to provide technical support.

Overall, recoveries generated by the MRC for services completed in FY22 ($204,424) increased relative to FY21 ($154,208), due to the lessening of the effects of the COVID-pandemic and increased funding on campus. In addition, there remains the continued trend of MRC

investigators selecting commercial vendors for completing NGS experiments. Decisions about which service provider to choose to perform NGS experiments are primarily price driven, as the MRC has not offered ultra high-throughput NGS platforms, which allow pricing to be based on high volume.

Since FY17, the core has lost NGS business from several PIs who are based in the GGI department (particularly for DNA-seq applications) to other academic cores or commercial providers (like Hudson Alpha, GeneWiz or BGI). These vendors use the Illumina NovaSeq or X10 platforms; the higher throughput of these instruments reduces the per sample price significantly. MRC can effectively compete with commercial vendors on turnaround time since our instruments are not currently used to full capacity. However, investigators tend to choose lower price over faster turnaround time due to extramural funding constraints. The purchase of a NextSeq 2000, an instrument with significantly higher throughput than the NextSeq 500 and reassessment of our current library pricing from FY 22 has begun in early FY 23, and should help narrow the gap between the charges from the MRC and those of commercial vendors.

The MRC offers a few pieces of equipment for campus use without recharge that may not otherwise be available in individual labs, including the Nanodrop Spectrophotometer, the Spectramax M2e plate reader, the Covaris S2 sonicator, the Genepix microarray scanner, and the Eppendorf EPmotion robot. These pieces of equipment are used predominantly by UTHSC investigators, but are used occasionally by other local labs (UofM or Rhodes).

Overall, our user base in FY22 included 71 unique internal investigators from UTHSC and six external users from three external academic institutions,. The MRC processed over 9,100 service units for these researchers. Many of the external users maintain active collaborations with UTHSC faculty and utilize our services because of the competitive pricing and the excellent recommendation of the MRC by the UTHSC community. We offer a competitive markup rate for these “friends of UTHSC” at the MRC, which is currently 10% above internal user rates.

Competitive Analysis

The MRC is one of two academic genomics shared resource facilities in the Memphis area. The other core, located at St. Jude Children’s Research Hospital, does not take outside samples. In addition, many commercial services offer large-scale NGS services and can provide competitive pricing due to economy of scale (GeneWiz, South Plainfield, NJ; BGI, Beijing, China, Novagene, Davis, CA, and HudsonAlpha, Birmingham, AL). However, the *value-added of the MRC* is direct personal interaction and the ability of the MRC to assist in troubleshooting protocols, services that these organizations do not provide. In addition, the MRC provides enhanced data security, and a direct pipeline to feed raw data generated in the MRC for downstream analysis by the Molecular Bioinformatics Core, which is adjacent to the MRC in TSRB Suite 110.

Marketing Plans to Obtain New Business

We will continue to encourage our clients to tell their collaborators and colleagues about our services; many of our external clients have resulted from such interactions. To showcase the MRC, the core will continue to participate in several campus-wide activities, such as attending new faculty orientation sessions, organizing vendor seminars, and providing presentations to postdoctoral fellows and graduate students. The MRC has been highlighted at local and national meetings focused on core facility resources management, including the regional Southeastern Association of Shared Resources (SEASR) annual meeting in Atlanta, GA in June of 2019 and the ABRF national annual meeting in 2018. UTHSC served as a gold institutional sponsor of the 2021 virtual SEASR annual meeting and was a gold institutional sponsor of the 2022 SEASR

meeting in Nashville, TN, held in June of 2022. At this meeting, the MRC and its partner cores (mBIO and the PMC/MPMS) were advertised. It should be noted that duplication of genomics resources in other departments as part of faculty recruitment packages (including sequencers provided in startup packages that are to be managed by individual faculty and that will not be recharge centers) may pose a direct threat to the continued demand for NGS technologies.

Forecasted Volumes for New Business

The university has also recruited, and is still recruiting, new research faculty, many using genomic techniques, so this effort is expected to increase campus utilization of the MRC. Increased core usage by new faculty and existing faculty in-house may also lead to increased external usage as users recommend the MRC to external investigators as a result of collaborations with other institutions. Although total support from grants and contracts for the UTHSC campus increased significantly from FY21 to FY22 (~$126M to $134M), there is typically a significant lag time between the award of funds and the generation of samples for genomic profiling by research laboratories.

In October of 2020, UTHSC entered into a formal agreement with Novogene, a commercial provider, to provide “bulk discount” or “new user” NGS pricing to all UTHSC MRC core customers. The MRC has served as one conduit for sample submissions to Novogene and recharges a small fee via iLab to manage the relationship with the vendor on behalf of our price-sensitive customers. The goals of this strategy were to better understand the volume of NGS needs on campus, to serve our price-sensitive and our time-sensitive customers and to offer competitive pricing to all investigators without the need for each individual investigator to set up a contract with Novogene directly, which can be a roadblock to generating data quickly. However, in FY22, due to poor customer service experienced post-pandemic, our contract with Novogene for NGS services was not renewed due. Our researchers identified several problems with turnaround and with data quality. To offset the loss of access to Novogene, the MRC has agreed to purchase a new Next-Gen sequencer from Illumina (NextSeq 2000), that will enable the MRC to offer more competitive pricing in FY23. In addition to the new instrument the MRC will also reduce the pricing of our NGS libraries further enabling better value for our clientele.

There have been no available sources of institutional funds dedicated to MRC equipment purchases in several years; therefore, the purchase of any new genomics instruments, such as the 10X Genomics single cell sequencing platform or the Oxford Nanopore PromethION long-read sequencer, or the Nanostring GeoMx spatial genomics system, all recommended by the MRC IAB, have not been feasible to date. These instruments were also recommended as key to executing cross-cutting platform initiatives in the original and second versions of the Operational Strategic Plan for Research, which was approved by Chancellor Schwab.

Overall, MRC revenues in FY23 are expected to remain stable, or to slightly increase, relative to FY22, as research activities continue to increase after the adaptation to the COVID-19 pandemic, and in response to increased extramural awards. We predict that revenues will return to FY19 levels. However, revenues from internal customers and income from external customers may decrease to levels more similar to FY20-FY22 if the volume of NGS sequencing and microarray service requests does not increase in FY23.

Molecular Bioinformatics Core (mBIO) Institutional Research Core Facility Analysis Report- FY22

Written by Daniel Johnson, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?
The mBIO core designation as an institutional core is appropriate since it served 50 unique UTHSC researchers across 17 departments and five colleges (COM, COP, COD, COPH and CGHS).

2. Does the core pass the multi-departmental, multi-investigator litmus test?
Yes. In FY22, this core processed 741 analysis requests including 34 hours of custom data mining or custom scripting on behalf of 50 unique users across 17 departments and three colleges (COM, COP, and CGHS). The departments with the largest number of users were in the College of Graduate Health Sciences (CGHS, 13), followed by the Department of Physiology (COM, 7 users) and the Department of Pharmaceutical Science (COP, 4 users). The top five users, based on the percentage of invoices for completed work in FY22, were Dr. Liza Makowski (Medicine/Hematology, COM, 36.58%), Ramesh Narayanan (Medicine/Hematology, COM, 16.15%), Kazuko Sakata (Pharmacology, COM, 7.91%), Rajasingh Johnson (Bioscience Research, COD, 6.92%), and Jianyang Du (Anatomy and Neurobiology, COM, 4.94%). The other users accounted for 37.50% of total core revenues.

3. Is there sufficient intra- and inter-departmental use and if not, why?
Yes, 50 researchers were served across 17 departments and five colleges.

4. Can the services for the core be outsourced more economically?
No. The internal prices are very competitive relative to other similar academic cores (UTHSC is in the bottom quartile), or to commercial vendors.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g. grants funded through investigator use, publications, etc.)?
Yes. In FY22, core activities led to 57 total PubMed-indexed publications, two of which were co-authored by Dr. Johnson, 12 letters of support provided for grant applications, and four pending grant applications that included Dr. Johnson as a paid co-I. The core supported 30 active grants and contracts. In addition, Dr. Johnson provided workshops and seminars related to bioinformatics that were well- attended.

6. Is the core currently self-sufficient or is it subsidized by the institution?
In FY22, the core was subsidized by the institution. The net subsidy after the state appropriation was zero.

Accomplishments this past year:

- The mBIO core was well-received in its seventh year of operation as the inaugural institutional molecular bioinformatics core on the UTHSC campus.
- Dr. Johnson was included as an author on two publications and he supported multiple grant applications. He also received salary support from one award.
- The mBIO interfaced well with the Molecular Resource Center and the Proteomics and Metabolomics institutional cores, establishing a streamlined, collaborative and "one-stop shop" approach to support genomics and proteomics experiments from experimental

design to data analysis. The mBIO also actively participated in joint staffing sessions with the Biostats, Epidemiology, and Research Design clinic, which provides referrals to the mBIO core, when appropriate.

- Dr. Johnson was an invited speaker at the Arkansas Bioinformatics COVID-19 AI meeting. Dr. Johnson also attended the SEASR 2022 annual meeting in Nashville, TN.

Financial Overview – FY22:

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues	30,046	16,661	15,784	17,241	15,847
Expenses	(132,520)	(163,119)	(156,125)	(111,321)	(159,347)
Income (Subsidy)	(102,474)	(146,458)	(140,341)	(94,080)	(143,500)
Other Costs	0	0	0	0	0
Income (Subsidy)	(102,474)	(146,458)	(140,341)	(94,080)	(143,500)
State Appropriation	62,302	121,971	123,980	150,538	191,580
Net Income (Subsidy)	(40,172)	(24,487)	(16,361)	56,458	48,080
Subsidy, % before State Appropriation	77%	89%	89%	85%	90%
Subsidy, % after State Appropriation	30%	15%	10%	0%	0%

7. Suggested outcomes:

It is recommended that mBIO continue as an institutional core.

Molecular Bioinformatics (mBIO) Institutional Core Facility
Summary of Institutional Core Activities for FY 2022
(July 1, 2020- June 30, 2022)

Written by Daniel Johnson, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

I. PUBLICATIONS (Journal publication dates: July 1, 2021 to June 30, 2022)
Full-length published articles (UTHSC faculty investigators are indicated in bold, the core director is underlined)

Kumar V, Kiran S, **Kumar S**, **Singh UP**. Extracellular vesicles in obesity and its associated inflammation. Int Rev Immunol. 2022;41(1):30-44. doi:10.1080/08830185.2021.1964497. Epub 2021 Aug 23. PMID: 34423733; PMCID: PMC8770589.

Starlard-Davenport A, Fitzgerald A, Pace BS. Exploring epigenetic and microRNA approaches for γ-globin gene regulation. Exp Biol Med (Maywood). 2021Nov;246(22):2347-2357. doi: 10.1177/15353702211028195. Epub 2021 Jul 22. PMID:34292080; PMCID: PMC8606961.

Pagliuca S, Gurnari C, Awada H, Kishtagari A, Kongkiatkamon S, Terkawi L, Zawit M, Guan Y, LaFramboise T, Jha BK, Patel BJ, Hamilton BK, Majhail NS, Lundgren S, Mustjoki S, Sauntharajah Y, Visconte V, Chan TA, **Yang CY**, Lenz TL, Maciejewski JP. The similarity of class II HLA genotypes defines patterns of autoreactivity in idiopathic bone marrow failure disorders. Blood. 2021 Dec30;138(26):2781-2798. doi: 10.1182/blood.2021012900. PMID: 34748628; PMCID: PMC8718627.

Siegel EM, Ajidahun A, Berglund A, Guerrero W, Eschrich S, Putney RM, Magliocco A, Riggs B, Winter K, Simko JP, Ajani JA, Guha C, Okawara GS, AbdallaI, Becker MJ, Pizzolato JF, Crane CH, Brown KD, **Shibata D**. Genome-wide host methylation profiling of anal and cervical carcinoma. PLoS One. 2021 Dec9;16(12):e0260857. doi: 10.1371/journal.pone.0260857. PMID: 34882728; PMCID: PMC8659695.

Singla B, Aithabathula RV, Kiran S, Kapil S, **Kumar S**, **Singh UP**. Reactive oxygen species in Regulating Lymphangiogenesis and Lymphatic Function. Cells.2022 May 26;11(11):1750. doi: 10.3390/cells11111750. PMID: 35681445; PMCID: PMC9179518.

Perkins RS, Suthon S, Miranda-Carboni GA, **Krum SA**. WNT5B in cellular signaling pathways. Semin Cell Dev Biol. 2022 May;125:11-16. doi:10.1016/j.semcdb.2021.09.019. Epub 2021 Oct 9. PMID: 34635443.

Ingram H, Dogan M, Eason JD, Kuscu C, **Kuscu C**. MicroRNAs: Novel Targets in Hepatic Ischemia-Reperfusion Injury. Biomedicines. 2022 Mar 29;10(4):791. doi:10.3390/biomedicines10040791. PMID: 35453542; PMCID: PMC9028838.

Chen K, **Sun Z**. Estrogen inhibits renal Na-Pi Co-transporters and improves klotho deficiency-induced acute heart failure. Redox Biol. 2021 Nov;47:102173.doi: 10.1016/j.redox.2021.102173. Epub 2021 Oct 18. PMID: 34678656; PMCID: PMC8577443.

Zhao S, Browning J, **Cui Y**, Wang J. Using machine learning to classify patients on opioid use. J Pharm Health Serv Res. 2021 Oct 19;12(4):502-508. doi:10.1093/jphsr/rmab055. PMID: 35003334; PMCID: PMC8697024.

Chintanaphol M, Orgil BO, Alberson NR, **Towbin JA**, **Purevjav E**. Restrictive cardiomyopathy: from genetics and clinical overview to animal modeling. Rev Cardiovasc Med. 2022 Mar 17;23(3):108. doi: 10.31083/j.rcm2303108. PMID:35345275.

Xu F, Gao J, Orgil BO, Bajpai AK, Gu Q, **Purevjav E, Davenport AS**, Li K, **Towbin JA**, Black DD, Pierre JF, Lu L. Ace2, and Tmprss2 Expressions Are Regulated by Dhx32 and Influence the Gastrointestinal Symptoms Caused by SARS-CoV-2. J Pers Med. 2021 Nov 16;11(11):1212. doi: 10.3390/jpm11111212.PMID: 34834564; PMCID: PMC8621576.

Samak G, Rao R, **Rao R**. Lactobacillus casei and Epidermal growth factor Prevent Osmotic Stress-Induced Tight Junction Disruption in Caco-2 cell monolayers. Cells. 2021 Dec 18;10(12):3578. doi: 10.3390/cells10123578. PMID:34944085; PMCID: PMC8700399.

Mitachi K, Mingle D, Effah W, Sánchez-Ruiz A, **Hevener KE**, **Narayanan R**, Clemons WM Jr, Sarabia F, **Kurosu M**. Concise Synthesis of Tunicamycin V and discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID:35594368; PMCID: PMC9329268.

Kundu S, Shetty A, **Gomes-Solecki M**. Necroptosis Contributes to Persistent Inflammation During Acute Leptospirosis. Front Immunol. 2022 Mar 22;13:810834.doi: 10.3389/fimmu.2022.810834. PMID: 35392072; PMCID: PMC8980737.

Shetty A, Kundu S, Vernel-Pauillac F, Ratet G, Werts C, **Gomes-Solecki M**. Transient Presence of Live Leptospira interrogans in Murine Testes. MicrobiolSpectr. 2022 Jun 29;10(3):e0277521. doi: 10.1128/spectrum.02775-21. Epub 2022 Apr 21. PMID: 35446113; PMCID: PMC9241917.

Kiran S, Rakib A, **Singh UP**. The NLRP3 Inflammasome Inhibitor Dapansutrile Attenuates Cyclophosphamide-Induced Interstitial Cystitis. Front Immunol. 2022Jun 3;13:903834. doi: 10.3389/fimmu.2022.903834. PMID: 35720309; PMCID: PMC9205468.

Howard LM, Edwards KM, Zhu Y, Williams DJ, Self WH, Jain S, Ampofo K, Pavia AT, Arnold SR, **McCullers JA**, Anderson EJ, Wunderink RG, Grijalva CG. Parainfluenza Virus Types 1-3 Infections Among Children and Adults Hospitalized With Community-acquired Pneumonia. Clin Infect Dis. 2021 Dec6;73(11):e4433-e4443. doi: 10.1093/cid/ciaa973. PMID: 32681645; PMCID: PMC8662767.

Kumar A, Sinha N, Kodidela S, Zhou L, **Singh UP**, **Kumar S**. Effect of benzo (a)pyrene on oxidative stress and inflammatory mediators in astrocytes and HIV-infected macrophages. PLoS One. 2022 Oct 14;17(10):e0275874. doi:10.1371/journal.pone.0275874. PMID: 36240258; PMCID: PMC9565757.

Meena AS, Shukla PK, Bell B, Giorgianni F, Caires R, Fernández-Peña C, Beranova S, Aihara E, Montrose MH, Chaib M, **Makowski L**, Neeli I, Radic MZ, Vásquez V, Jaggar JH, Cordero-Morales JF, **Rao R**. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID: PMC9250449.

Victor AK, Donaldson M, **Johnson D**, Miller W, **Reiter LT**. Molecular Changes in Prader-Willi Syndrome Neurons Reveals Clues About Increased Autism Susceptibility. Front Mol Neurosci.

2021 Oct 29;14:747855. doi:10.3389/fnmol.2021.747855. PMID: 34776864; PMCID: PMC8586424.

Wang X, Bajpai AK, Gu Q, Centeno A, **Starlard-Davenport A**, Prins P, Xu F, Lu L. A systems genetics approach delineates the role of Bcl2 in leukemia pathogenesis. Leuk Res. 2022 Mar;114:106804. doi: 10.1016/j.leukres.2022.106804.Epub 2022 Feb 9. PMID: 35182904; PMCID: PMC9272521.

Starlard-Davenport A, Gu Q, Pace BS. Targeting Genetic Modifiers of HBG Gene Expression in Sickle Cell Disease: The miRNA Option. Mol Diagn Ther. 2022 Sep;26(5):497-509. doi: 10.1007/s40291-022-00589-z. Epub 2022 May 12. PMID:35553407; PMCID: PMC9098152.

Alleboina S, Aljouda N, **Miller M**, **Freeman KW**. Therapeutically targeting oncogenic CRCs facilitates induced differentiation of NB by RA and the BET bromodomain inhibitor. Mol Ther Oncolytics. 2021 Sep 25;23:181-191. doi:10.1016/j.omto.2021.09.004. PMID: 34729395; PMCID: PMC8526497.

Trebska-McGowan K, Chaib M, Alvarez MA, Kansal R, Pingili AK, **Shibata D**, **Makowski L**, **Glazer ES**. TGF-β Alters the Proportion of Infiltrating Immune Cells in a Pancreatic Ductal Adenocarcinoma. J Gastrointest Surg. 2022Jan;26(1):113-121. doi: 10.1007/s11605-021-05087-x. Epub 2021 Jul 14. PMID:34260016.

Berglund A, Muenyi C, Siegel EM, Ajidahun A, Eschrich SA, Wong D, Hendrick LE, Putney RM, Kim S, Hayes DN, **Shibata D**. Characterization of Epigenomic Alterations in HPV16+ Head and Neck Squamous Cell Carcinomas. Cancer Epidemiol biomarkers Prev. 2022 Apr 1;31(4):858-869. doi: 10.1158/1055-9965.EPI-21-0922.PMID: 35064062; PMCID: PMC8983563.

Gu Q, Xu F, Orgil BO, Khuchua Z, Munkhsaikhan U, Johnson JN, Alberson NR, Pierre JF, Black DD, Dong D, Brennan JA, Cathey BM, Efimov IR, **Towbin JA**, **Purevjav E**, Lu L. Systems genetics analysis defines importance of TMEM43/LUMA for cardiac- and metabolic-related pathways. Physiol Genomics. 2022 Jan 1;54(1):22-35. doi: 10.1152/physiolgenomics.00066.2021. Epub2021 Nov 12. PMID: 34766515; PMCID: PMC8721901.

Shukla PK, Meena AS, **Rao R**. Prevention and mitigation of alcohol-induced neuroinflammation by Lactobacillus plantarum by an EGF receptor-dependent mechanism. Nutr Neurosci. 2022 Apr;25(4):871-883. doi:10.1080/1028415X.2020.
1819105. Epub 2020 Sep 18. PMID: 32945721; PMCID: PMC7969470.

Bhuniya R, Yuan X, Bai L, Howie KL, Wang R, Li W, Park F, **Yang CY**. Design, Synthesis, and Biological Evaluation of Apcin-Based CDC20 Inhibitors. ACS Med Chem Lett. 2022 Jan 18;13(2):188-195. doi: 10.1021/acsmedchemlett.1c00544. PMID:35178174; PMCID: PMC8842116.

Gao Y, **Cui Y**. Clinical time-to-event prediction enhanced by incorporating compatible related outcomes. PLOS Digit Health. 2022;1(5):e0000038. doi:10.1371/journal.pdig.0000038. Epub 2022 May 26. PMID: 35757279; PMCID: PMC9222982.

Krutilina RI, Playa H, Brooks DL, Schwab LP, Parke DN, Oluwalana D, Layman DR, Fan M, **Johnson DL**, Yue J, Smallwood H, **Seagroves TN**. HIF-Dependent CKB Expression Promotes Breast Cancer Metastasis, Whereas Cyclocreatine Therapy Impairs Cellular Invasion and

Improves Chemotherapy Efficacy. Cancers (Basel).2021 Dec 22;14(1):27. doi: 10.3390/cancers14010027. PMID: 35008190; PMCID:PMC8749968.

Kurosu M, Mitachi K, Yang J, Pershing EV, Horowitz BD, Wachter EA, Lacey JW3rd, Ji Y, Rodrigues DJ. Antibacterial Activity of Pharmaceutical-Grade Rose Bengal: An Application of a Synthetic Dye in Antibacterial Therapies. Molecules. 2022 Jan 5;27(1):322. doi: 10.3390/molecules27010322. PMID: 35011554; PMCID: PMC8746496.

Camors EM, Roth AH, Alef JR, Sullivan RD, Johnson JN, **Purevjav E**, **Towbin JA**. Progressive Reduction in Right Ventricular Contractile Function Attributable to Altered Actin Expression in an Aging Mouse Model of Arrhythmogenic Cardiomyopathy. Circulation. 2022 May 24;145(21):1609-1624. doi:10.1161/CIRCULATIONAHA. 120.049261. Epub 2022 Apr 19. PMID: 35437032; PMCID: PMC9133220.

Lin Y, **Sun Z**. Klotho deficiency-induced arterial calcification involves osteoblastic transition of VSMCs and activation of BMP signaling. J Cell Physiol. 2022 Jan;237(1):720-729. doi: 10.1002/jcp.30541. Epub 2021 Aug 8. PMID:34368951; PMCID: PMC8810603.

Shukla PK, Meena AS, Pierre JF, **Rao R**. Central role of intestinal epithelial glucocorticoid receptor in alcohol- and corticosterone-induced gut permeability and systemic response. FASEB J. 2022 Jan;36(1):e22061. doi:10.1096/fj.202101424R. PMID: 34861075; PMCID: PMC8647846.

Munkhsaikhan U, Kwon Y, Sahyoun AM, Ait-Aissa K, Kassan A, **Kassan M**. The microsomal triglyceride transfer protein inhibitor lomitapide improves vascular function in mice with obesity. Obesity (Silver Spring). 2022 Apr;30(4):893-901.doi: 10.1002/oby.23389. Epub 2022 Mar 6. PMID: 35253407; PMCID: PMC8957593.

Sutton S, Lin J, Perkins RS, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**. Estrogen receptor alpha and NFATc1 bind to a bone mineral density-associated SNP to repress WNT5B in osteoblasts. Am J Hum Genet. 2022 Jan 6;109(1):97-115. doi:10.1016/j.ajhg.2021.11.018. Epub 2021 Dec 13. PMID: 34906330; PMCID: PMC8764205.

Rana M, Kansal R, Chaib M, Teng B, Morrison M, Hayes DN, Stanfill AG, **Shibata D**, Carson JA, **Makowski L**, **Glazer ES**. The pancreatic cancer immune tumor microenvironment is negatively remodeled by gemcitabine while the TGF-β receptor plus dual checkpoint inhibition maintains antitumor immune cells. Mol Carcinog.2022 Jun;61(6):549-557. doi: 10.1002/mc.23401. Epub 2022 Mar 23. PMID: 35319799.

Di L, Akther S, Bezrucenkovas E, Ivanova L, Sulkow B, Wu B, Mneimneh S, **Gomes-Solecki M**, Qiu WG. Maximum antigen diversification in a lyme bacterial population and evolutionary strategies to overcome pathogen diversity. ISME J.2022 Feb;16(2):447-464. doi: 10.1038/s41396-021-01089-4. Epub 2021 Aug 19. PMID:34413477; PMCID: PMC8376116.

Kiran S, Rakib A, Moore BM, **Singh UP**. Cannabinoid Receptor 2 (CB2) Inverse Agonist SMM-189 Induces Expression of Endogenous CB2 and Protein Kinase A That Differentially Modulates the Immune Response and Suppresses Experimental Colitis. Pharmaceutics. 2022 Apr 26;14(5):936. doi:10.3390/pharmaceutics14050936. PMID: 35631522; PMCID: PMC9147685.

Poje JE, Azevedo JF, Nair N, Mahachi K, Frank LE, Sherpa P, Krizek RS, Baccam T, **Gomes-Solecki M**, Petersen CA. Borrelia burgdorferi (Spirochaetales:Spirochaetaceae) Infection

Prevalence and Host Associations of Ticks Found on Peromyscus spp. in Maryland. J Med Entomol. 2022 Mar 16;59(2):752-757. doi:10.1093/jme/tjab206. PMID: 34971369; PMCID: PMC8924970.

Kiran S, Rakib A, Kodidela S, **Kumar S**, **Singh UP**. High-Fat Diet-Induced Dysregulation of Immune Cells Correlates with Macrophage Phenotypes and Chronic Inflammation in Adipose Tissue. Cells. 2022 Apr 13;11(8):1327. doi:10.3390/cells11081327. PMID: 35456006; PMCID: PMC9031506.

Suthon S, Perkins RS, Lin J, Crockarell JR Jr, Miranda-Carboni GA, **Krum SA**.GATA4 and estrogen receptor alpha bind at SNPs rs9921222 and rs10794639 to regulate AXIN1 expression in osteoblasts. Hum Genet. 2022 Jun 9. doi:10.1007/s00439-022-02463-8. Epub ahead of print. PMID: 35678873.

Drake JA, Fleming AM, Behrman SW, **Glazer ES**, Deneve JL, Yakoub D, Tsao MW, Dickson PV. Tumor Location in the Pancreatic Tail Is Associated with Decreased Likelihood of Receiving Chemotherapy for Pancreatic Adenocarcinoma. J Gastrointest Surg. 2022 Oct;26(10):2136-2147. doi: 10.1007/s11605-022-05381-2.Epub 2022 Jun 29. PMID: 35768717.

Kassan A, Ait-Aissa K, **Kassan M**. Gut Microbiota Regulates the Sympathetic Nerve Activity and Peripheral Serotonin Through Hypothalamic MicroRNA-204 in Order to Increase the Browning of White Adipose Tissue in Obesity. Cureus. 2022Feb 4;14(2):e21913. doi: 10.7759/cureus.21913. PMID: 35155042; PMCID:PMC8820388.

Hollingsworth TJ, Wang X, White WA, Simpson RN, **Jablonski MM**. Chronic Proinflammatory Signaling Accelerates the Rate of Degeneration in a Spontaneous Polygenic Model of Inherited Retinal Dystrophy. Front Pharmacol. 2022 Mar21;13:839424. doi: 10.3389/fphar.2022.839424. PMID: 35387333; PMCID: PMC8978607.

Fili CV, Lin L, Chapman J, **Hamilton D**, Yates CR. Methylsulfonylmethane and Sesame Seed Oil Improve Dyslipidemia and Modulate Polyunsaturated Fatty Acid Metabolism in Two Mouse Models of Diabetes. J Med Food. 2022 Jun;25(6):607-617.doi: 10.1089/jmf.2021.0196. PMID: 35708633; PMCID: PMC9247677.

Yuan X, Chinnaswamy K, Stuckey JA, **Yang CY**. Computational Cosolvent Mapping Analysis Leads to Identify Salicylic Acid Analogs as Weak Inhibitors of ST2 and IL33 Binding. J Phys Chem B. 2022 Mar 31;126(12):2394-2406. doi:10.1021/acs.jpcb.2c00341. Epub 2022 Mar 16. PMID: 35294837; PMCID: PMC9354565.

Fortes-Gabriel E, Guedes MS, Shetty A, Gomes CK, Carreira T, Vieira ML, Esteves L, Mota-Vieira L, **Gomes-Solecki M**. Enzyme immunoassays (EIA) for serodiagnosis of human leptospirosis: specific IgG3/IgG1 isotyping may further inform the diagnosis of acute disease. PLoS Negl Trop Dis. 2022 Feb23;16(2):e0010241. doi: 10.1371/journal.pntd.0010241. PMID: 35196321; PMCID: PMC8901056.

Chen K, Wang S, **Sun Z**. In Vivo Cardiac-specific Expression of Adenylyl Cyclase 4 Gene Protects against Klotho Deficiency-induced Heart Failure. Transl Res. 2022 Jun;244:101-113. doi: 10.1016/j.trsl.2022.01.006. Epub 2022 Jan 31.PMID: 35114419; PMCID: PMC9119924.

Chaib M, Sipe LM, Yarbro JR, Bohm MS, Counts BR, Tanveer U, Pingili AK, Daria D, Marion TN, Carson JA, Thomas PG, **Makowski L**. PKC agonism restricts innate immune suppression,

promotes antigen cross-presentation and synergizes with agonistic CD40 antibody therapy to activate CD8+ T cells in breast cancer. Cancer Lett. 2022 Apr 10;531:98-108. doi:10.1016/j.canlet.2022.01.017. Epub 2022 Jan 21. PMID: 35074498.

Collier DA, Fitzpatrick D, Dell M, Snideman SS, Marsicano CR, Kelchen R, Wells KE. We Want You Back: Uncovering the Effects on In-Person Instructional Operations in Fall 2020. Res High Educ. 2022;63(5):741-767. doi:10.1007/s11162-021-09665-5. Epub 2021 Nov 30. PMID: 34866763; PMCID: PMC8631564.

Collyer J, Xu F, Munkhsaikhan U, Alberson NF, Orgil BO, Zhang W, Czosek RJ, Lu L, Jefferies JL, **Towbin JA**, **Purevjav E**. Combining whole exome sequencing within silico analysis and clinical data to identify candidate variants in pediatric left ventricular noncompaction. Int J Cardiol. 2022 Jan 15;347:29-37. doi:10.1016/j.ijcard.2021.11.001. Epub 2021 Nov 6. PMID: 34752814.

Huo X, Zhang W, Zhao G, Chen Z, Dong P, Watari H, **Narayanan R**, Tillmanns TD, Pfeffer LM, Yue J. FAK PROTAC Inhibits Ovarian Tumor Growth and Metastasis by Disrupting Kinase Dependent and Independent Pathways. Front Oncol. 2022 Apr 28;12:851065. doi: 10.3389/fonc.2022.851065. PMID: 35574330; PMCID: PMC9095959.

Koffman EE, Kruse CM, Singh K, Naghavi FS, Curtis MA, Egbo J, Houdi M, LinB, Lu H, Debiec J, **Du J**. Acid-sensing ion channel 1a regulates the specificity of reconsolidation of conditioned threat responses. JCI Insight. 2022 Feb22;7(4):e155341. doi: 10.1172/jci.insight.155341. PMID: 35025766; PMCID: PMC8876458.

Mahat U, Garg B, **Yang CY**, Mehta H, Hanna R, Rogers HJ, Flagg A, Ivanov AI, Corey SJ. Lymphocyte cytosolic protein 1 (L-plastin) I232F mutation impairs granulocytic proliferation and causes neutropenia. Blood Adv. 2022 Apr26;6(8):2581-2594. doi: 10.1182/bloodadvances.2021006398. PMID: 34991157; PMCID: PMC9043934.

Beasley MM, Gunawan T, **Tunstall BJ**, Kearns DN. Intermittent access training produces greater motivation for a non-drug reinforcer than long access training. Learn Behav. 2022 Feb 7. doi: 10.3758/s13420-022-00512-w. Epub ahead of print.PMID: 35132517.

Han X, **Sun Z**. Adult Mouse Kidney Stem Cells Orchestrate the De Novo Assembly of a Nephron via Sirt2-Modulated Canonical Wnt/β-Catenin Signaling. Adv Sci (Weinh). 2022 May;9(15): e2104034. doi: 10.1002/advs.202104034. Epub 2022 Mar 22. PMID: 35315252; PMCID: PMC9130916.

II. Conferences / Presentations

Artificial Intelligence in Medicine with the Arkansas Bioinformatics Group

III. PRESENTATIONS GIVEN TO PROMOTE CORE RESOURCES AND CORE USAGE

A. Tours

Twelve tours for new faculty were given. Dr. Johnson met with seven postdocs to discuss core services and bioinformatics analysis.

B. Courses and Internal Presentations

Co-Course Director, PATH942, Web-Based Bioinformatics and Computational Biology Tools (Dr. Johnson also developed the course materials.)

IV. SUMMARY OF ACTIVITIES

A. Personnel

Director: Daniel L. Johnson, PhD (100% effort)

B. Oversight Committee

The following faculty were members of the FY22 Molecular Bioinformatics Core Internal Advisory Board:

Lawrence Reiter (Neurology), *IAB Chair*
Ramesh Narayanan (Medicine – Hematology)
Megan Mulligan (Genetics, Genomics, and Informatics)
Salvatore Mancarella (Physiology)

C. Equipment

Equipment	Cost	Funding Source	Year of Purchase
Analysis Server	$3,400	Office of Research	2015
Analysis Server	$3,400	Office of Research	2015
Analysis Server	$3,400	Recharge Fees, mBIO	2016
Analysis Server	$3,400	Recharge Fees, mBIO	2016
Deep Storage System	$5,400	Office of Research	2017
Windows 10 Server for SPSS and GSEA software	$2,100	Recharge Fees, mBIO	2018
Software Development Center	$2,300	Recharge Fees, mBIO	2018
Analysis Server	$3,200	Recharge Fees, mBIO	2021
Analysis Server	$3,200	Recharge Fees, mBio	2021
File Storage (for individual PIs to access)	$30,000	Office of the Chancellor (initial core investment)	2015

D. Service Contracts

No service contracts are needed since all equipment is maintained locally by Dr. Johnson. In FY22, mBIO funds were used to pay for a portion of the Thermo Electron Orbitrap agreement on behalf of the PMIC.

E. FY22 Usage Volumes by Service Request Type

- Alignment: 219
- Biostatistics: 20
- Custom Scripting: 20
- Data Mining: 14
- Gene Ontology: 3
- Gene Set Enrichment Analysis: 3
- GraphPad Prism 7 licenses: 130
- Heatmap: 32
- iPathway Guide: 21
- Normalization: 17
- Peak Annotation: 26
- Peak Calling: 24

- Peak Modeling: 0
- Pearson's Correlation: 17
- Principle Component Analysis: 17
- Quality Control: 152
- String Analysis: 2
- Venn Diagram: 5
- Volcano Plot: 17

Overall usage of the Core:
741 service requests including 34 hours of custom data mining or custom scripting on behalf of 50 unique research laboratories across 17 departments and five colleges (COM, COP, COD, COHP, and CGHS. Dr. Johnson provided 16 letters of support for grant submissions.

Departments that requested services, FY22
Anatomy and Neurobiology (COM): 2 investigators
Bioscience Research (COD): 1 investigator
Comparative Medicine (COM): 1 investigator
Diagnostic and Heath Science (COHP); 1 investigator
Genetics, Genomics, Informatics (COM): 3 investigators
Graduate Health Science (CGHS): 13 investigators
Medicine (COM): 2 investigators
MIB (COM): 3 investigators
Neurology (COM): 2 investigators
Ophthalmology (COM): 2 investigators
Orthopedic Surgery (COM): 1 investigator
Pathology (COM): 2 investigators
Pediatrics (COM): 3 investigators
Pharmaceutical Science (COP): 4 investigators
Physiology (COM): 7 investigators
Surgery (COM): 2 investigators
Transplant Surgery: 1 investigator

F. Multi-year trends (Bioinformatics)
FY22 was the seventh full fiscal year of service for the mBIO Core. Service requests and revenues have increased for FY22 compared to FY21.

G. FY22 Fee Structure
In FY18, per recommendation of the mBIO Internal Advisory Board, the core moved to a flat-fee schedule rather than an hourly or custom scripting/data mining fee structure. The chart below shows the FY22 service fees associated with each type of service task.

Type of service:	Cost
• Advanced Clustering:	$51.50 per experiment
• Alignment to the genome:	$10.30 per sample
• Biostatistics:	$34.90 per paired condition
• Custom Scripting:	$45.02 per hour
• Data Mining:	$81.03 per hour
• David Pathway Analysis:	$57.40
• De novo Assembly:	$1,320

- GEO setup and deposit: $231.86
- Gene set enrichment analysis: $86.66 per paired condition
- GraphPad Prism 9 license: $110 per license
- Heatmap analysis: $12.28 per image
- iPathway Guide analysis: $81.86 per paired condition
- Normalization workflow: $23.64 per experiment
- Pearson's Correlation calculation: $12.28 per image
- Principle Component analysis: $23.64 per image
- Quality Assurance analysis: $5.15 per sample
- SNP Analysis: $86.66 per sample
- String Analysis: $56.28 per paired condition
- Venn Diagram: $12.28 per image
- Volcano Plot: $12.28 per image

V. GRANTS THAT SUPPORTED THE CORE, FY22

Abidi, Ammaar
Oxnard Foundation

Chizhikov, Viktor
USPHS NIH Grant NS-093009, Mesenchymal-neuroepithelial interactions in the developing telencephalon

Collier, Daniel
USPHS NIH Grant HL-133451, Trauma Induced Endothelial Cell Ca2+ Signaling

Cui, Yan
USPHS Grant CA-262296, Algorithm-based prevention and reduction of cancer health disparity arising from data inequality

Dale, James
USPHS NIH Grant AI-132117, Structure-Based Design of a Broadly Protective Group A Streptococcal Vaccine

Davenport, Athena S
USPHS NIH Grant DK-144641, MicroRNA-based epigenetic approach to induce fetal hemoglobin

Methodist Mission Support Fund

Du, Jianyang
USPHS Grant NIH MH-113986, CO2 inhalation enhances the lability of fear memory

Freeman, Kevin
USPHS NIH Grant CA-216394, Dissecting the contribution of the transcriptional regulators of SNS fate to neuroblastoma oncogenesis

Gadiparthi, Rao
USPHS NIH Grant HL-069908, NFATs and Vascular Injury

Gomes-Solecki, Maria
Univ Iowa Subcontract to USPHS NIH AI-39267, Field trial and modeling of transmission-blocking vaccine to prevent Lyme disease

Hevener, Kirk
Army Grant W81XWH2010296 Hevener, Development and evaluation of inhibitors of the C. difficile enzyme, FabK, as microbiome-sparing antibacterials

Jablonski, Monica
USPHS NIH Grant EY-029950, Novel Extended Release Glaucoma Therapy for Once Daily Dosing

Johnson, Rajasingh
American Heart Association Grant 20TPA35490215, Selective inhibition of HDAC6 attenuates angiotensin-II induced cardiac hypertrophy by suppressing autophagy

Kassan, Modar
USPHS NIH Grant Hl-150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Laribee, Ronald
USPHS NIH Grant CA-233028, Endolysosomal-nuclear communication mediated through V-ATPase and NHE9 dependent epigenetic signaling

Makowski, Liza
USPHS NIH Grant CA-253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

Mancarella, Salvatore
USPHS NIH Grant HL-153638, Defining the roles of Orai3 channel in cardiomyocytes and cardiomyopathy

Narayanan, Ramesh
Army Grant W81XWH- 21-1-0055, Androgen Receptor-Targeted Treatment for Therapeutically Challenging Breast Cancer

USPHS NIH Grant CA-229164, Novel Degraders of the Androgen Receptor (AR) and AR Splice Variants (AR-SVs)

Nowak Jr, Thaddeus S
USPHS NIH Grant NS-113957, Genetics of stroke vulnerability in C57BL/6 mouse substrains

Parfenova, Elena
USPHS NIH Grant NS-105655, Endothelial Vasoprotection by Hypothermia

Rao, Radhakrishna
USPHS NIH Grant DK-055532, Intestinal Mucosal Protection by Epidermal Growth Factor

Reiter, Lawrence
USPHS NIH Grant NS-115776, The role of UBE3A in gliopathic seizures

Sakata, Kazuko
USPHS NIH Grant NS-101703, Heat shock factor HSF1 regulation of promoter-specific BDNF transcription

Seagroves, Tiffany
Army Grant W81XWH2010019, Discovery of Orally Bioavailable Tubulin Inhibitors to Overcome Taxane Resistance in Metastatic Breast Cancer

Shibata, David
Univ of Utah subcontract to USPHS NIH CA-206110, Transdisciplinary Team Science in Colorectal Cancer Prognosis - the ColoCare Study

Singh, Udai
USPHS Grant AI-140405, Adipose T cell microRNAs (miRs) regulate macrophage function during obesity

Sun, Zhongjie
USPHS NIH Grant HL-154147, Investigation into Arterial Stiffness and Hypertension

USPHS NIH Grant AG-049780, Investigation into Heart Aging

Towbin, Jeffrey Allen
USPHS NIH Grant HL-151438, Discovery of modifier genes in cardiomyopathy

VI. BUSINESS DEVELOPMENT

A. Market Assessment

In FY22, the mBIO core completed 741 service requests including 34 hours of custom data mining or custom scripting on behalf of 51 unique research laboratories across 17 departments and five colleges (COM, COP, COD, COHP, and CGHS). Dr. Johnson provided 12 letters of support for grant submissions. The core provided office hours and consultations for >50 investigators and students. To reach out to external customers, the director attended the Arkansas Artificial Intelligence campus meeting and attended the Southeastern Association of Shared Resources annual meeting in Nashville, TN in June of 2022.

B. Marketing Plans to Obtain New Business

The focus of marketing for the mBIO core in FY23 will be to continue expanding the core customer base throughout the UTHSC system and the Mid-South/Delta region. We will continue participating in events sponsored by the Office of Research, holding local seminars and workshops, and expanding the mBIO core website. Dr. Johnson presents a series of talks each spring in order to educate new researchers in bioinformatics workflows, and to advertise the mBIO core services.

C. Forecasted Volumes for New Business and Recommendations for FY23

The core increased pricing 3% for the FY23 period over FY22. This new rate structure became effective July 1, 2022 and continues to place UTHSC in the bottom-third of peer academic institutions that offer bioinformatics services. Based on the IAB recommendations in FY18, the core moved to a flat fee structure in FY19 for all services other than custom scripting and data mining. We will continue the trend of sample-based fee rather than hourly rates.

In FY17, iPathway Guide, which maps pathway interactomes, was purchased by the mBIO core. The pricing structure was set to charge for individual analyses. This analysis tool can be accessed anywhere online, although Dr. Johnson's account must manage the initial analysis request. He is then able to share the results with PIs online through a web interface. In FY22, demand for iPathway Guide network mapping software increased as did the resale of Prism (GraphPad) statistics and graphing software, which is offered as a renewable institutional site license through the mBIO core (must be renewed each year). However, iPathway Guide has increased its pricing for FY23 and will likely be discontinued. Instead, core users can access analysis tools online or offered at no additional cost with Affymetrix.

The external customer markup rate for services will continue to be 20%, which is the rate approved for the mBIO service center, and the rate approved by the Office of Finance in 2017. This level of markup is consistent with other regional cores that offer bioinformatics services to external customers.

In FY22, the core replaced two aging data analysis systems, added a new large data storage array, and created a single-cell analysis pipeline as well as ATAC seq pipeline for users.

To obtain external customers, Dr. Johnson will continue to advertise the core at national and regional meetings, including the Southeastern Association of Shared Resources annual meeting in June of 2023 (Atlanta, GA) and by attending the ABRF national meeting in Boston, MA in May of 2023. Overall, it is expected the volume of services will remain the same in FY23 as in FY22, unless newly recruited faculty begin to use the mBIO, MRC, and PMC cores.

VI. Actual Budget FY22 (July 1, 2021 to June 30, 2022)

FY2022	DEBITS	CREDITS
Salaries	91,315	
Supplies	32,118	
Service Contracts	35,914*	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***159,347***	
FY22 Internal Recoveries		15,847
FY22 External Recoveries		0
TOTAL CREDITS		***15,847***
Income / (Subsidy)	(143,500)	
State Appropriation	191,580	
Net Income / (Subsidy)	**48,080**	

*Service Contracts expenditures include a portion of the PMC Thermo Electron Orbitrap maintenance agreement invoice in FY22, which totaled $59,367. The amount of $35,914 was paid from the Molecular Bioinformatics account.

Proteomics and Metabolomics (PMC) Institutional Research Core Facility Analysis Report, Including the Metabolic Phenotyping Mass Spectrometry Unit (MPMS)- FY22

Written by David Kakhniashvili, PhD; Michelle Puchowicz, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?

The PMC designation as an institutional core is appropriate. The Proteomics and Untargeted Metabolomics Unit (abbreviated as "Proteomics" herein) served nine system users (eight on the Memphis campus and one on the UT Institute for Agriculture campus) across seven UTHSC departments and two UTHSC colleges (Memphis, COM and COP) and one user in the Department of Animal Science on the UIA campus. One external academic user from Michigan State University was also served. The MPMS Unit served four internal investigators from two colleges (COM, COP) and two external academic users (University of Pittsburg and the University of Illinois, Chicago).

2. Does the core pass the multi-departmental, multi-investigator litmus test?

Yes. The Proteomics Unit served eight internal users across seven departments within two colleges and three external users. The MPMS Unit served five internal investigators within two colleges and two external academic users (University of Pittsburg and the University of Illinois, Chicago).

The top three users of the Proteomics Unit, as a percentage of total invoices for completed services ($38,933.46) were: 1) Daniel Matthew (UIA, 33.82%), 2) Ramesh Narayanan (31.32%, Medicine/Hematology, COM), and 3) Zhonjue Sun (10.84%, Physiology, COM). The other PMC users accounted for 24.02% of the Proteomics Unit invoices. The top three users of the MPMS Unit as a percentage of the total invoices issued for all completed services ($19,030) were: 1) Rhonda Kineman (external, UIC, 41.93%), 2) Modar Kassan (16.18%, Physiology, COM) and 3) Kirk Hevener (10.09%, Pharmaceutical Sciences, COP). The other users accounted for 31.8% of MPMS invoices. Of note, the PMC includes two units, and the budgets for each unit are independent, since the costs and revenues are shared with the Department of Pediatrics only for the MPMS Unit.

3. Is there sufficient intra- and inter-departmental use and if not, why?

Yes, use of the Proteomics Unit has increased over FY21 levels and there are recurring laboratory users across several departments and at least two colleges year over year. In contrast, historically, the MPMS Unit has been exclusively used by either COM investigators (FY20-FY22), or external users. One staff member responsible for sample preparation left the MPMS Unit in June of FY21 (Dr. Sethuraman). Therefore, in FY22, sample processing and analysis was performed by one senior staff scientist (Dr. Pralad Rao) with support from the director. Although the MPMS Unit was able to maintain daily functions during the first half of FY22, it was unable to take on new large-scale projects, including developing new or specialized assays for UTHSC users. Several grants were recently awarded requiring PMC services (predominantly the proteomics/untargeted metabolomics, with only one grant relying on MPMS).

4. Can the services for the core be outsourced more economically?

No. The core's prices for all services remain within the bottom half to third relative to our academic peer institutions. Commercial vendors that offer proteomics (Biognosys, MS

Bioworks, etc.) or metabolomics (like Metabolon) cannot compete with academic pricing. Although there are six NIH-funded regional comprehensive metabolomics cores in the country, these centers also recharge for services (for example, the Southeast Center for Integrated Metabolomics at the University of Florida, http://secim.ufl.edu/services/). In addition, for the MPMS Unit, Dr. Puchowicz has unique skill sets in the analysis of isotope-labeled specimens that most cores will not accept for analysis.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g., grants funded through investigator use, publications, etc.)?

Yes. Reviewers of federal grant applications expect that investigators have local access to proteomics and metabolomics technologies and local experts for project consultation and data analysis. Data generated in the PMC led to one grant awarded in FY22. In addition, in FY22, the PMC Unit provided 11 letters of support for new grant applications and the MPMS Unit provided 14 letters of support. These proposals either included core services deemed essential to complete the proposed scientific aims, or included preliminary data generated in the PMC to support the proposed hypotheses; grant submissions are detailed in the core activities report. In FY22, each unit supported 12 PubMed-indexed publications. The Proteomics Unit also supported four grant awards, and the MPMS Unit supported two internal grant awards and two external grant awards.

6. Is the core currently self-sufficient or is it subsidized by the institution?

Both units of the PMC are subsidized by the institution. In FY22, the PMC Proteomics Unit was subsidized by the state of Tennessee and the institution. The total net income of the PMC was $60,200 after subsidy. FY22 ended with a net deficit of $21,576 for the MPMS, after accounting for sharing of expenses and revenues sharing with the Department of Pediatrics, under the MOU, which created an equal partnership between the Department of Pediatrics and the Office of Research. The $21,576 deficit for the MPMS unit was entirely offset by the Office of Research.

7. Accomplishments, FY22

- The PMC supported 13 publications, with additional manuscripts either in review or in preparation for submission by internal investigators.
- The MPMS supported 10 publications, with additional manuscripts either in review or in preparation for submission by internal investigators.
- The MPMS Unit of the PMC began invoicing for a full line of targeted metabolic assay services FY21, and in FY22, further expanded service offerings to include specialized assays to meet the needs of local users across six departments (including: Physiology, Pharmaceutical Sciences, Pharmacology, Bioscience Research and Operative Dentistry, Pediatrics, Genetics, Genomics and Informatics).
- Both units participated in the Hot Topics in Research series to advertise core resources.

Financial Overview – FY22:

PMC, Proteomics and Untargeted Metabolomics Unit:

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues	37,827	40,930	26,237	15,326	40,136
Expenses	(163,712)	(139,814)	(163,774)	(110,341)	(130,261)
Income (Subsidy)	(125,885)	(98,884)	(137,537)	(95,015)	(90,125)
Other Costs	0	0	0	0	0
Income (Subsidy)	(125,885)	(98,884)	(137,537)	(95,015)	(90,125)
State Appropriation	93,360	95,694	97,608	138,942	150,325
Net Income (Subsidy)	(32,525)	(3,190)	(39,929)	43,927	60,200
Subsidy, % before State Appropriation	77%	71%	84%	86%	70%
Subsidy, % after State Appropriation	20%	2%	24%	0%	0%

MPMS Unit (Unit opened FY20)

TOTALS	FY20	FY21	FY22
Revenues	44,710	41,216	21,140
Expenses	(66,970)	(80,841)	(53,358)
Income (Subsidy)	(22,260)	(39,625)	(32,218)
Other Costs	0	0	0
Income (Subsidy)	(22,260)	(39,625)	(32,218)
State Appropriation	0	7,828	10,642
Net Income (Subsidy)	(22,260)	(31,797)	(21,576)
Subsidy, % before State Appropriation	33%	49%	60%
Subsidy, % after State Appropriation	33%	39%	40%

7. Suggested outcomes:

It is recommended that the Proteomics Unit of PMC continue as an institutional core. However, it is recommended that the MPMS Unit become a college- or departmental-aligned shared resource since the MPMS Unit has primarily served COM and external users since FY20.

Proteomics & Metabolomics Core (PMC)
Summary of Institutional Core Activities for FY22

Written by David Kakhniashvili, PhD; Michelle Puchowicz, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

I. PUBLICATIONS:

Full-length published articles (UTHSC investigator appears in bold and external users in italics; the core director is underlined)

Proteomics and Untargeted Metabolomics Unit:

Liao FF, Lin G, Chen X, Chen L, Zheng W, Raghow R, Zhou FM, Shih AY, Tan XL. Endothelial Nitric Oxide Synthase-Deficient Mice: A Model of Spontaneous Cerebral Small-Vessel Disease. Am J Pathol. 2021 Nov;191(11):1932-1945. doi:10.1016/j.ajpath.2021.02.022. Epub 2021 Mar 10. PMID: 33711310; PMCID:PMC8647425.

Chen K, **Sun Z**. Estrogen inhibits renal Na-Pi Co-transporters and improves klotho deficiency-induced acute heart failure. Redox Biol. 2021 Nov;47:102173.doi: 10.1016/j.redox.2021.102173. Epub 2021 Oct 18. PMID: 34678656; PMCID:PMC8577443.

Victor AK, Donaldson M, Johnson D, Miller W, **Reiter LT**. Molecular Changes in Prader-Willi Syndrome Neurons Reveals Clues About Increased Autism Susceptibility. Front Mol Neurosci. 2021 Oct 29;14:747855. doi:10.3389/fnmol.2021.747855. PMID: 34776864; PMCID: PMC8586424.

Mitachi K, Mingle D, Effah W, Sánchez-Ruiz A, **Hevener KE**, **Narayanan R**, Clemons WM Jr, Sarabia F, Kurosu M. Concise Synthesis of TunicamycinV and Discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID:35594368; PMCID: PMC9329268.

Lin Y, **Sun Z**. Klotho deficiency-induced arterial calcification involves osteoblastic transition of VSMCs and activation of BMP signaling. J Cell Physiol. 2022 Jan;237(1):720-729. doi: 10.1002/jcp.30541. Epub 2021 Aug 8. PMID:34368951; PMCID: PMC8810603.

Ahmed HA, Ismael S, Salman M, Devlin P, McDonald MP, **Liao FF**, Ishrat T. Direct AT2R Stimulation Slows Post-stroke Cognitive Decline in the 5XFADAlzheimer's Disease Mice. Mol Neurobiol. 2022 Jul;59(7):4124-4140. doi:10.1007/s12035-022-02839-x. Epub 2022 Apr 29. PMID: 35486224.

Meena AS, Shukla PK, Bell B, **Giorgianni F**, Caires R, Fernández-Peña C, Beranova S, Aihara E, Montrose MH, Chaib M, Makowski L, Neeli I, Radic MZ, Vásquez V, Jaggar JH, Cordero-Morales JF, Rao R. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID:PMC9250449.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, Yue J, Benyó Z, **Tigyi GJ**. Prometastatic Effect of ATX Derived from Alveolar Type II Pneumocytes andB16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi:10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.
Guo H, Zhang W, Wang J, Zhao G, Wang Y, Zhu BM, Dong P, Watari H, Wang B, LiW, **Tigyi G**,

Yue J. Cryptotanshinone inhibits ovarian tumor growth and metastasis by degrading c-Myc and attenuating the FAK signaling pathway. Front Cell Dev Biol. 2022 Sep 28;10:959518. doi: 10.3389/fcell.2022.959518. PMID: 36247016;PMCID: PMC9554091.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, Yue J, Zhang W. Adipose-Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal Transition Through Activating the TGF-β Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276;PMCID: PMC8727693.

Chen K, Wang S, **Sun Z**. In Vivo Cardiac-specific Expression of Adenylyl Cyclase 4 Gene Protects against Klotho Deficiency-induced Heart Failure. Transl Res. 2022 Jun;244:101-113. doi: 10.1016/j.trsl.2022.01.006. Epub 2022 Jan 31.PMID: 35114419; PMCID: PMC9119924.

Huo X, Zhang W, Zhao G, Chen Z, Dong P, Watari H, **Narayanan R**, Tillmanns TD, Pfeffer LM, Yue J. FAK PROTAC Inhibits Ovarian Tumor Growth and Metastasis by Disrupting Kinase Dependent and Independent Pathways. Front Oncol. 2022 Apr28;12:851065. doi: 10.3389/fonc.2022.851065. PMID: 35574330; PMCID: PMC9095959.

Han X, **Sun Z**. Adult Mouse Kidney Stem Cells Orchestrate the De Novo Assembly of a Nephron via Sirt2-Modulated Canonical Wnt/β-Catenin Signaling. Adv Sci (Weinh). 2022 May;9(15):e2104034. doi: 10.1002/advs.202104034. Epub 2022 Mar 22.PMID: 35315252; PMCID: PMC9130916.

MPMS Unit:

Mitachi K, Mingle D, Effah W, Sánchez-Ruiz A, **Hevener KE**, **Narayanan R**, Clemons WM Jr, Sarabia F, Kurosu M. Concise Synthesis of TunicamycinV and Discovery of a Cytostatic DPAGT1 Inhibitor. Angew Chem Int Ed Engl. 2022 Aug 1;61(31):e202203225. doi: 10.1002/anie.202203225. Epub 2022 Jun 10. PMID: 35594368; PMCID: PMC9329268.

Munkhsaikhan U, Kwon Y, Sahyoun AM, Ait-Aissa K, Kassan A, **Kassan M**. The microsomal triglyceride transfer protein inhibitor lomitapide improves vascular function in mice with obesity. Obesity (Silver Spring). 2022 Apr;30(4):893-901. doi: 10.1002/oby.23389. Epub 2022 Mar 6. PMID: 35253407; PMCID: PMC8957593.

Kassan A, Ait-Aissa K, **Kassan M**. Gut Microbiota Regulates the Sympathetic Nerve Activity and Peripheral Serotonin Through Hypothalamic MicroRNA-204 in Order to Increase the Browning of White Adipose Tissue in Obesity. Cureus. 2022 Feb 4;14(2):e21913. doi: 10.7759/cureus.21913. PMID: 35155042; PMCID: PMC8820388.

Sethuraman A, Rao P, Pranay A, Xu K, LaManna JC, **Puchowicz MA**. Chronic Ketosis Modulates HIF1α-Mediated Inflammatory Response in Rat Brain. Adv Exp Med Biol. (2021). 1269:3-7.

Ranea-Robles P, Chen H, Stauffer B, Yu C, Bhattacharya D, Friedman SL, **Puchowicz M**, Houten SM. The peroxisomal transporter ABCD3 plays a major role in hepatic dicarboxylic fatty acid metabolism and lipid homeostasis*. J Inherit Metab Dis*. (2021) Sep 26. Online ahead of print. PMID: 34564857

Ranea-Robles P, Violante S, Argmann C, Dodatko T, Bhattacharya D, Chen H, Yu C, Friedman SL, **Puchowicz M**, Houten SM. Murine deficiency of peroxisomal L-bifunctional protein (EHHADH) causes medium-chain 3-hydroxydicarboxylic aciduria and perturbs hepatic cholesterol homeostasis*. Cell Mol Life Sci.* (2021) Jul;78(14):5631-5646. PMCID: PMC8263512

Govatati S, Pichavaram P, Mani AM, Kumar R, Sharma D, Dienel A, Meena S, **Puchowicz MA**, Park EA, Rao GN. Novel role of xanthine oxidase-dependent H2O2 production in 12/15-lipoxygenase-mediated de novo lipogenesis, triglyceride biosynthesis and weight gain*. Redox Biol.* (2021) Nov. PMCID: PMC8577505

Salman M, Ismael S, Li L, Ahmed HA, **Puchowicz MA**, Ishrat T. Endothelial Thioredoxin-Interacting Protein Depletion Reduces Hemorrhagic Transformation in Hyperglycemic Mice after Embolic Stroke and Thrombolytic Therapy. *Pharmaceuticals (Basel)*. 2021 Sep 27;14(10):983. PMCID: PMC8537904

Kumari R, Irudayam MJ, Al Abdallah Q, Jones TL, Mims TS, **Puchowicz MA**, Pierre JF, Brown CW. SMAD2 and SMAD3 differentially regulate adiposity and the growth of subcutaneous white adipose tissue. *FASEB J.* (2021) Dec;35(12):e22018. PMID: 34681207

Salman M, Ismael S, Lexiao L, Ahmed HA, **Puchowicz MA**, Ishrat T. Acute Hyperglycemia Exacerbates Hemorrhagic Transformation after Embolic Stroke and Reperfusion with tPA: A Possible Role of TXNIP-NLRP3 Inflammasome. *J Stroke Cerebrovasc Dis*. (2022) Feb;31(2):106226. Epub 2021 Nov 27. PMCID: PMC8792268

Ranea-Robles P, Pavlova NN, Bender A, Pereyra AS, Ellis JM, Stauffer B, Yu C, Thompson CB, Argmann C, **Puchowicz M**, Houten SM. A mitochondrial long-chain fatty acid oxidation defect leads to tRNA uncharging and activation of the integrated stress response in the mouse heart. *Cardiovasc Res*. (2022) Apr 7: PMID: 35388887 DOI: 10.1093/cvr/cvac050.

Response to immune checkpoint blockade improved in pre-clinical model of breast cancer after bariatric surgery. Sipe LM, Chaib M, Korba EB, Jo H, Lovely MC, Counts BR, Tanveer U, Holt JR, Clements JC, John NA, Daria D, Marion TN, Bohm MS, Sekhri R, Pingili AK, Teng B, Carson JA, Hayes DN, Davis MJ, Cook KL, **Pierre JF, Makowski L**. *Elife*. 2022 Jul 1;11:e79143. PMCID: PMC9342954.

II. PRESENTATIONS GIVEN TO PROMOTE CORE USAGE

Three PMC tours for investigators by Dr. Kakhniashvili

10-12-2021 Fall 2021: mBIO Core Bioinformatics Workshop Series:
"Common Molecular Tools and Data Analysis Workflow to Accelerate Your Research"

1. "Proteomics and Pathway Analysis"
   Presented by Dr. Johnson, Molecular Bioinformatics Core
2. "PMC: Instrumentation, Applications, and Services"
   Presented by Dr. Kakhniashvili

05-03-2022 Hot Topics

1. "Mapping the Proximity Interaction Network of STIM1 Reveals New Mechanisms of Cytoskeletal Regulation"
   Presented by Dr. Mancarella
2. "PMC: Instrumentation, Applications, and Services"
   Presented by Dr. Kakhniashvili

III. SUMMARY OF ACTIVITIES

A. Personnel

PMC Core Director: David Kakhniashvili, PhD (100% effort)
MPMS Unit Director: Michelle Puchowicz (50% effort)
MPMS Unit Staff: Prahlad Rao, PhD, mass spectrometry applications specialist (80% effort)

Oversight Committee (Internal Advisory Board)
Sarka Beranova, PhD (Pharmaceutical Sciences)
Ivan Gerling, PhD (Medicine-Endocrinology)
Lawrence Reiter, PhD (Neurology)
Heather Smallwood, PhD (Pediatrics); *CHAIR*
Salvatore Mancarella, PhD (Physiology)

B. Equipment Used

Equipment	Cost	Funding Source; Fiscal Year Purchased
Mass Spectrometer – Thermo Fisher Orbitrap Fusion Lumos* + UHPLC units*	$1,027150	Office of Research 2016
UHPLC – Thermo Fisher UltiMate 3000 RSLC Nano*		Office of Research 2016
UHPLC – Thermo Fisher Vanquish*		Office of Research 2016
SpeedVac – Thermo Fisher SPD1010-115	$10,629	Office of Research 2016
NanoDrop One – Thermo Fisher	$8,984	Office of Research 2016
Server Computer	$6,272	Office of Research 2016
SW – Protein Metrics Bionic	$7,700	Office of Research 2016
Micro-centrifuge Legend Micro 21R Sorvall w/RTR	$5,356	Office of Research 2017
Agilent Mass Spectrometer* 7000 QQQ MS/MS EI/CI	$92,726	Pediatrics 2017
Agilent GC custom series*	$19,320	Pediatrics

7890B		2017
Agilent Auto Injector 7693A w/ tray*	$12,266	Pediatrics 2017
NIST MS Library Bundle / Mass Profiler Professional*	$4,339	Pediatrics 2017
Total cost of equipment (>$5,000)	**$1,194,742**	

*Equipment necessary to launch the core

C. Service Contracts

Proteomics and Untargeted Metabolomics Unit:

Service Contract #	**Equipment Covered**	**Vendor**	**Cost, $**
40374276	Mass spectrometer Orbitrap Fusion Lumos	Thermo Electron North America	57,218
	UHPLC Ultimate 3000RSLCnano Pump		6,013
	UHPLC Ultimate 3000RSLCnano Auto-sampler WPS-3000TPL RS		2,733
Sub-Total			65,964
Discount, 10%			-6,596.40
Total			**$59,367.60**

MPMS Unit:

Service Contract #	**Equipment Covered**	**Vendor**	**Cost, $**
9500084997	GC7000 QQQ MS/MS system	Ion Technology Support, Inc. – Morrisville, NC	
	7890B GC system		
	UHPLC Ultimate 3000RSLCnano Auto-sampler WPS-3000TPL RS		
	7693 Auto injector & Tray		
Total			**$10,500**

D. Usage Volumes (Invoices by Service Type, PI and Department), FY22

Proteomics and Untargeted Metabolomics Services:

Internal (UTHSC) Users		**Usage Volume, $**	
College, Department	**PI**	**PI, Total**	**UTHSC only Departments Total**
COM, Medicine	Narayanan, R.	12,195.45	12,195.45
COM, Physiology	Sun, Z.	4,220.63	4,985.99
	Tigyi, G.	765.36	
COM, Diagnostic and Health Sci.	Mohamed, J.	2,566.08	2,566.08
COM, Neurology	Reiter, L.	1,654.53	1,654.53

COP, Pharmaceutical Sci.	Giorgianni, F.	1,519.48	1,519.48
COM, Pharmacology	Liao, F-F.	1,024.22	1,024.22
UTK (Matthew, D. and McCord, R.)		13,924.14	
Internal Users, Total		**37,869.87**	**23,945.73**
External Users		**Usage Volume, $**	
Institution	**PI**	**PI, Total**	**Institution**
Michigan State University	Ashkarran, A.	1,063.57	
External Users, Total		**1,063.57**	
Total Invoiced (Internal and External Users)		**38,933.46**	

MPMS Unit:

Internal (UTHSC) Users		**Usage Volume, $**	
College, Department	**PI**	**PI, Total**	**Department, Total**
COM, Physiology	Kassan, Modar	3,080	3,080
COP, Pharmaceutical Sciences	Hevener, Kirk	1,920	1,920
Internal Users, Total		**5,000**	**5,000**
External Users		**Usage Volume, $**	
Institution	**PI**	**PI**	**Institution**
University of Illinois, Chicago	Kineman, Rhonda	7,980	7,980
University of Pittsburgh	Dutta, Partha	1,870	1,870
External Users, Total		**9,850**	**9,850**
Grand Total Invoiced (Internal and External Users)		**14,850**	**14,850**

PMC: PROTEOMICS AND UNTARGETED METABOLOMICS UNIT:

Protein iTRAQ (isobaric tags for relative and absolute quantification)/TMT (tandem mass tags) labeling:

4-plex:	$787.86
6-plex:	$1,125.51
8-plex:	$1,406.89
10-plex	$1,519.44
11-plex	$1,596.50
16-plex	$1,850.00

Protein identification:
LC/MS/MS, DB search, note: does not include sample digestion/preparation)

RP LC/MS/MS (30 min):	$78.78/run
RP LC/MS/MS (60 min):	$123.81/run
RP LC/MS/MS (120 min):	$202.59/run
RP LC/MS/MS (240 min):	$337.65/run

Protein identification and mapping of specified post-translational modifications (PTM):
LC/MS/MS, DB/PTM search, note: does not include sample digestion/preparation

RP LC/MS/MS (60 min):	$123.81/sample
RP LC/MS/MS (120 min):	$202.59/sample
RP LC/MS/MS (240 min):	$337.65/sample
Search for specified PTMs:	$33.76/PTM

Differential protein expression analysis by iTRAQ/PMT (reporter ion quantification):
LC/MS/MS, DB search/quantification, note: does not include sample labeling/preparation

Unfractionated mixture of labeled peptides, 2hr RP-LC/MS/MS:	$225.11/run
Unfractionated mixture of labeled Peptides, 4hr RP-LC/MS/MS:	$371.42/run

Differential protein expression analysis by SILAC analysis (precursor ion quantification):
LC/MS/MS, DB search/quantification, note: does not include sample labeling/preparation

Unfractionated mixture of labeled peptides, 2hr RP-LC/MS/MS:	$225.11/run
Unfractionated mixture of labeled Peptides, 4hr RP-LC/MS/MS:	$371.42/run

Protein differential expression analysis, MudPIT:
MudPit, DB search, note: does not include sample digestion/preparation;
2hr RP-LC/MS/MS/fraction:

6 (SCX or HpHRP) step fractions	$168.83
7-12 (SCX or HpHRP) step fractions:	$163.19
>12 (SCX or HpHRP) step fractions:	$157.58

Absolute quantification of specified (targeted) proteins (parallel reaction monitoring):
PRM analysis for peptide quantification, note: does not include sample digestion/preparation

LC/MC/MS (30 min)	$90.04/run
LC/MS/MS (60 min)	$140.69/run
LC/MS/MS (120 min)	$225.11/run

Absolute quantification of specified metabolites/small molecules:
LC/MS/MS, post-acquisition analysis, calibration Curve, internal standard, AUC quantification

LC/MS/MS (15 min):	$19.14/run
LC/MS/MS (30 min):	$33.76/run

Differential quantification of metabolites – untargeted analysis
LC/HRAM-MS/MS, post-acquisition analysis, HRAM AUC Quantification, MS/MS identification

LC/MS/MS (15 min):	$33.76/run
LC/MS/MS (30 min):	$56.28/run

Consultation (initial consult-no cost): $103/consult

Volume Discount for PMC Bulk MS runs:

The volume MS "run" discount rate does not include reagents or kits, such as the TMT kit for isobaric labeling, or labor-intensive steps, such as sample processing, but will be applied to MS "runs". The below volume discount rate will be applied if samples are submitted simultaneously for processing in bulk*, or after the volume threshold has been met for the current FY.

30-49 MS runs, for a single project:	10% discount, all MS runs
50-99 MS runs, for a single project:	15% discount, all MS runs
100+ MS runs, for a single project:	20% discount, all MS runs

*If samples are submitted piecemeal, then the volume discount will be applied only for those MS runs that exceed the discount threshold. For example, if a PI submits three sets of samples requiring 15, then 10, then 20 MS runs, for a total of 45 MS runs that are completed at different times on separate iLab service requests, then the discount would be applied at MS run #31 onwards.

METABOLIC PHENOTYPING MASS SPECTROMETRY (MPMS) UNIT:

Citric Acid Cycle- related intermediates

Metabolite concentrations:	$100/run
Metabolite enrichments -MPE (2H, 13C):	$75/run
Both concentration/MPE:	$150/run
Search for specified PTMs:	Please inquire

Total Protein / Protein Turnover

Via D20 water method:	$50/run
Tracer infusion method:	$150/run

Glucose or Glycerol:

Concentrations:	$50/run
Enrichments -MPE (2H, 13C):	$35/run
Glucose and Glycerol:	$100/run

Lipids:

Total fatty acid profile (C10-C18/sat./unsat.:	$125/run
Fatty acid /Cholesterol:	$125/run
Isotopomer analysis (MPE):	$100/run
Sterols special-select	$80/run
Synthesis- fractional rates (D20 method):	$150/run

Use of GC-MS/MS by Trained Users (at discretion of the MPMS Director):

Standard-EI mode (60 min):	$110/run
Extended-CI mode (60 min):	$150/run
Duplicate runs:	$50/run

Consultation: **$100/consult**

High volume discounts, MPMS:

High-volume discounts will be provided to core users as negotiated with the MPMS core director and as approved by the associate vice chancellor for Research-Cores (typically >100 samples).

IV. GRANTS AND CONTRACTS SUPPORTED BY THE CORE

Proteomics and Untargeted Metabolomics Unit, FY22 users:

Giorgianni, Francesco
Retina Research Foundation, CD5L-mediated autophagocytosis in RPE cells

Liao, Francesca-Fang
USPHS NIH Grant AG-058467, Novel mechanistic link between metabolic changes and dementia potential role of miRNA21

Narayanan, Ramesh
USPHS NIH Grant CA-229164, Novel Degraders of the Androgen Receptor (AR) and AR Splice Variants (AR-SVs)

Reiter, Lawrence
USPHS NIH Grant NS-115776, The role of UBE3A in gliopathic seizures.

Proteomics and Untargeted Metabolomics Unit, recently awarded, services listed as essential to proposal:

Zhao, Q.*
NIH R01 started January 28, 2021
Intensive Lifestyle Intervention, Metabolomics, and Risk of Frailty Fracture in Overweight or Obese Patients with Type 2 Diabetes

**Includes salary coverage for the PMC Director*

Reiter, Lawrence T.
ROHHAD Association 11/02/2019-10/31/2021
"Rapid-onset Obesity with Hypothalamic Dysfunction, Hypoventilation, and autonomic Dysregulation (ROHHAD): Stem Cell Models to Investigate Cause and Consequences."

MPMS Unit, recently awarded, services listed as essential to proposal:

Makowski, Liza; Pierre, JF
NCI R01 CA253329 08/01/2020 – 04/30/2025
Role of microbial-modulated bile acid receptor signaling in breast cancer.

MPMS Unit, FY22 Users:

Internal users, FY22:
Kassan, Modar
USPHS NIH Grant HI-150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Makowski, Liza; Pierre, Joseph
USPHS NIH Grant CA-253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

External MPMS users, FY22:
Kineman, Rhonda (University of Illinois, Chicago)
USPHS NIH Grant DK-116878, Hormonal Regulation of Liver Metabolism

Dutta, Partha (Pitt)
USPHS NIH Grant HL0142629, Mechanisms of myelopoiesis after myocardial infarction

B. LETTERS OF SUPPORT

Letters of support were provided for 11 grant applications by the Proteomics and Untargeted Metabolomics Unit:

PI	Institution, College, Department	Date
Internal Users	UTHSC, COM, 4 Departments	
Liao, F	UTHSC, COM, Pharmacology	07-08-2021
Freeman, K.	UTHSC, COM, Genetics Genomics and Informatics	09-27-2021
Laribee, R.	UTHSC, COM, Pathology	10-21-2021
Laribee, R.	UTHSC, COM, Pathology	10-22-2021
Laribee, R.	UTHSC, COM, Pathology	01-18-2022
Bukiya, A.	UTHSC, COM, Pharmacology	01-22-2022
Zhao, Q*	UTHSC, COM, Preventive Medicine	02-23-2022
Chen, H.	UTHSC, COM, Pharmacology	02-23-2022
External Users		
Cordero-Morales, J. and Vasquez, V.	UT Knoxville	09-07-2021
White, Jennell	Wayne State University, Detroit, MI	10-05-2021
San Martin, R.	UT Knoxville	01-31-2022

**Starred applications included dedicated support for Dr. Kakhniashvili as a co-investigator.*

Letters of support were provided for 14 grant applications by the MPMS Unit:

PI	Institution, College, Department	Date
Internal Users		
Kassen, Modar	UTHSC, COM, Physiology	05-06-2021
Feng Liu-Smith	UTHSC, COM, Preventative Medicine	07-02-2021
Abidi, Ammaar	UTHSC, COD, Bioscience Research and Operative Dentistry	10-22-2021
Johnson, Jeremiah G.	UT Knoxville, Microbiology	10-22-2021
Smallwood, Heather	UTHSC, COM, Pediatrics	01-15-2022
Bukiya, Anna	UTHSC, COM, Pharmacology	01-19-2022
Malik, Kafait U.*	UTHSC, COM, Pharmacology	06-20-2022
External Users		
Kineman, Rhonda*	UIC, Chicago, Medicine	07-10-2021
Houten, Sander*	Mount Sinai-NY, Icahn SOM, Genetics	08-26-2021
Maharjan, Pramir	Tennessee State, COA, Agriculture-Envr.	01-14-2022
Cordoba-Chacon, Jose*	UIC, Chicago, Medicine	01-18-2022
Dutta, Partha	U.Pittsburgh, SOM, Medicine	01-25-2022
Stephenson, Erin	Midwestern University, Chicago	02-15-2022
Sandlers, Yana	Cleveland State, Chemistry	06-22-2022

**Starred items included dedicated support for Dr. Puchowicz as a co-investigator.*

V. BUSINESS DEVELOPMENT PLAN

A. Market Assessment

The primary mission of the Proteomics and Metabolomics Core (PMC) is to provide investigators at UTHSC, in the Memphis area and regionally/nationally with access to state-of-the-art proteomics, metabolomics, lipidomics and glycomics technologies and services. Dr. Steven Goodman created the new PMC in FY16 to meet the needs of the basic and clinical researchers at UTHSC and to help develop the precision medicine initiative on campus. In Q1 of FY20, the Metabolic Phenotyping Mass Spectrometry (MPMS) Unit was added in partnership with the Department of Pediatrics. This unit offers analysis of targeted metabolites focused on cellular metabolism and isotype-labeled sample analysis.

The PMC is defined as an institutional core based on its service to multiple colleges and departments within UTHSC. The potential additional customers for our user base include UTHSC, University of Memphis, the VA, Le Bonheur Hospital and other commercial and academic partners in the Memphis metropolitan area. Investigators from St. Jude are also potential customers since the queue for their internal proteomics core is currently several weeks long. Our core also has capacity to analyze samples for regional/national academic or commercial customers.

Currently, there is not a dedicated MS instrument in the PMC for untargeted metabolomics; these projects are referred to UT-Knoxville, or to other academic cores. Our Lumos Orbitrap MS is left in a proteomics profiling mode, without “flipping” the instrument to a metabolomics mode, as per the recommendation of the PMC Internal Advisory Board. This recommendation was made after discovering that the Orbitrap instrument/HPLC required substantial downtime for cleaning every time a “flip” was executed. To address unmet untargeted metabolomics needs, Drs. Kakhniashvili, Puchowicz, Smallwood, and Seagroves actively served as consultants to the lead PI (Dr. Robert Williams, Genetics) on a S10 instrumentation grant proposal to acquire a second MS instrument for the PMC for dedicated untargeted metabolomics and lipidomics profiling to support discovery-based research projects. Though scored and discussed, the proposal was not funded. Revision of this proposal is currently on hold while investigators generate additional preliminary data as recommended by the S10 review panel.

B. Competitive Analysis

Typically, the biggest threats to proteomics and metabolomics cores are other academic core facilities that accept external samples, NIH-funded Regional Comprehensive Metabolomics Resource Cores, and, particularly for metabolomics, commercial vendors like Metabolon. The PMC, including the MPMS Unit, offers value-added services that include the scientific expertise and breadth of training of the directors, analysis of isotype-labeled samples, quick turnaround time and state of the art instrumentation that most core facilities in the United States have not yet adopted. The Proteomics and MPMS units are also highly desired campus resources of several newly recruited faculty, or candidates who have recently interviewed for key positions on campus. The closest proteomics/metabolomics core facilities are located at St. Jude Children’s Hospital, which is available for use only by those UTHSC faculty who directly collaborate with St. Jude investigators.

C. Marketing Plans to Obtain New Business

A primary focus of the PMC, including the MPMS Unit, will be to continue advertisement of services to the UTHSC campus, throughout the Memphis medical center and throughout the University of Tennessee system. The branding strategy will involve local advertisement on the campus. The core will continue participation in the Hot Topics in Research seminar series, and the Office of Research-sponsored events to faculty (technology fairs, etc.). The PMC will also continue to host seminars by commercial vendors to advertise onboarding of new equipment or to educate users about proteomics and metabolic/metabolomic approaches and technologies.

D. Forecasted Volumes for New Business

In FY23, we project, that internal recoveries from PMC proteomics-based services will increase 50% over FY22 levels, based on estimated demand and knowledge of upcoming projects by the director. Since the MPMS Unit is no longer accepting samples, it is projected there will be no additional revenues from this unit in FY23.

E. Budgets

PMC: Proteomics and Untargeted Metabolomics Services

PMC –Proteomics Unit, FY2022 Budget

FY2022	DEBITS	CREDITS
Salaries	92,577	
Supplies	14,231	
Service Contracts	23,453*	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***130,261***	
FY22 Internal Recoveries		37,870
FY22 External Recoveries		2,266
TOTAL CREDITS		***40,136***
Income / (Subsidy)	(90,125)	
State Appropriation	150,325	
Net Income / (Subsidy)	**60,200**	

*Service Contracts/Maintenance expenditures included a Thermo Electron invoice, which totaled $59,367 for FY22. However, $35,914 of this expense was paid from the Molecular Bioinformatics account.

Subsidy, % before State Appropriation	70%
Subsidy, % after State Appropriation	0%

MPMS Unit– FY2022 Core Activities, Budget, After Revenue and Expenses Share with Dept. of Pediatrics

FY2022	DEBITS	CREDITS
SALARIES (Dr. Pralad Rao)*	22,139	
SUPPLIES (Includes Payments To Pediatrics For Shared Revenues)	20,719	
SERVICE CONTRACTS**	10,500	
EQUIPMENT (> $5,000)	0	
OTHER EXPENSES	0	
TOTAL EXPENSES	***53,358***	
FY22 INTERNAL RECOVERIES		5,000
FY22 EXTERNAL RECOVERIES		16,140
TOTAL CREDITS (BEFORE COST SHARE)		***21,140***
INCOME / (SUBSIDY)	(32,218)	
STATE APPROPRIATION	10,642	
NET INCOME / (SUBSIDY)* **	**(21,576)**	

*In FY22, 25% of Prahlad K. Rao's salary was directly paid from this account.
**Service contracts/maintenance expenditures included an Ion Technology Support, Inc. invoice, which totaled $10,500 for FY22.
***100% of the deficit of $21,576 was subsidized by the Office of Research/institution.

Subsidy, % before state appropriation 60%
Subsidy, % after state appropriation 40%

Flow Cytometry and Cell Sorting (FCCS) Institutional Research Core Facility Analysis Report- FY22

Written by Deidre Daria, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?
The FCCS Core's designation as an institutional core is appropriate since it has served 63 total users across 40 internal laboratories representing 18 departments and four colleges (COM, COP, COD, COHP) in FY22. The core also served one laboratory at the University of Memphis.

2. Does the core pass the multi-departmental, multi-investigator litmus test?
Yes. In FY22, this core processed 208 cytometry projects on the ZE5, 30 flow sorting projects, and 29 data analysis requests from 41 individual users corresponding to 29 labs across 18 departments and four colleges (COM, COP, COD, and COHP). The college with the largest number of individual users was the College of Medicine with 21 laboratories from 8 departments. The top five laboratories, based on the percentage of invoices for completed services in FY22, accounted for 55.7% of total revenues. These investigators were: 1) Cem Kuscu (Pediatrics, COM, 22.1%), 2) Amber Smith (Surgery, COM, 13.1%), 3) Elizabeth Fitzpatrick (MIB, COM, 7.5%), 4) Kevin Freeman (Clinical Pharmacy and Translational Science, COP, 6.7%), and 5) Marko Radic (MIB, COM 6.3%). The other 24 laboratories accounted for 44.3% of invoices. Thirty-two individuals from 22 UTHSC laboratories and one individual from the University of Memphis took advantage of the flow cytometry courses offered at no charge through the core.

3. Is there sufficient intra- and inter-departmental use and if not, why?
Yes. Sixty-three individual users from 18 departments and four colleges were served.

4. Can the services for the core be outsourced more economically?
No. It should be noted that live, stained cells cannot be shipped to other cores or commercial entities for flow cytometry analysis or cell sorting without compromising data integrity or cell viability, respectively, and samples must be processed locally. St. Jude's core facility is only available on a select basis to the outside community and the University of Memphis does not have cell sorting capabilities. Samples may be run at the VA on the new analyzer, but users are expected to run and analyze their own samples unassisted. None of these outside sources provide data analysis support.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting (e.g., grants funded through investigator use, publications, etc.)?
Yes. In FY22, core activities led to 82 unique PubMed-indexed publications and supported 13 awarded extramural grant and contracts and multiple intramural grants and startup funding packages. Reviewers of federal grant applications (NIH) expect that the investigators will have local access to flow cytometry facilities as verified in support letters provided by the FCCS Core. In addition, 32 individuals participated in the flow cytometry classes and hands-on cytometry training was provided to six new core users.

6. Is the core currently self-sufficient, or is it subsidized by the institution?
In FY22, the core was subsidized by the institution, not including salary of the former director (Dr. Tony Marion), which was entirely provided by the Department of Microbiology, Immunology and Biochemistry (MIB). Dr. Daria also provided assistance to the RBL upon request and ~3% of her salary was subsidized by the RBL core budget. Overall, FY22 ended with a net required subsidy of $151,075 (79%) after state appropriation of $9,598.

Accomplishments this past year:

- 12 new or lost labs (>3yrs) utilized the core educational or charged services in FY22.
- A four-part flow cytometry lecture series was offered in-person every other month for five months in FY22. Class sizes were at maximum capacity four out of the five months. Thirty course reviews were received rating either the individual class or the series in its entirety; of these, 29 surveys indicated overall ratings of excellent, with only one negative review received.
- An analysis computer and refrigerator/freezer were replaced with new equipment.
- Dr. Tony Marion continued to serve as president and member of the executive council for SEFCIG (Southeast Flow Cytometry Interest Group), a regional chapter of ISAC.
- Dr. Deidre Daria served as secretary for SEASR (Southeastern Association of Shared Resources), a regional chapter of ABRF. In 2022-2023, she will serve as chapter treasurer-elect.
- Dr. Deidre Daria attended the high-dimensional data analysis workshops, “Getting started with Flow Cytometry Data Science” and “Tailoring Cytometry Data Science Workflows” offered through ISAC (International Society for Advancement of Cytometry), which is accredited by the American Society for Clinical Pathology.
- Both Drs. Marion and Daria participated in SEFCIG2022, which focused on high-dimensional data and new technologies.
- Dr. Daria participated in Cyto2022, which focused on recent developments in flow, mass, and image cytometry.

Financial Overview – FY22:

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues	28,892	25,745	30,499	32,824	31,533
Expenses	(166,094)	(126,532)	(199,646)	(217,136)	(192,206)
Income (Subsidy)	(137,202)	(100,787)	(169,147)	(184,312)	(160,673)
Other Costs	0	0	0	0	0
Income (Subsidy)	(137,202)	(100,787)	(169,147)	(184,312)	(160,673)
State Appropriation	0	0	0	64,760	9,598
Net Income (Subsidy)	(137,202)	(100,787)	(169,147)	(119,552)	(151,075)
Subsidy, % before State Appropriation	82.6%	80%	85%	85%	84%
Subsidy, % after State Appropriation	82.6%	80%	85%	55%	79%

7. Suggested outcomes:

The FCCS Core should continue to be operated as an institutional core. The institutional funding allocated to the FCCS core should be increased in FY23 back to FY21 levels (~$65,760).

Flow Cytometry and Cell Sorting (FCCS) Institutional Core Facility Summary of Institutional Core Activities for FY22

Written by Deidre Daria, PhD; Natalie Smith, MS; and Tiffany Seagroves, PhD

PUBLICATIONS (Full-length published articles; Journal publication dates: July 1, 2021 to June 30, 2022; UTHSC investigators are bolded; core director is underlined)

Ackermann M, Anders HJ, Bilyy R, Bowlin GL, Daniel C, De Lorenzo R, EgebladM, Henneck T, Hidalgo A, Hoffmann M, Hohberger B, Kanthi Y, Kaplan MJ, KnightJS, Knopf J, Kolaczkowska E, Kubes P, Leppkes M, Mahajan A, Manfredi AA,Maueröder C, Maugeri N, Mitroulis I, Muñoz LE, Narasaraju T, Naschberger E,Neeli I, Ng LG, **Radic MZ**, Ritis K, Rovere-Querini P, Schapher M, Schauer C,Simon HU, Singh J, Skendros P, Stark K, Stürzl M, van der Vlag J, Vandenabeele P, Vitkov L, von Köckritz-Blickwede M, Yanginlar C, Yousefi S, Zarbock A, SchettG, Herrmann M. Patients with COVID-19: in the dark-NETs of neutrophils. CellDeath Differ. 2021 Nov;28(11):3125-3139. doi: 10.1038/s41418-021-00805-z. Epub2021 May 24. PMID: 34031543; PMCID: PMC8142290.

Liao FF, Lin G, Chen X, Chen L, Zheng W, Raghow R, Zhou FM, Shih AY, Tan XL. Endothelial Nitric Oxide Synthase-Deficient Mice: A Model of Spontaneous Cerebral Small-Vessel Disease. Am J Pathol. 2021 Nov;191(11):1932-1945. doi:10.1016/j.ajpath.2021.02.022. Epub 2021 Mar 10. PMID: 33711310; PMCID:PMC8647425.

Zhang L, Hu J, Meshkat BI, Liechty KW, **Xu J**. LncRNA MALAT1 Modulates TGF-β1-Induced EMT in Keratinocyte. Int J Mol Sci. 2021 Oct 30;22(21):11816.doi: 10.3390/ijms222111816. PMID: 34769245; PMCID: PMC8584148.

Pabla N, **Bajwa A**. Role of Mitochondrial Therapy for Ischemic-Reperfusion Injury and Acute Kidney Injury. Nephron. 2022;146(3):253-258. doi:10.1159/000520698. Epub 2021 Dec 9. PMID: 34883481; PMCID: PMC9090938.

Starlard-Davenport A, Fitzgerald A, Pace BS. Exploring epigenetic and microRNA approaches for γ-globin gene regulation. Exp Biol Med (Maywood). 2021Nov;246(22):2347-2357. doi: 10.1177/15353702211028195. Epub 2021 Jul 22. PMID:34292080; PMCID: PMC8606961.

Bai Y, Kim JY, Bisunke B, Jayne LA, Silvaroli JA, Balzer MS, Gandhi M, Huang KM, Sander V, Prosek J, Cianciolo RE, Baker SD, Sparreboom A, Jhaveri KD,Susztak K, **Bajwa A**, Pabla NS. Kidney toxicity of the BRAF-kinase inhibitor vemurafenib is driven by off-target ferrochelatase inhibition. Kidney Int. 2021Dec;100(6):1214-1226. doi: 10.1016/j.kint.2021.08.022. Epub 2021 Sep 15. PMID:34534550; PMCID: PMC8608726.

Hama T, Nagesh PK, Chowdhury P, Moore BM 2nd, Yallapu MM, Regner KR, Park F.DNA damage is overcome by TRIP13 overexpression during cisplatin nephrotoxicity. JCI Insight. 2021 Nov 22;6(22):e139092. doi: 10.1172/jci.insight.139092. PMID:34806647; PMCID: PMC8663775.

Sumida K, Han Z, Chiu CY, Mims TS, **Bajwa A**, Demmer RT, Datta S, Kovesdy CP, Pierre JF. Circulating Microbiota in Cardiometabolic Disease. Front Cell Infect Microbiol. 2022 May 3;12:892232. doi: 10.3389/fcimb.2022.892232. PMID: 35592652;PMCID: PMC9110890.

Pagliuca S, Gurnari C, Awada H, Kishtagari A, Kongkiatkamon S, Terkawi L, Zawit M, Guan Y, LaFramboise T, Jha BK, Patel BJ, Hamilton BK, Majhail NS, Lundgren S, Mustjoki S, Sauntharajah Y, Visconte V, Chan TA, **Yang CY**, Lenz TL, Maciejewski JP. The similarity of class II HLA genotypes defines patterns of autoreactivity in idiopathic bone marrow failure disorders. Blood. 2021 Dec30;138(26):2781-2798. doi: 10.1182/blood.2021012900. PMID: 34748628; PMCID:PMC8718627.

Siegel EM, Ajidahun A, Berglund A, Guerrero W, Eschrich S, Putney RM, Magliocco A, Riggs B, Winter K, Simko JP, Ajani JA, Guha C, Okawara GS, AbdallaI, Becker MJ, Pizzolato JF, Crane CH, Brown KD, Shibata D. Genome-wide host methylation profiling of anal and cervical carcinoma. PLoS One. 2021 Dec9;16(12):e0260857. doi: 10.1371/journal.pone.0260857. PMID: 34882728; PMCID:PMC8659695.

Tang BH, Guan Z, Allegaert K, Wu YE, Manolis E, Leroux S, Yao BF, Shi HY, LiX, Huang X, Wang WQ, Shen AD, Wang XL, Wang TY, Kou C, Xu HY, Zhou Y, Zheng Y,Hao GX, Xu BP, Thomson AH, Capparelli EV, Biran V, Simon N, **Meibohm B**, Lo YL, Marques R, Peris JE, Lutsar I, Saito J, Burggraaf J, Jacqz-Aigrain E, van denAnker J, Zhao W. Drug Clearance in Neonates: A Combination of Population Pharmacokinetic Modelling and Machine Learning Approaches to Improve Individual Prediction. Clin Pharmacokinet. 2021 Nov;60(11):1435-1448. doi:10.1007/s40262-021-01033-x. Epub 2021 May 27. PMID: 34041714.

Nagy-Szakal D, Couto-Rodriguez M, Wells HL, Barrows JE, Debieu M, Butcher K,Chen S, Berki A, Hager C, Boorstein RJ, Taylor MK, **Jonsson CB**, Mason CE, O'Hara NB. Targeted Hybridization Capture of SARS-CoV-2 and Metagenomics Enables Genetic Variant Discovery and Nasal Microbiome Insights. Microbiol Spectr. 2021Oct 31;9(2):e0019721. doi: 10.1128/Spectrum.00197-21. Epub 2021 Sep 1. PMID:34468193; PMCID: PMC8557865.

Pierre JF, Phillips GJ, Chandra LC, Rendina DN, Thomas-Gosain NF, Lubach GR, Lyte M, Coe CL, **Gosain A**. Lyticase Facilitates Mycobiome Resolution Without Disrupting Microbiome Fidelity in Primates. J Surg Res. 2021 Nov;267:336-341.doi: 10.1016/j.jss.2021.06.023. Epub 2021 Jun 26. PMID: 34186310; PMCID:PMC8678161.

Chen K, **Sun Z**. Estrogen inhibits renal Na-Pi Co-transporters and improves klotho deficiency-induced acute heart failure. Redox Biol. 2021 Nov;47:102173.doi: 10.1016/j.redox.2021.102173. Epub 2021 Oct 18. PMID: 34678656; PMCID:PMC8577443.

Xue Y, Yang D, Vogel P, Stabenow J, Zalduondo L, Kong Y, Ravi Y, Sai-Sudhakar CB, Parvathareddy J, Hayes E, Taylor S, **Fitzpatrick E**, **Jonsson CB**. Cardiopulmonary Injury in the Syrian Hamster Model of COVID-19. Viruses. 2022Jun 27;14(7):1403. doi: 10.3390/v14071403. PMID: 35891384; PMCID: PMC9316644.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y, Vogel P, Channappanavar R, **Jonsson CB**, **Smith AM**. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infections During SARS-CoV-2.Front Immunol. 2022 May 12;13:894534. doi: 10.3389/fimmu.2022.894534. PMID:35634338; PMCID: PMC9134015.

Bhuniya R, Yuan X, Bai L, Howie KL, Wang R, **Li W**, Park F, **Yang CY**. Design, Synthesis, and Biological Evaluation of Apcin-Based CDC20 Inhibitors. ACS MedChem Lett. 2022 Jan 18;13(2):188-195. doi: 10.1021/acsmedchemlett.1c00544. PMID:35178174; PMCID: PMC8842116.

Bansal S, **Jonsson CB**, Taylor SL, Figueroa JM, Dugour AV, Palacios C, Vega JC. Iota-carrageenan and xylitol inhibit SARS-CoV-2 in Vero cell culture. PLoS One. 2021 Nov 19;16(11):e0259943. doi: 10.1371/journal.pone.0259943. PMID:34797868; PMCID: PMC8604354.

Samak G, Rao R, **Rao R**. Lactobacillus casei and Epidermal Growth Factor Prevent Osmotic Stress-Induced Tight Junction Disruption in Caco-2 Cell Monolayers. Cells. 2021 Dec 18;10(12):3578. doi: 10.3390/cells10123578. PMID:34944085; PMCID: PMC8700399.

Kneller DW, Li H, Phillips G, Weiss KL, Zhang Q, Arnould MA, **Jonsson CB**, Surendranathan S, Parvathareddy J, Blakeley MP, Coates L, Louis JM, Bonnesen PV, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors ofSARS-CoV-2 main protease. Nat Commun. 2022 Apr 27;13(1):2268. doi:10.1038/s41467-022-29915-z. PMID: 35477935; PMCID: PMC9046211.

Albadari N, Deng S, Chen H, Zhao G, Yue J, Zhang S, Miller DD, Wu Z, **Li W**. Synthesis and biological evaluation of selective survivin inhibitors derived from the MX-106 hydroxyquinoline scaffold. Eur J Med Chem. 2021 Nov15;224:113719. doi: 10.1016/j.ejmech.2021.113719. Epub 2021 Jul 30. PMID:34371464; PMCID: PMC8511083.

Adams A, Murphy QM, Dougherty OP, Sawyer AM, Bai F, Edholm CJ, Williams EP, Allen LJS, **Jonsson CB**. Data-driven models for replication kinetics of Orthohantavirus infections. Math Biosci. 2022 Jul;349:108834. doi:10.1016/j.mbs.2022.108834. Epub 2022 May 19. PMID: 35598641.

Kundu S, Shetty A, **Gomes-Solecki M**. Necroptosis Contributes to PersistentI nflammation During Acute Leptospirosis. Front Immunol. 2022 Mar 22;13:810834.doi: 10.3389/fimmu.2022.810834. PMID: 35392072; PMCID: PMC8980737.

Shiah YJ, Shan L, Radin DI, **Huang GT**. Effects of intentionally treated water on the growth of mesenchymal stem cells: An exploratory study. Explore (NY).2021 Nov 24:S1550-8307(21)00242-1. doi: 10.1016/j.explore.2021.11.007. Epub ahead of print. PMID: 34887234.

Shetty A, Kundu S, Vernel-Pauillac F, Ratet G, Werts C, **Gomes-Solecki M**. Transient Presence of Live Leptospira interrogans in Murine Testes. Microbiol Spectr. 2022 Jun 29;10(3):e0277521. doi: 10.1128/spectrum.02775-21. Epub 2022Apr 21. PMID: 35446113; PMCID: PMC9241917.

Suthon S, Lin J, Perkins RS, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**. Estrogen receptor alpha and NFATc1 bind to a bone mineral density-associated SNP to repress WNT5B in osteoblasts. Am J Hum Genet. 2022 Jan 6;109(1):97-115. doi:10.1016/j.ajhg.2021.11.018. Epub 2021 Dec 13. PMID: 34906330; PMCID: PMC8764205.

MacKay CE, Floen M, Leo MD, Hasan R, Garrud TAC, Fernández-Peña C, Singh P, **Malik KU**, Jaggar JH. A plasma membrane-localized polycystin-1/polycystin-2complex in endothelial cells elicits vasodilation. Elife. 2022 Mar 1;11:e74765.doi: 10.7554/eLife.74765. PMID: 35229718; PMCID: PMC8933003.

Odobasic D, Hawkins CL, **Radic M**. Editorial: New roles of neutrophils and granulocytic MDSC in autoimmune diseases, inflammation, and anti-microbial immunity. Front Immunol. 2022 Jul 29;13:974062. doi: 10.3389/fimmu.2022.974062.PMID: 35967293; PMCID: PMC9372723.

Smith AP, Williams EP, Plunkett TR, Selvaraj M, Lane LC, Zalduondo L, Xue Y,Vogel P, Channappanavar R, **Jonsson CB**, **Smith AM**. Time-Dependent Increase in Susceptibility and Severity of Secondary Bacterial Infection during SARS-CoV-2Infection. bioRxiv [Preprint]. 2022 Mar 1:2022.02.28.482305. doi:10.1101/2022.02.28.482305. Update in: Front Immunol. 2022 May 12;13:894534.PMID: 35262077; PMCID: PMC8902874.

Anesi SD, Tauber J, Nguyen QD, Chang P, Berdy GJ, Lin CC, Chu DS, Levine HT, Fernandez AD, Roy N, **Asbell PA**, Kantor AM, Chang AT, Singh B, Youngblood BA, Jeng BH, Jhanji V, Rasmussen HS, Foster CS. Lirentelimab for severe and chronic forms of allergic conjunctivitis. J Allergy Clin Immunol. 2022Sep;150(3):631-639. doi: 10.1016/j.jaci.2022.03.021. Epub 2022 Apr 4. PMID:35390403.

Banerjee S, Yadav S, Banerjee S, Fakayode SO, Parvathareddy J, Reichard W, Surendranathan S, Mahmud F, Whatcott R, Thammathong J, **Meibohm B**, Miller DD, **Jonsson CB**, Dubey KD. Drug Repurposing to Identify Nilotinib as a PotentialSARS-CoV-2 Main Protease Inhibitor: Insights from a Computational and InVitro Study. J Chem Inf Model. 2021 Nov 22;61(11):5469-5483. doi:10.1021/acs.jcim.1c00524. Epub 2021 Oct 20. PMID: 34666487; PMCID: PMC8547516.

Meena AS, Shukla PK, Bell B, Giorgianni F, Caires R, Fernández-Peña C,Beranova S, Aihara E, Montrose MH, Chaib M, **Makowski L**, Neeli I, **Radic MZ**,Vásquez V, Jaggar JH, Cordero-Morales JF, **Rao R**. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID:PMC9250449.

Myers LK, Winstead M, Kee JD, Park JJ, Zhang S, **Li W**, Yi AK, Stuart JM, Rosloniec EF, Brand DD, Tuckey RC, Slominski AT, Postlethwaite AE, Kang AH.1,25-Dihydroxyvitamin D3 and 20-Hydroxyvitamin D3 Upregulate LAIR-1 and Attenuate Collagen Induced Arthritis. Int J Mol Sci. 2021 Dec 12;22(24):13342.doi: 10.3390/ijms222413342. PMID: 34948139; PMCID: PMC8709360.

Wang X, Bajpai AK, Gu Q, Centeno A, **Starlard-Davenport A**, Prins P, Xu F, LuL. A systems genetics approach delineates the role of Bcl2 in leukemia pathogenesis. Leuk Res. 2022 Mar;114:106804. doi: 10.1016/j.leukres.2022.106804.Epub 2022 Feb 9. PMID: 35182904; PMCID: PMC9272521.

Glazer ES. TGF-β Alters the Proportion of Infiltrating Immune Cells in a Pancreatic Ductal Adenocarcinoma. J Gastrointest Surg. 2022Jan;26(1):113-121. doi: 10.1007/s11605-021-05087-x. Epub 2021 Jul 14. PMID:34260016.

Alleboina S, Aljouda N, Miller M, **Freeman KW**. Therapeutically targeting oncogenic CRCs facilitates induced differentiation of NB by RA and the BET bromodomain inhibitor. Mol Ther Oncolytics. 2021 Sep 25;23:181-191. doi:10.1016/j.omto.2021.09.004. PMID: 34729395; PMCID: PMC8526497.

Shukla PK, Meena AS, **Rao R**. Prevention and mitigation of alcohol-induced neuroinflammation by Lactobacillus plantarum by an EGF receptor-dependent mechanism. Nutr Neurosci. 2022 Apr;25(4):871-883. doi:10.1080/1028415X.2020.1819105. Epub 2020 Sep 18. PMID: 32945721; PMCID:PMC7969470.

Xu J, Hu J, Idlett-Ali S, Zhang L, Caples K, Peddibhotla S, Reeves M, ZgheibC, Malany S, Liechty KW. Discovery of Small Molecule Activators of Chemokine Receptor CXCR4 That Improve Diabetic Wound Healing. Int J Mol Sci. 2022 Feb16;23(4):2196. doi: 10.3390/ijms23042196. PMID: 35216311; PMCID: PMC8879702.

Ahmed HA, Ismael S, Salman M, Devlin P, McDonald MP, **Liao FF**, Ishrat T. Direct AT2R Stimulation Slows Post-stroke Cognitive Decline in the 5X-FAD Alzheimer's Disease Mice. Mol Neurobiol. 2022 Jul;59(7):4124-4140. doi:10.1007/s12035-022-02839-x. Epub 2022 Apr 29. PMID: 35486224.

Krutilina RI, Playa H, Brooks DL, Schwab LP, Parke DN, Oluwalana D, Layman DR, Fan M, Johnson DL, Yue J, **Smallwood H**, **Seagroves TN**. HIF-Dependent CKB Expression Promotes Breast Cancer Metastasis, Whereas Cyclocreatine Therapy Impairs Cellular Invasion and Improves Chemotherapy Efficacy. Cancers (Basel).2021 Dec 22;14(1):27. doi: 10.3390/cancers14010027. PMID: 35008190; PMCID:PMC8749968.

Brown Lobbins ML, Slominski AT, Hasty KA, Zhang S, Miller DD, **Li W**, Kim TK, Janjetovic Z, Tuckey RC, Scott IO, Myers LK, Postlethwaite AE. Modulation by17,20S(OH)2 pD of Fibrosis-Related Mediators in Dermal Fibroblast Lines from Healthy Donors and from Patients with Systemic Sclerosis. Int J Mol Sci. 2021 Dec 29;23(1):367. doi: 10.3390/ijms23010367. PMID: 35008794; PMCID:PMC8745512.

Stewart KL, Gigic B, Himbert C, Warby CA, Ose J, Lin T, Schrotz-King P,Boehm J, Jordan KC, Metos J, Schneider M, Figueiredo JC, Li CI, Shibata D,Siegel E, Toriola AT, Hardikar S, Ulrich CM. Association of Sugar Intake with Inflammation- and Angiogenesis-Related Biomarkers in Newly Diagnosed Colorectal Cancer Patients. Nutr Cancer. 2022;74(5):1636-1643. doi:10.1080/01635581.2021.1957133. Epub 2021 Aug 9. PMID: 34369225; PMCID:PMC8825879.

Temiz-Resitoglu M, Guden DS, Senol SP, Vezir O, Sucu N, Kibar D, Yılmaz SN, Tunctan B, **Malik KU**, Sahan-Firat S. Pharmacological Inhibition of Mammalian Target of Rapamycin Attenuates Deoxycorticosterone Acetate Salt-Induced Hypertension and Related Pathophysiology: Regulation of Oxidative Stress, Inflammation, and Cardiovascular Hypertrophy in Male Rats. J CardiovascPharm acol. 2022 Mar 1;79(3):355-367. doi: 10.1097/FJC.0000000000001187. PMID:34840266.

Sanchez V, Galor A, Jensen K, Mondal K, **Mandal N**. Relationships between ocular surface sphingomyelinases, Meibum and Tear Sphingolipids, and clinical parameters of meibomian gland dysfunction. Ocul Surf. 2022 Jul;25:101-107. doi:10.1016/j.jtos.2022.06.003. Epub 2022 Jun 14. PMID: 35714913.

Kneller D, Li H, Phillips G, Weiss K, Zhang Q, Arnould M, **Jonsson C**, Surendranathan S, Parvathareddy J, Blakeley M, Coates L, Louis J, Bonnesen P, Kovalevsky A. Covalent narlaprevir- and boceprevir-derived hybrid inhibitors ofSARS-CoV-2 main protease: room-temperature X-ray and neutron crystallography, binding thermodynamics, and antiviral activity. Res Sq [Preprint]. 2022 Feb11:rs.3.rs-1318037. doi: 10.21203/rs.3.rs-1318037/v1. Update in: Nat Commun.2022 Apr 27;13(1):2268. PMID: 35169792; PMCID: PMC8845512.

Lin Y, **Sun Z**. Klotho deficiency-induced arterial calcification involves osteoblastic transition of VSMCs and activation of BMP signaling. J Cell Physiol. 2022 Jan;237(1):720-729. doi: 10.1002/jcp.30541. Epub 2021 Aug 8. PMID:34368951; PMCID: PMC8810603.

Shukla PK, Meena AS, Pierre JF, **Rao R**. Central role of intestinal epithelial glucocorticoid receptor in alcohol- and corticosterone-induced gut permeability and systemic response. FASEB J. 2022 Jan;36(1):e22061. doi:10.1096/fj.202101424R. PMID: 34861075; PMCID: PMC8647846.

Nagib MM, Zhang S, Yasmen N, Li L, Hou R, Yu Y, Boda VK, Wu Z, **Li W**, Jiang J. Inhibition of TRPC3 channels by a novel pyrazole compound confers anti seizure effects. Epilepsia. 2022 Apr;63(4):1003-1015. doi: 10.1111/epi.17190. Epub 2022Feb 18. PMID: 35179226; PMCID: PMC9007831.

Mondal K, Takahashi H, Cole J 2nd, Del Mar NA, Li C, Stephenson DJ, AllegoodJ , Cowart LA, Chalfant CE, Reiner A, **Mandal N**. Systemic Elevation of n-3Polyunsaturated Fatty Acids (n-3-PUFA) Is Associated with Protection against Visual, Motor, and Emotional Deficits in Mice following Closed-Head Mild Traumatic Brain Injury. Mol Neurobiol. 2021 Nov;58(11):5564-5580. doi:10.1007/s12035-021-02501-y. Epub 2021 Aug 8. PMID: 34365584; PMCID: PMC8655834.

Yoon TW, **Fitzpatrick EA**, Snyder JD, Lee S, Kim YI, Zacheaus C, Yi AK. Contribution of Protein Kinase D1 on Acute Pulmonary Inflammation and Hypersensitivity Pneumonitis Induced by Saccharopolyspora rectivirgula Immunohorizons. 2022 Mar 10;6(3):224-242. doi: 10.4049/immunohorizons.2200017.PMID: 35273098.

Aksel H, Sarkar D, Lin MH, Buck A, **Huang GT**. Cell-derived Extracellular Matrix Proteins in Colloidal Microgel as a Self-Assembly Hydrogel for Regenerative Endodontics. J Endod. 2022 Apr;48(4):527-534. doi:10.1016/j.joen.2022.01.011. Epub 2022 Jan 22. PMID: 35077752.

Kneller DW, Li H, Galanie S, Phillips G, Labbé A, Weiss KL, Zhang Q, Arnould MA, Clyde A, Ma H, Ramanathan A, **Jonsson CB**, Head MS, Coates L, Louis JM, Bonnesen PV, Kovalevsky A. Structural, Electronic, and Electrostatic Determinants for Inhibitor Binding to Subsites S1 and S2 in SARS-CoV-2 Main Protease. J Med Chem. 2021 Dec 9;64(23):17366-17383. doi:10.1021/acs.jmedchem.1c01475. Epub 2021 Oct 27. PMID: 34705466; PMCID:PMC8565456.

Merigeon EY, Yang D, Ihms EA, Bassit LC, **Fitzpatrick EA**, **Jonsson CB**, Schinazi RF, Block DS, Olsen HS. An ACE2-IgG4 Fc Fusion Protein Demonstrates Strong Binding to All Tested SARS-CoV-2 Variants and Reduced Lung Inflammation in Animal Models of SARS-CoV-2 and Influenza. Pathog Immun. 2022 Aug23;7(1):104-121. doi: 10.20411/pai.v7i1.491. PMID: 36072571; PMCID: PMC9438944.

Guo H, **Zhang W**, Wang J, Zhao G, Wang Y, Zhu BM, Dong P, Watari H, Wang B, LiW, **Tigyi G**, Yue J. Cryptotanshinone inhibits ovarian tumor growth and metastasis by degrading c-Myc and attenuating the FAK signaling pathway. Front Cell Dev Biol. 2022 Sep 28;10:959518. doi: 10.3389/fcell.2022.959518. PMID: 36247016;PMCID: PMC9554091.

Aksel H, Zhu X, Gauthier P, **Zhang W**, Azim AA, **Huang GT**. A new direction in managing avulsed teeth: stem cell-based de novo PDL regeneration. Stem Cell Res Ther. 2022 Jan 28;13(1):34. doi: 10.1186/s13287-022-02700-x. PMID: 35090556;PMCID: PMC8796335.

Kim S, Kim YE, Song I, Ujihara Y, Kim N, Jiang YH, Yin HH, Lee TH, **Kim IH**. Neural circuit pathology driven by Shank3 mutation disrupts social behaviors. Cell Rep. 2022 Jun 7;39(10):110906. doi: 10.1016/j.celrep.2022.110906. PMID:35675770; PMCID: PMC9210496.

Agrawal M, Rasiah PK, **Bajwa A**, Rajasingh J, **Gangaraju R**. Mesenchymal Stem Cell Induced Foxp3(+) Tregs Suppress Effector T Cells and Protect against Retinal Ischemic Injury. Cells. 2021 Nov 4;10(11):3006. doi:10.3390/cells10113006. PMID: 34831229; PMCID: PMC8616393.
Ryan MC, Kim E, Cao X, Reichard W, Ogorek TJ, Das P, **Jonsson CB**, Baudry J, Chung D, Golden JE. Piperazinobenzodiazepinones: New Encephalitic Alphavirus Inhibitors via Ring Expansion of 2-Dichloromethylquinazolinones. ACS Med ChemLett. 2022 Mar 14;13(4):546-553. doi: 10.1021/acsmedchemlett.1c00539. PMID:35450382; PMCID: PMC9014857.

Di L, Akther S, Bezrucenkovas E, Ivanova L, Sulkow B, Wu B, Mneimneh S, **Gomes-Solecki M**, Qiu WG. Maximum antigen diversification in a lyme bacterial population and evolutionary strategies to overcome pathogen diversity. ISME J.2022 Feb;16(2):447-464. doi: 10.1038/s41396-021-01089-4. Epub 2021 Aug 19. PMID:34413477; PMCID: PMC8376116.

Asbell PA, Sanfilippo CM, Mah FS. Antibiotic susceptibility of bacterial pathogens isolated from the aqueous and vitreous humour in the Antibiotic Resistance Monitoring in Ocular micro organisms (ARMOR) Surveillance Study:2009-2020 update. J Glob Antimicrob Resist. 2022 Jun;29:236-240. doi:10.1016/j.jgar.2022.03.010. Epub 2022 Mar 23. PMID: 35339737.

Rana M, Kansal R, Chaib M, Teng B, Morrrison M, Hayes DN, Stanfill AG,Shibata D, Carson JA, **Makowski L**, **Glazer ES**. The pancreatic cancer immune tumor microenvironment is negatively remodeled by gemcitabine while TGF-β receptor plus dual checkpoint inhibition maintains antitumor immune cells. Mol Carcinog.2022 Jun;61(6):549-557. doi: 10.1002/mc.23401. Epub 2022 Mar 23. PMID: 35319799.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, Yue J, Benyó Z, **Tigyi GJ.** Prometastatic Effect of ATX Derived from Alveolar Type II Pneumocytes andB16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi:10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.

Suthon S, Perkins RS, Lin J, Crockarell JR Jr, **Miranda-Carboni GA**, **Krum SA**.GATA4 and estrogen receptor alpha bind at SNPs rs9921222 and rs10794639 to regulate AXIN1 expression in osteoblasts. Hum Genet. 2022 Jun 9. doi:10.1007/s00439-022-02463-8. Epub ahead of print. PMID: 35678873.

Slayden AV, Dyer CL, Ma D, **Li W**, Bukiya AN, Parrill AL, Dopico AM. Discovery of agonist-antagonist pairs for the modulation of Ca2+ and voltage-gated K+ channels of large conductance that contain beta1subunits. Bioorg Med Chem. 2022 Aug 15;68:116876. doi:10.1016/j.bmc.2022.116876. Epub 2022 Jun 13. PMID: 35716586.

Whittington KB, Prislovsky A, Beaty J, Albritton L, **Radic M**, Rosloniec EF. CD8 T Cells Expressing an HLA-DR1 Chimeric Antigen Receptor Target Autoimmune CD4+ T Cells in an Antigen-Specific Manner and Inhibit the Development of Autoimmune Arthritis. J Immunol. 2022 Jan 1;208(1):16-26. doi:10.4049/jimmunol.2100643. Epub 2021 Nov 24. PMID: 34819392; PMCID: PMC8702470.

Zhou Q, Verne GN. Disruption of the Mucosal Serotonin Reuptake Transporter(SERT) Through Gut Dysbiosis. Gastroenterology. 2022 Jun;162(7):1833-1834. doi:10.1053/j.gastro.2022.03.029. Epub 2022 Mar 24. PMID: 35341788.

Brizuela C, **Huang GT**, Diogenes A, Botero T, Khoury M. The Four Pillars for Successful Regenerative Therapy in Endodontics: Stem Cells, Biomaterials, Growth Factors, and Their Synergistic Interactions. Stem Cells Int. 2022 Sep19;2022:1580842. doi: 10.1155/2022/1580842. PMID: 36193253; PMCID: PMC9526564.

Drake JA, Fleming AM, Behrman SW, **Glazer ES**, Deneve JL, Yakoub D, Tsao MW, Dickson PV. Tumor Location in the Pancreatic Tail Is Associated with Decreased Likelihood of Receiving Chemotherapy for Pancreatic Adenocarcinoma. J Gastrointest Surg. 2022 Oct;26(10):2136-2147. doi: 10.1007/s11605-022-05381-2.Epub 2022 Jun 29. PMID: 35768717.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, Yue J, **Zhang W**. Adipose-Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal Transition Through Activating the TGF-β Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276;PMCID: PMC8727693.

Yuan X, Chinnaswamy K, Stuckey JA, **Yang CY**. Computational Cosolvent Mapping Analysis Leads to Identify Salicylic Acid Analogs as Weak Inhibitors of ST2 andIL33 Binding. J Phys Chem B. 2022 Mar 31;126(12):2394-2406. doi:10.1021/acs.jpcb.2c00341. Epub 2022 Mar 16. PMID: 35294837; PMCID: PMC9354565.

Galor A, Sanchez V, Jensen A, Burton M, Maus K, Stephenson D, Chalfant C, **Mandal N**. Meibum sphingolipid composition is altered in individuals with meibomian gland dysfunction-a side by side comparison of Meibum and Tear Sphingolipids. Ocul Surf. 2022 Jan;23:87-95. doi: 10.1016/j.jtos.2021.11.011.Epub 2021 Nov 30. PMID: 34861426; PMCID: PMC8792295.

Mondal K, Porter H, Cole J 2nd, Pandya HK, Basu SK, Khanam S, Chiu CY, Shah V, Stephenson DJ, Chalfant CE, **Mandal N**. Hydroxychloroquine Causes Early Inner Retinal Toxicity and Affects Autophagosome-Lysosomal Pathway and Sphingolipid Metabolism in the Retina. Mol Neurobiol. 2022 Jun;59(6):3873-3887. doi:10.1007/s12035-022-02825-3. Epub 2022 Apr 15. Erratum in: Mol Neurobiol. 2022Oct;59(10):6611. PMID: 35426574.

Fortes-Gabriel E, Guedes MS, Shetty A, Gomes CK, Carreira T, Vieira ML, Esteves L, Mota-Vieira L, **Gomes-Solecki M**. Enzyme immunoassays (EIA) for serodiagnosis of human leptospirosis: specific IgG3/IgG1 isotyping may further inform diagnosis of acute disease. PLoS Negl Trop Dis. 2022 Feb23;16(2):e0010241. doi: 10.1371/journal.pntd.0010241. PMID: 35196321; PMCID:PMC8901056.

Swanson ML, Regner KR, Moore BM, **Park F**. Cannabinoid Type 2 Receptor Activation Reduces the Progression of Kidney Fibrosis Using a Mouse Model of Unilateral Ureteral Obstruction. Cannabis Cannabinoid Res. 2022 Feb 23. doi:10.1089/can.2021.0127. Epub ahead of print. PMID: 35196117.

Chen K, Wang S, **Sun Z**. In Vivo Cardiac-specific Expression of Adenylyl Cyclase 4 Gene Protects against Klotho Deficiency-induced Heart Failure. Transl Res. 2022 Jun;244:101-113. doi: 10.1016/j.trsl.2022.01.006. Epub 2022 Jan 31.PMID: 35114419; PMCID: PMC9119924.

Gaur AH, Panetta JC, **Smith AM**, Dallas RH, Freeman BB 3rd, Stewart TB, TangL, John E, Branum KC, Patel ND, Ost S, Heine RN, Richardson JL, Hammill JT, Bebrevska L, Gusovsky F, Maki N, Yanagi T, Flynn PM, McCarthy JS, Chalon S, Guy RK. Combining SJ733, an oral ATP4 inhibitor of Plasmodium falciparum, with the pharmacokinetic enhancer cobicistat: An innovative approach in antimalarial drug development. eBio Medicine. 2022 Jun;80:104065. doi: 10.1016/j.ebiom.2022.104065.Epub 2022 May 19. PMID: 35598441; PMCID: PMC9127571.

Chaib M, Sipe LM, Yarbro JR, Bohm MS, Counts BR, Tanveer U, Pingili AK, **Daria D**, Marion TN, Carson JA, Thomas PG, **Makowski L**. PKC agonism restricts innate immune suppression, promotes antigen cross-presentation and synergizes with agonistic CD40 antibody therapy to activate CD8+ T cells in breast cancer. Cancer Lett. 2022 Apr 10;531:98-108. doi:10.1016/j.canlet.2022.01.017. Epub 2022 Jan 21. PMID: 35074498.

Mahat U, Garg B, **Yang CY**, Mehta H, Hanna R, Rogers HJ, Flagg A, Ivanov AI, Corey SJ. Lymphocyte cytosolic protein 1 (L-plastin) I232F mutation impairs granulocytic proliferation and causes neutropenia. Blood Adv. 2022 Apr26;6(8):2581-2594. doi: 10.1182/bloodadvances.2021006398. PMID: 34991157; PMCID:PMC9043934.

Han X, **Sun Z**. Adult Mouse Kidney Stem Cells Orchestrate the De NoVo Assembly of a Nephron via Sirt2-Modulated Canonical Wnt/β-Catenin Signaling. AdvSci (Weinh). 2022 May;9(15):e2104034. doi: 10.1002/advs.202104034. Epub 2022 Mar22. PMID: 35315252; PMCID: PMC9130916.

Huo X, **Zhang W**, Zhao G, Chen Z, Dong P, Watari H, Narayanan R, Tillmanns TD, Pfeffer LM, Yue J. FAK PROTAC Inhibits Ovarian Tumor Growth and Metastasis by Disrupting Kinase Dependent and Independent Pathways. Front Oncol. 2022 Apr28;12:851065. doi: 10.3389/fonc.2022.851065. PMID: 35574330; PMCID: PMC9095959.

Song CY, Singh P, Motiwala M, Shin JS, Lew J, Dutta SR, Gonzalez FJ, Bonventre JV, **Malik KU**. 2-Methoxyestradiol Ameliorates Angiotensin II-Induced Hypertension by Inhibiting Cytosolic Phospholipase A₂α Activity in Female Mice. Hypertension. 2021 Nov;78(5):1368-1381. doi:10.1161/HYPERTENSIONAHA.121.18181. Epub 2021 Oct 11. PMID: 34628937; PMCID:PMC8516072.

Adhikari P, Shukla PK, Alharthi F, **Rao R**, Pradhan P. Photonic technique to study the effects of probiotics on chronic alcoholic brain cells by quantifying their molecular specific structural alterations via confocal imaging. J Biophotonics. 2022 Mar;15(3):e202100247. doi: 10.1002/jbio.202100247. Epub 2021Dec 2. PMID: 34786860.

I. PRESENTATIONS, AND MEETINGS TO PROMOTE CORE USAGE AND FUNCTION

A. Meetings to support core functions and instrumentation

Since his election in 2019, Dr. Marion continues to serve as the president of the Southeast Flow Cytometry Interest Group (SEFCIG), a professional organization associated with the International Society for Advancement of Cytometry (ISAC) which promotes research, development, and applications in analytical cytometry. In March of 2022 SEFCIG held an in-person meeting in Raleigh-Durham, NC. Topics included cutting edge technologies, microparticle flow cytometry, and the complexities of working with high-dimensional data. It also provided an opportunity to interact with new flow cytometer core directors, managers, and technical staff who have recently upgraded

their instruments to spectral-based analyzers, which is a goal of the UTHSC FCCS. A Thermo Bigfoot spectral and conventional laser flow sorter was proposed in a pending S10 instrumentation grant proposal in May of 2022.

In June of 2022 Dr. Daria attended virtually the CYTO2022 meeting held by ISAC. The meeting began with data analysis workshops, focusing on machine-learning tools and analysis platforms. The conference included more than 20 presentations with topics ranging from best practices for shared resource laboratories, to image cytometry and flow cytometry for immune therapy and vaccine trials. The meeting also provided access to experts in the field to discuss image and mass-based cytometry and various high parameter (35+ colors) data analysis platforms.

Dr. Daria served as secretary for a regional chapter of the ABRF organization, SEASR (Southeast Association of Shared Resources), and she attended the annual meeting in June of 2022 in Nashville, TN. SEASR provides a forum for core directors, managers, and technical staff to discuss common issues associated with SRLs. The meeting program included both scientific and administrative topics relevant to flow cores, such as high-dimensional data analysis, service fee rate-setting, and managing collaborations.

B. Continuing Education

In FY22 Dr. Daria attended two workshops offered by ISAC, “Best Practices for User Consultation” and “Getting Started with Flow Cytometry Data Science.”

C. Instrument/Software Training and Seminars

Dr. Daria taught a four-part seminar series entitled “Flow Cytometry Basics” every other month for five months during FY22. A total of 32 UTHSC personnel from 23 UTHSC laboratories and one individual from the University of Memphis attended. In addition, six new UTHSC users were trained to operate the ZE5 analyzer independently and two users were trained in to analyze raw data using FlowJo software.

SUMMARY OF ACTIVITIES

A. Personnel

Scientific Director: Tony Marion, PhD, professor (40% effort; no salary provided by the core operating budget). Note, Dr. Marion retired June 30, 2022.

Technical Director: Deidre Daria, PhD, research specialist (FY22 effort: 97% effort, FCCS core, >3% effort RBL core). Dr. Daria was selected as the incoming core director in August of 2022 (FY23).

B. FCCS Internal Advisory Board (IAB)

The FY22 FCCS core advisory committee consists of the following members:

David Brand (Medicine-Rheumatology, COM and VAMC)
Maria Gomes-Solecki (MIB, COM)
Rajashekhar Gangaraju (Ophthalmology, COM)
Liza Makowski (Medicine-Hematology, COM); *CHAIR*

C. Equipment and research resources

FY22 equipment located in the FCCS lab:

Equipment	Cost	Funding Source
FACSAria IIu sorter	$483,000	S10 RR022465 (PI: Marion), 2008
AMO aerosol maintenance		included with FACSAria
Lauda recirculating bath		included with FACSAria
Bio-Rad ZE5*	$286,592*	VC Research startup, 2016
Amnis FlowSight[#]	$0	Kindly donated by UTHSC Dept. of Ophthalmology

*after discount and LSR II trade-in, List $355,342
[#]not operational at this time

FY22 equipment owned by the RBL, and operated in part by the FCCS

Equipment	Cost	Funding Source
FACSAria II sorter*	$367,940	E0701655001, 2009
AMO aerosol maintenance		included with FACSAria
Lauda recirculating bath		included with FACSAria
BioProtect III Bio-containment enclosure	$44,400	E0701655001, 2009
Cytex Aurora	$242,138	G20 1G20AI167349-01 (PI:Jonsson), 2021

*The FACSAria II was removed from the RBL and gifted to the FCCS in Q2 of FY22 due to the replacement with a spectral cytometer from Cytek in Q2 of FY23.

D. Service Contracts

BD Biosciences Aria IIu sorter $33,161
(Specialty Underwriters)

BD Biosciences Aria II sorter (RBL) $29,842*
(Specialty Underwriters)
*discontinued in Q4 of FY21 due to planned replacement with the RBL Aria II sorter

Bio-Rad ZE5 $27,000
(Bio-Rad)

E. Usage Volumes

Service Types	FY19, units	FY19, h	FY20, units	FY21, units	FY21, units	FY21, h	FY22, units	FY22, h
Flow cytometry	193	189	242	239	239	309.5	208	269.5

Cell sorting	47	101.5	20	28	28	99.5	30	95
Data Analysis	89	109	51	34	34	22.5	29	23.5
Training	9	14	16	8	8	21.5	6	15.5
RBL Live/Cell Sorting				1	1	0.5		
RBL Flow Cytometry				6	6	23.75	7	14.5

F. Multi-year trends

FY period	UTHSC users (# labs)	External or commercial users (# labs)	Flow cytometry (total # uses)	Cell sorting (total # uses)
FY22	40	1	208	30
FY21	29	0	239	28
FY20	31	1	242	20
FY19	23	0	193	47
FY18	25	0	193	29
FY17	23	1	148	26
FY16	24	1	287	29
FY15	23	2	283	28
FY14	15	2	163	27
FY13	20	2	347	28
FY12	18	2	279	28
FY11	25	2	318	37

G. Fee Structure

In FY22, the FY21 service prices were escalated by 3%.

FACSAria (Cell Sorter)	UTHSC	External, Academic	Commercial
2- or 4-way Sorting	$138.51	$207.77	Negotiated agreement
Sorting to Plates or Single Cell Sorting	$138.51	$207.77	Negotiated agreement
Small Particle sorting	$172.20	$258.20	Negotiated agreement
FACSAria (RBL Cell Sorter)	**UTHSC**	**External, Academic**	**Commercial**

2- or 4-way Sorting/Live cell acquisition	$230.84	$277.02	Negotiated agreement
Investigator-operated cytometry (billed in 30-minute increments)	$59.55	$89.33	N/A
Operator-assisted cytometry (billed in 30-minute increments)	$81.08	$121.62	Negotiated agreement
Bio-Rad ZE5 (Flow Cytometer)	**UTHSC**	**External, Academic**	**Commercial**
Investigator-operated cytometry (billed in 30-minute increments)	$59.55	$89.33	N/A
Operator-assisted cytometry (billed in 30-minute increments)	$81.08	$121.62	Negotiated agreement
Raw Data Analysis (30-minute minimum, then billed in 15-minute increments)	$59.55	$89.33	Negotiated agreement
Training	**UTHSC**	**External, Academic**	**Commercial**
Cytometry instruments and software training (per hour)	$92.34	$138.51	N/A

**Training on instruments does not include cell sorting.*
Only the FCCS operator or director may use the cell sorters.

II. GRANTS
A. GRANTS SUPPORTED BY THE CORE, FY22

Gomes-Solecki, Maria
University of Iowa Subcontract to USPHS NIH Grant AI-39267, Field trial and modeling of transmission-blocking vaccine to prevent Lyme disease

Jonsson, Colleen
USPHS NIH Grant AI-142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

Liao, Francesca-Fang
USPHS NIH Grant AG058467, Novel mechanistic link between metabolic changes and dementia potential role of miRNA21

USPHS NIH Grant NS-120327, Blood-brain-barrier and white matter mechanisms underlying dementia

Kim, Il Hwan
USPHS NIH Grant MH-117429, Genes, Neural Circuits and Behavior

Radic, Marko
Viela Bio., Sponsored Research Agreement, Evaluation of FCRL5 as Therapeutic Target in Experimental Lupus

Triumvira Immunologies, Sponsored Research Agreement, Evaluation of Anti-CD19 TAC-T cell Efficacy in SLE Patient Cell Cultures

Rao, Radhakrishna
Mississippi State University Subcontract to USPHS NIH Grant CA-260147, Photonics probing of DNA mass density spatial structure for cancer diagnostics

Smith, Amber
USPHS NIH Grant AI-139088, Predictive Modeling of Influenza-Pneumococcal Coinfection

Sun, Zhongjie
USPHS NIH Grant AG-062375, Epigenetic Regulation of Kidney Function and Blood Pressure

USPHS NIH Grant HL-154147, Investigation into Arterial Stiffness and Hypertension

Tigyi, Gabor
USPHS NIH Grant CA-092160, Anticancer Strategies Targeting the Autotaxin-LPA Receptor Axis

University of Maryland Subcontract to USPHS NIH Grant AI-150574, Intercollaborative Radiation Countermeasure (INTERACT) Consortium for Advanced Development of Medical Countermeasures to Mitigate/Treat Acute and Delayed Radiation Syndromes

B. GRANT APPLICATIONS TO SUPPORT THE CORE

Effective in their FY24, BD Bioscience has announced that they will no longer repair the FACSAria IIu model of cell sorters, such as those currently located within the FCCS core facility. The instruments have reached their 10-12-year durable life span and will each need to be replaced by an instrument capable of cell sorting within the next 1-2 years for UTHSC to remain current in flow-based technologies relative to our academic peers.

In FY22 Dr. Marion submitted as PI a revised NIH S10 shared instrumentation grant proposal to acquire a new sorter (Thermo Bigfoot) with specifications that align with the mission of the FCCS core to provide the latest in flow cytometry technology and to provide access to state-of-the-art instrumentation. The proposed sorter would also serve as a second analyzer. The proposal was supported by several major/minor users representing 16 UTHSC laboratories from 11 departments and one external laboratory at St. Jude Children's Research Hospital. The Bigfoot instrument is a spectral analyzer.

III. BUSINESS DEVELOPMENT

A. FCCS Core history

The UTHSC Flow Cytometry and Cell Sorting (FCCS) laboratory was established in 2003. The mission of the Flow Cytometry and Cell Sorting laboratory and the FCCS Core is to provide the UTHSC and Memphis research community with access to state-of-the-art instruments, expertise, instruction and assistance with experimental design, and data analysis for digital, multicolor flow cytometry and cell sorting, including indexed

single-cell sorting. Prior to 2003, flow cytometry and cell sorting services were part of the Molecular Resource Center (MRC). The acquisition of the BD Biosciences LSR II flow cytometer in 2003 with a S10 shared equipment grant from NIH NCRR (PI: Tony Marion) provided UTHSC researchers with the first capability for the now standard digital "multicolor" flow cytometry. Flow cytometry was separated from the MRC at that time to become an independent shared research support laboratory. The core laboratory was expanded to include cell sorting in 2008 with the acquisition of the newly developed and state-of-the-art BD Biosciences FACSAria cell sorter also with NIH NCRR S10 grant support (PI: Tony Marion). Dr. Marion initiated the movement to modernize flow cytometry and cell sorting at UTHSC, was PI for both instrumentation grants, and has been director of the core laboratory since its inception.

In 2016, the BD Biosciences LSR II flow cytometer was replaced with the Bio-Rad ZE5 21-color cytometer (formally known as the Propel Yeti). This ZE5 has provided the campus with a highly technically sophisticated flow cytometer with a yellow-green laser (561 nm), which the LSR II did not have. That deficiency had previously limited the usefulness of PE and PE-tandem fluorophores and the potential to incorporate red fluorescence proteins and "fruit dyes" into experiments that require those fluorophores, in most cases only excited by the 561 nm laser. The potential to quantify red fluorescence protein expression in single cells augments protocols that employ red fluorescence protein expression in *in vivo* imaging studies. In addition to the yellow-green laser with seven fluorescence detectors, the ZE5 has a violet, 405 nm; blue, 488 nm; and red, 640nm lasers with 7, 4, 7 and 3 fluorescence detectors for a total of 21 fluorescence detectors. The ZE5 also has a FALS (forward angle light scatter) detector on the violet laser to improve detection of small, subcellular particles, such as extracellular vesicles and bacteria.

In 2018, Dr. Deidre Daria replaced Dr. Terry-Ann Milford, PhD as the full-time flow cytometry specialist dedicated to assisting users in the planning and execution of flow cytometry and cell sorting experiments.

In 2019, the FCCS was tasked with the operation, training, and maintenance of the RBL FACSAria II cell sorter. Prior to this time, the RBL FACSAria was not in use and was not operational. The RBL FACSAria was repaired in FY20, but because the room where the repaired RBL FACSAria was housed was inaccessible for most of FY20 (September 2019 to March 2020) due to a roof leak, the instrument was inaccessible for most of FY20. Although repaired and functional in FY21, the RBL sorter has reached its durable lifespan, was transferred to the FCCS in January of FY22, and is scheduled to be replaced in FY23 with a Cytek Aurora instrument, which will be exclusively operated by RBL users and staff, with the ability to request assistance from the FCCS core, if needed. Since the RBL gifted the FACSAria II to the FCCS, it has no longer been covered by a service agreement, rather, it is being held to be sold as used equipment or to be used as a trade-in towards a new sorter.

In 2021, the FCCS accepted the gift of the AMNIS FlowSight Imaging Cytometer from the Department of Ophthalmology. The FlowSight was not in use, nor was it operational, prior to the time of acquisition by the FCCS. The FlowSight will be repaired and placed in service only if sufficient need is demonstrated.

B. Market Assessment

The FCCS Core provides access to state-of-the-art multicolor flow cytometry and fluorescence-activated cell sorting (FACS) for the UTHSC and Memphis research community. Services offered by the FCCS Core include training in the use of the flow cytometer in the FCCS laboratory as well as advice and assistance for multicolor flow cytometry experimental design and data analysis. The core can also perform two- and four-way FACS for BSL1/2 samples and index single-cell FACS into microwells or onto microscope slides. The research services provided by the FCCS Core are competitive with similar flow cytometry and cell sorting research cores at other major research institutions. Pricing for services in the FCCS Core is likewise competitive with southeast regional research institutions. However, some of the instrumentation is nearing the end of their lifetime.

The FCCS Core has experienced relatively stable use of both flow cytometry and cell sorting services for the past five years (Section III.F). Over those five years, the FCCS Core has provided services for 31+ individual research laboratories from five colleges and five outside academic institutions or commercial companies. Since the transition to the YETI (ZE5) flow cytometer in 2017, the core has trained 55 new users. The FCCS Core is a critical resource for the grant-supported research mission at UTHSC as well as local, external researchers who depend upon the FCCS Core for data collection.

C. Competitive Analysis

There are other flow cytometers and cell sorters available in the Memphis medical district. Within the UTHSC campus, a Miltenyi MACSQuant flow cytometer is housed at the Translational Science Research Building, an Agilent Novocyte and Luminex Guava easyCyte are located within the College of Pharmacy and a Cytek Aurora is located within the RBL. Users of these instruments participate in the educational seminars, but rarely pay for fee-based services in the FCCS Core. Outside of the UTHSC campus, housed within either the Le Bonheur Children's Hospital, the Children's Research Foundation, or the Memphis VA Medical Center (VAMC), are a BD Biosciences LSR II flow cytometer, a Sony SH800 FACS sorter, a Bio-Rad S3 FACS sorter, a Cytek Aurora, and a FACSAria FACS sorter. Users who choose these resources do so either because of convenience, or because use of the other instruments is free of charge (at the VAMC or within departmental "cores"). Although these other services do not advertise their services, or actively compete with the FCCS Core, they do siphon away users who might otherwise use the FCCS Core.

D. Marketing Plans to Obtain New Business

The technical capabilities of the FCCS Core are sustained and continually expanded by Drs. Marion and Daria, who have more than 40 years of combined experience in all aspects of flow cytometry and cell sorting.

The capabilities of the FCCS Core, particularly in the area of high-dimensional single-cell analysis and its role in multi-omics research require communication to the research community. Each version of the Operational Strategic Plan for Research has recognized the importance of including single-cell analyses into research protocols in all areas of research that involve analyses of cellular phenotypes and their manipulation, and the diversity of gene expression among individual cells with similar phenotype or origin. High-dimensional analysis platforms can be established with only 12-14 parameters, which is within the current capabilities of the core. The FCCS Core has the capability to perform indexed single cell sorting based upon up to 12 different fluorescence

parameters and the ZE5 can comfortably analyze 14+ parameters. Because the number of parameters measured at the single-cell level is continually increasing, the core will need to establish an optimized panel for use on our current instruments, capable of expanding upon acquisition of new instrumentation, and flexible enough for investigators to tailor towards their specific needs. In turn, an optimized panel will provide the datasets needed to establish the machine-learning tools for high-dimensional data analysis and provide a framework panel for the future experiments. It will also reduce the time and money spent by the investigator to optimize a panel and aid in training.

The BD Biosciences LSR II flow cytometer was replaced in Q1 of FY17 with the Propel YETI (Bio-Rad ZE5) 21-color cytometer. As an early adopter, we had unlimited technical support and service from Propel. Bio-Rad acquired rights to manufacture and service the Yeti in 2017, rebranded as the ZE5. Bio-Rad also acquired rights to the Propel EVO software, now named Everest, also in 2017. The ZE5 has provided the campus with a highly technically sophisticated flow cytometer with a yellow-green laser (561 nm), which the LSR II did not have. Yellow-green laser excitation of several fluorophores will eliminate, or at least vastly reduce the problem of autofluorescence generated by the 488 nm laser. The potential to quantify red fluorescence protein expression in single cells will also augment protocols that employ red fluorescence protein expression in *in vivo* imaging studies. It is sufficient to meet current needs and capabilities can be expanded with additional lasers/PMTs.

The NIH S10 grant application re-submitted by Dr. Marion identified the Thermo Fisher Scientific Bigfoot Spectral Cell Sorter as the best option. This instrument would be functionally compatible with the existing FCCS SRL Bio-Rad ZE5 flow cytometer and provide a “backup” when the ZE5 is either not operational or committed to scheduled use. The Bigfoot sorter will also solve the limitations of the current Aria II sorter by the addition of a 561nm laser. The Bigfoot sorter will also advance our available technology by allowing the choice between newly developed full spectrum cytometry (spectral unmixing) or conventional compensation to increase the choice of reagents and markers (35+) that would not otherwise be compatible for sub-population analysis.

Workshops and/or “Hot Topics” dedicated to emphasizing the capabilities of the FCCS Core and how those capabilities can expand the research capabilities of research labs that utilize cell isolation and analysis will be expanded in order to support the research mission at UTHSC and the viability of the FCCS Core. To continue the education objective and increase visibility, the FCCS Core will continue with its four-part lecture series designed to educate users in the basics of flow cytometry, panel design, compensation, and gating and will advertise these classes campus-wide. Education in data analysis with emphasis on high-dimensional data analysis, in the form of webinars, lectures, practice datasets, and discussion groups will be worked out in FY23. In addition, the core will sponsor Shared Resources Technology Talks from guest speakers and webinars from vendors on new technologies related to flow cytometry. These objectives will provide users with additional educational support and maintain the core’s mission of providing the latest technologies and expertise.

To address the many important technical requirements of flow cytometry, the FCCS Core established a UTHSC FCCS sharepoint site for all UTHSC personnel and continues to release additional basic flow cytometry protocols as well as “Tech notes” through this portal. The information on this site will provide some of the educational and technical support needed by researchers and highlights the capabilities of the core.

E. Forecasted Volumes for New Business

As panel design and complexity increase so too does the time and effort involved in designing and optimizing a high-quality panel fit for downstream high-dimensional data analysis. Optimization can take weeks or months, discouraging investigators and leading them to seek alternative approaches. An optimized panel specifically for core instruments is expected to entice new investigators by reducing time and effort spent in development and retain current investigators with designs specific to core instruments. In addition, choice of fluorochromes and antibody concentrations are highly specific to the individual flow cytometry instrument further encouraging users to utilize the core instruments as opposed to other sources.

Because of the success of the educational classes, the core will continue provide basic flow cytometry classes and expand to offer data analysis educational opportunities using the core optimized panels. These classes serve as a marketing tool as well as maintain the core's mission of providing cutting edge service and technology.

We will also continue to participate in events sponsored by SEFCIG, ISAC, SEASR and ABRF to further expand our expertise and visibility to an external customer base. We will also continue to participate in the Office of Research Hot Topics seminar series and to recruit guest speakers for the cores' special technology seminars focused on flow cytometry.

FY2022	DEBITS	CREDITS
Salaries	103,529	
Supplies	21,720	
Service Contracts	66,957*	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***192,206***	
FY22 Internal Recoveries		31,533
FY22 External Recoveries		0
TOTAL CREDITS		***31,533***
Income / (Subsidy)	(160,673)	
State Appropriation	9,598	
Net Income / (Subsidy)	**(151,075)**	

*Service contracts/maintenance expenditures included BD Biosciences (through Specialty Underwriters) invoices, which totaled $39,957 and Bio-Rad Laboratories, which totaled $27,000 for FY22.

Subsidy, % before state appropriation 84%
Subsidy, % after state appropriation 79%

Research Histology Core (RHC) Institutional Research Core Facility Analysis Report- FY22

Written by Natalie Smith, MS and Tiffany Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?

The RHC core designation as an institutional core is appropriate since it served 23 UTHSC laboratories across 10 departments and three colleges (COM, COP and COD).

2. Does the core pass the multi-departmental, multi-investigator litmus test?

Yes. In FY22, this core processed 3,750 service item requests for 23 unique laboratories across 10 departments and three colleges (COM, COP and COD). There were five unique users in the departments of Physiology, Pediatrics and Pharmaceutical Sciences. The top five users, based on the percentage of invoiced service requests were: 1) Dr. Amandeep Bajwa (Pediatrics, COM, 19.9%), 2) Dr. Gabor Tigyi (Physiology, COM, 9.57%), 3) Dr. Wei Li (Pharmaceutical Sciences, COP, 7.57%), 4) Dr. Bernd Meibohm (Pharmaceutical Sciences, COP, 7.44%) and 5) Dr. Joseph Pierre (Pediatrics, COM, 5.93%). The other 18 users accounted for the remaining 49.59% of invoices for completed projects.

3. Is there sufficient intra- and inter-departmental use and if not, why?

Yes, 23 unique users were served across multiple departments and three colleges.

4. Can the services for the core be outsourced more economically?

No. The service fee structure is very competitive relative to other similar academic cores in our region (UTHSC is in the bottom quartile), or to commercial vendors. In addition, shipment of grossed specimens in either ethanol-based or formaldehyde solutions to outside vendors for tissue processing is highly regulated and requires unique shipping and handling compliance and recordkeeping, which can be burdensome and expensive.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting? (e.g., grants funded through investigator use, publications, etc.)?

Yes. In FY22, core activities led to 46 publications and supported 14 grants or contracts. In addition, Ms. Natasha Jones, University Clinical Health manager, provided expert consultation on project design at no cost to the investigators.

6. Is the core currently self-sufficient or is it subsidized by the institution?

In FY22, the core was subsidized by the institution; the net subsidy after state appropriation was $37,466 (56.0%).

Accomplishments this past year:

- The RHC continued its fourth full year of operation as a partnership between the Office of Research and the Department of Pathology/UCH, supporting 23 unique internal laboratories.
- Expenses decreased in FY22 relative to all prior FY periods.
- The core supported 46 publications and 14 extramural grant awards/contracts.

Financial Overview – FY22:

TOTALS	FY18	FY19	FY20	FY21	FY22
Revenues*	19,663	11,018	24,136	23,568	13,261
Expenses**	(94,718)	(129,931)	(75,345)	(79,927)	(67,373)
Income (Subsidy)	(75,055)	(118,913)	(51,209)	(56,359)	(54,112)
Other Costs	0	0	0	0	0
Income (Subsidy)	(75,055)	(118,913)	(51,209)	(56,359)	(54,112)
State Appropriation	18,434	0	0	12,045	16,646
Net Income (Subsidy)	(56,621)	(118,913)	(51,209)	(44,314)	(37,466)
Subsidy, % before State Appropriation	79%	91%	68%	71%	80%
Subsidy, % after State Appropriation	60%	91%	68%	55%	56%

*Revenues after 50:50 share with UCH per the negotiated MOU.
**Includes salary support for the UCH-based histotechnician and 50% of the total expenses for supplies and equipment maintenance, after pro-rating with UCH based on the volume of research-specific projects.

7. Suggested outcomes:
It is recommended that RHC continue as an institutional core.

Research Histology Core (RHC) Institutional Core Facility
Summary of Institutional Core Activities for FY 2022

Written by Natalie Smith, MS and Tiffany Seagroves, PhD

I. PUBLICATIONS

Full-length published articles (UTHSC faculty investigators invoiced by the core are indicated in bold)

Kumar V, Kiran S, Kumar S, **Singh UP**. Extracellular vesicles in obesity and its associated inflammation. Int Rev Immunol. 2022;41(1):30-44. doi:10.1080/08830185.2021.1964497. Epub 2021 Aug 23. PMID: 34423733; PMCID:PMC8770589.

Zhang L, Hu J, Meshkat BI, Liechty KW, **Xu J**. LncRNA MALAT1 Modulates TGF-β1-Induced EMT in Keratinocyte. Int J Mol Sci. 2021 Oct 30;22(21):11816.doi: 10.3390/ijms222111816. PMID: 34769245; PMCID: PMC8584148.

Pabla N, **Bajwa A**. Role of Mitochondrial Therapy for Ischemic-Reperfusion Injury and Acute Kidney Injury. Nephron. 2022;146(3):253-258. doi:10.1159/000520698. Epub 2021 Dec 9. PMID: 34883481; PMCID: PMC9090938.

Kumari R, Irudayam MJ, Al Abdallah Q, Jones TL, Mims TS, Puchowicz MA, **Pierre JF**, **Brown CW**. SMAD2 and SMAD3 differentially regulate adiposity and the growth of subcutaneous white adipose tissue. FASEB J. 2021 Dec;35(12):e22018. doi:10.1096/fj.202101244R. PMID: 34731499.

Sumida K, Han Z, Chiu CY, Mims TS, **Bajwa A**, Demmer RT, Datta S, Kovesdy CP, **Pierre JF**. Circulating Microbiota in Cardiometabolic Disease. Front Cell Infect Microbiol. 2022 May 3;12:892232. doi: 10.3389/fcimb.2022.892232. PMID: 35592652;PMCID: PMC9110890.

Hama T, Nagesh PK, Chowdhury P, Moore BM 2nd, Yallapu MM, Regner KR, **Park F**. DNA damage is overcome by TRIP13 overexpression during cisplatin nephrotoxicity. JCI Insight. 2021 Nov 22;6(22):e139092. doi: 10.1172/jci.insight.139092. PMID:34806647; PMCID: PMC8663775.

Pierre JF, Phillips GJ, Chandra LC, Rendina DN, Thomas-Gosain NF, Lubach GR, Lyte M, Coe CL, Gosain A. Lyticase Facilitates Mycobiome Resolution Without Disrupting Microbiome Fidelity in Primates. J Surg Res. 2021 Nov;267:336-341.doi: 10.1016/j.jss.2021.06.023. Epub 2021 Jun 26. PMID: 34186310; PMCID:PMC8678161.

Chen K, **Sun Z**. Estrogen inhibits renal Na-Pi Co-transporters and improves klotho deficiency-induced acute heart failure. Redox Biol. 2021 Nov;47:102173.doi: 10.1016/j.redox.2021.102173. Epub 2021 Oct 18. PMID: 34678656; PMCID:PMC8577443.

Singla B, Aithabathula RV, Kiran S, Kapil S, Kumar S, **Singh UP**. Reactive Oxygen Species in Regulating Lymphangiogenesis and Lymphatic Function. Cells.2022 May 26;11(11):1750. doi: 10.3390/cells11111750. PMID: 35681445; PMCID:PMC9179518.

Xu F, Gao J, Orgil BO, Bajpai AK, Gu Q, Purevjav E, Davenport AS, Li K, Towbin JA, Black DD, **Pierre JF**, Lu L. Ace2 and Tmprss2 Expressions Are Regulated by Dhx32 and Influence the Gastrointestinal Symptoms Caused by SARS-CoV-2. J Pers Med. 2021 Nov 16;11(11):1212.

doi: 10.3390/jpm11111212.PMID: 34834564; PMCID: PMC8621576.

Suthon S, Lin J, Perkins RS, Crockarell JR Jr, Miranda-Carboni GA, **Krum SA**. Estrogen receptor alpha and NFATc1 bind to a bone mineral density-associated SNP to repress WNT5B in osteoblasts. Am J Hum Genet. 2022 Jan 6;109(1):97-115. doi:10.1016/j.ajhg.2021.11.018. Epub 2021 Dec 13. PMID: 34906330; PMCID: PMC8764205.

Kiran S, Rakib A, **Singh UP**. The NLRP3 Inflammasome Inhibitor Dapansutrile Attenuates Cyclophosphamide-Induced Interstitial Cystitis. Front Immunol. 2022Jun 3;13:903834. doi: 10.3389/fimmu.2022.903834. PMID: 35720309; PMCID:PMC9205468.

Xue Y, Yang D, Vogel P, Stabenow J, Zalduondo L, Kong Y, Ravi Y, Sai-Sudhakar CB, Parvathareddy J, Hayes E, Taylor S, **Fitzpatrick E**, Jonsson CB. Cardiopulmonary Injury in the Syrian Hamster Model of COVID-19. Viruses. 2022Jun 27;14(7):1403. doi: 10.3390/v14071403. PMID: 35891384; PMCID: PMC9316644.

Albadari N, Deng S, Chen H, Zhao G, Yue J, Zhang S, Miller DD, Wu Z, **Li W**. Synthesis and biological evaluation of selective survivin inhibitors derived from the MX-106 hydroxyquinoline scaffold. Eur J Med Chem. 2021 Nov15;224:113719. doi: 10.1016/j.ejmech.2021.113719. Epub 2021 Jul 30. PMID:34371464; PMCID: PMC8511083.

Kumar A, Sinha N, Kodidela S, Zhou L, **Singh UP**, Kumar S. Effect of benzo(a)pyrene on oxidative stress and inflammatory mediators in astrocytes and HIV-infected macrophages. PLoS One. 2022 Oct 14;17(10):e0275874. doi:10.1371/journal.pone.0275874. PMID: 36240258; PMCID: PMC9565757.

Myers LK, Winstead M, Kee JD, Park JJ, Zhang S, **Li W**, Yi AK, Stuart JM, Rosloniec EF, Brand DD, Tuckey RC, Slominski AT, Postlethwaite AE, Kang AH.1,25-Dihydroxyvitamin D3 and 20-Hydroxyvitamin D3 Upregulate LAIR-1 and Attenuate Collagen Induced Arthritis. Int J Mol Sci. 2021 Dec 12;22(24):13342.doi: 10.3390/ijms222413342. PMID: 34948139; PMCID: PMC8709360.

Peixoto-Neves D, Kanthakumar P, Kumar R, Soni H, **Adebiyi A**. Loss of urotensin II receptor diminishes hyperglycemia and kidney injury in streptozotocin-treated mice. J Mol Endocrinol. 2022 Mar 25;68(3):167-178. doi:10.1530/JME-21-0199. PMID: 35244607; PMCID: PMC9334220.

Wu Y, Yang D, **Chen GY**. The role of the Siglec-G ITIM domain during bacterial infection. Cell Mol Biol (Noisy-le-grand). 2022 Jan 2;67(4):163-169. doi:10.14715/cmb/2021.67.4.18. PMID: 35809291.

Jha KA, Rasiah PK, Gentry J, Del Mar NA, Kumar R, **Adebiyi A**, Reiner A, **Gangaraju R**. Mesenchymal stem cell secretome protects against oxidative stress-induced ocular blast visual pathologies. Exp Eye Res. 2022 Feb;215:108930. doi:10.1016/j.exer.2022.108930. Epub 2022 Jan 10. PMID: 35016886.

Bhuniya R, Yuan X, Bai L, Howie KL, Wang R, **Li W**, **Park F**, Yang CY. Design, Synthesis, and Biological Evaluation of Apcin-Based CDC20 Inhibitors. ACS Med Chem Lett. 2022 Jan 18;13(2):188-195. doi: 10.1021/acsmedchemlett.1c00544. PMID:35178174; PMCID: PMC8842116.

Xu J, Hu J, Idlett-Ali S, Zhang L, Caples K, Peddibhotla S, Reeves M, ZgheibC, Malany S, Liechty KW. Discovery of Small Molecule Activators of Chemokine Receptor CXCR4 That Improve Diabetic Wound Healing. Int J Mol Sci. 2022 Feb16;23(4):2196. doi: 10.3390/ijms23042196. PMID: 35216311; PMCID: PMC8879702.

Wu Y, Yang D, **Chen GY**. Targeted disruption of Gdi2 causes early embryonic lethality. Placenta. 2022 Aug;126:17-25. doi: 10.1016/j.placenta.2022.05.005.Epub 2022 May 13. PMID: 35689892.

Krutilina RI, Playa H, Brooks DL, Schwab LP, Parke DN, Oluwalana D, Layman DR, Fan M, Johnson DL, Yue J, Smallwood H, **Seagroves TN**. HIF-Dependent CKB Expression Promotes Breast Cancer Metastasis, Whereas Cyclocreatine Therapy Impairs Cellular Invasion and Improves Chemotherapy Efficacy. Cancers (Basel).2021 Dec 22;14(1):27. doi: 10.3390/cancers14010027. PMID: 35008190; PMCID:PMC8749968.

Lin Y, **Sun Z**. Klotho deficiency-induced arterial calcification involves osteoblastic transition of VSMCs and activation of BMP signaling. J Cell Physiol. 2022 Jan;237(1):720-729. doi: 10.1002/jcp.30541. Epub 2021 Aug 8. PMID:34368951; PMCID: PMC8810603.

Shukla PK, Meena AS, **Pierre JF**, Rao R. Central role of intestinal epithelial glucocorticoid receptor in alcohol- and corticosterone-induced gut permeability and systemic response. FASEB J. 2022 Jan;36(1):e22061. doi:10.1096/fj.202101424R. PMID: 34861075; PMCID: PMC8647846.

Nagib MM, Zhang S, Yasmen N, Li L, Hou R, Yu Y, Boda VK, Wu Z, **Li W**, Jiang J. Inhibition of TRPC3 channels by a novel pyrazole compound confers antiseizure effects. Epilepsia. 2022 Apr;63(4):1003-1015. doi: 10.1111/epi.17190. Epub 2022Feb 18. PMID: 35179226; PMCID: PMC9007831.

Munkhsaikhan U, Kwon Y, Sahyoun AM, Ait-Aissa K, Kassan A, **Kassan M**. The microsomal triglyceride transfer protein inhibitor lomitapide improves vascular function in mice with obesity. Obesity (Silver Spring). 2022 Apr;30(4):893-901.doi: 10.1002/oby.23389. Epub 2022 Mar 6. PMID: 35253407; PMCID: PMC8957593.

Yoon TW, **Fitzpatrick EA**, Snyder JD, Lee S, Kim YI, Zacheaus C, Yi AK. Contribution of Protein Kinase D1 on Acute Pulmonary Inflammation and Hypersensitivity Pneumonitis Induced by Saccharopolyspora rectivirgula. Immunohorizons. 2022 Mar 10;6(3):224-242. doi: 10.4049/immunohorizons.2200017.PMID: 35273098.

Trebska-McGowan K, Chaib M, Alvarez MA, Kansal R, Pingili AK, Shibata D, **Makowski L**, Glazer ES. TGF-β Alters the Proportion of Infiltrating Immune Cells in a Pancreatic Ductal Adenocarcinoma. J Gastrointest Surg. 2022Jan;26(1):113-121. doi: 10.1007/s11605-021-05087-x. Epub 2021 Jul 14. PMID:34260016.

Meena AS, Shukla PK, Bell B, Giorgianni F, Caires R, Fernández-Peña C, Beranova S, Aihara E, Montrose MH, Chaib M, **Makowski L**, Neeli I, Radic MZ, Vásquez V, Jaggar JH, Cordero-Morales JF, Rao R. TRPV6 channel mediates alcohol-induced gut barrier dysfunction and systemic response. Cell Rep. 2022 Jun14;39(11):110937. doi: 10.1016/j.celrep.2022.110937. PMID: 35705057; PMCID:PMC9250449.

Agrawal M, Rasiah PK, **Bajwa A**, Rajasingh J, **Gangaraju R**. Mesenchymal Stem Cell Induced Foxp3(+) Tregs Suppress Effector T Cells and Protect against Retinal Ischemic Injury. Cells. 2021 Nov 4;10(11):3006. doi:10.3390/cells10113006. PMID: 34831229; PMCID: PMC8616393.

Kiran S, Rakib A, Moore BM, **Singh UP**. Cannabinoid Receptor 2 (CB2) Inverse Agonist SMM-189 Induces Expression of Endogenous CB2 and Protein Kinase A That Differentially Modulates the Immune Response and Suppresses Experimental Colitis. Pharmaceutics. 2022 Apr 26;14(5):936. doi:10.3390/pharmaceutics14050936. PMID: 35631522; PMCID: PMC9147685.

Merigeon EY, Yang D, Ihms EA, Bassit LC, **Fitzpatrick EA**, Jonsson CB, Schinazi RF, Block DS, Olsen HS. An ACE2-IgG4 Fc Fusion Protein Demonstrates Strong Binding to All Tested SARS-CoV-2 Variants and Reduced Lung Inflammation in Animal Models of SARS-CoV-2 and Influenza. Pathog Immun. 2022 Aug23;7(1):104-121. doi: 10.20411/pai.v7i1.491. PMID: 36072571; PMCID: PMC9438944.

Dacheux MA, Lee SC, Shin Y, Norman DD, Lin KH, E S, Yue J, Benyó Z, **Tigyi GJ**. Prometastatic Effect of ATX Derived from Alveolar Type II Pneumocytes andB16-F10 Melanoma Cells. Cancers (Basel). 2022 Mar 21;14(6):1586. doi:10.3390/cancers14061586. PMID: 35326737; PMCID: PMC8946623.

Guo H, Zhang W, Wang J, Zhao G, Wang Y, Zhu BM, Dong P, Watari H, Wang B, **LiW**, **Tigyi G**, Yue J. Cryptotanshinone inhibits ovarian tumor growth and metastasis by degrading c-Myc and attenuating the FAK signaling pathway. Front Cell Dev Biol. 2022 Sep 28;10:959518. doi: 10.3389/fcell.2022.959518. PMID: 36247016;PMCID: PMC9554091.

Kiran S, Rakib A, Kodidela S, Kumar S, **Singh UP**. High-Fat Diet-Induced Dysregulation of Immune Cells Correlates with Macrophage Phenotypes and Chronic Inflammation in Adipose Tissue. Cells. 2022 Apr 13;11(8):1327. doi:10.3390/cells11081327. PMID: 35456006; PMCID: PMC9031506.

Suthon S, Perkins RS, Lin J, Crockarell JR Jr, Miranda-Carboni GA, **Krum SA**.GATA4 and estrogen receptor alpha bind at SNPs rs9921222 and rs10794639 tor egulate AXIN1 expression in osteoblasts. Hum Genet. 2022 Jun 9. doi:10.1007/s00439-022-02463-8. Epub ahead of print. PMID: 35678873.

Liu X, Zhao G, Huo X, Wang Y, **Tigyi G**, Zhu BM, Yue J, Zhang W. Adipose-Derived Stem Cells Facilitate Ovarian Tumor Growth and Metastasis by Promoting Epithelial to Mesenchymal Transition Through Activating the TGF-β Pathway. Front Oncol. 2021 Dec 22;11:756011. doi: 10.3389/fonc.2021.756011. PMID: 35004276;PMCID: PMC8727693.

Peixoto-Neves D, Kanthakumar P, Afolabi JM, Soni H, Buddington RK, **Adebiyi** A. KV7.1 channel blockade inhibits neonatal renal autoregulation triggered by a step decrease in arterial pressure. Am J Physiol Renal Physiol.2022 Feb 1;322(2):F197-F207. doi: 10.1152/ajprenal.00568.2020. Epub 2022 Jan 10.PMID: 35001664; PMCID: PMC8816635.

Rana M, Kansal R, Chaib M, Teng B, Morrrison M, Hayes DN, Stanfill AG, Shibata D, Carson JA, **Makowski L**, Glazer ES. The pancreatic cancer immune tumor microenvironment is negatively remodeled by gemcitabine while TGF-β receptor plus dual checkpoint inhibition maintains antitumor immune cells. Mol Carcinog.2022 Jun;61(6):549-557. doi: 10.1002/mc.23401. Epub 2022 Mar 23. PMID: 35319799.

Kassan A, Ait-Aissa K, **Kassan M**. Gut Microbiota Regulates the Sympathetic Nerve Activity and Peripheral Serotonin Through Hypothalamic MicroRNA-204 in Order to Increase the Browning of White Adipose Tissue in Obesity. Cureus. 2022Feb 4;14(2):e21913. doi: 10.7759/cureus.21913. PMID: 35155042; PMCID:PMC8820388.

Slayden AV, Dyer CL, Ma D, **Li W**, Bukiya AN, Parrill AL, Dopico AM. Discovery of agonist-antagonist pairs for the modulation of Ca[2]+ and voltage-gated K+ channels of large conductance that contain beta1subunits. Bioorg Med Chem. 2022 Aug 15;68:116876. doi:10.1016/j.bmc.2022.116876. Epub 2022 Jun 13. PMID: 35716586.

Swanson ML, Regner KR, Moore BM, **Park F**. Cannabinoid Type 2 Receptor Activation Reduces the Progression of Kidney Fibrosis Using a Mouse Model of Unilateral Ureteral Obstruction. Cannabis Cannabinoid Res. 2022 Feb 23. doi:10.1089/can.2021.0127. Epub ahead of print. PMID: 35196117.

Chen K, Wang S, **Sun Z**. In Vivo Cardiac-specific Expression of Adenylyl Cyclase 4 Gene Protects against Klotho Deficiency-induced Heart Failure. Transl Res. 2022 Jun;244:101-113. doi: 10.1016/j.trsl.2022.01.006. Epub 2022 Jan 31.PMID: 35114419; PMCID: PMC9119924.

Chaib M, Sipe LM, Yarbro JR, Bohm MS, Counts BR, Tanveer U, Pingili AK, Daria D, Marion TN, Carson JA, Thomas PG, **Makowski L**. PKC agonism restricts innate immune suppression, promotes antigen cross-presentation and synergizes with agonistic CD40 antibody therapy to activate CD8⁺ T cells in breast cancer. Cancer Lett. 2022 Apr 10;531:98-108. doi:10.1016/j.canlet.2022.01.017. Epub 2022 Jan 21. PMID: 35074498.

Han X, **Sun Z**. Adult Mouse Kidney Stem Cells Orchestrate the De Novo Assembly of a Nephron via Sirt2-Modulated Canonical Wnt/β-Catenin Signaling. Adv Sci (Weinh). 2022 May;9(15):e2104034. doi: 10.1002/advs.202104034. Epub 2022 Mar 22.PMID: 35315252; PMCID: PMC9130916.

II. PRESENTATIONS GIVEN TO PROMOTE CORE RESOURCES AND CORE USAGE

No presentations were given in FY22.

III. SUMMARY OF ACTIVITIES

A. Personnel

Medical Director: Due to clinical staff turnover, there is currently no medical director oversight of the research-only specimens.

Laboratory Manager: Ms. LaShwan Barnett was replaced by Ms. Natasha Jones, who is the direct contact for investigators to arrange core services. She is directly involved in processing research specimens and interacts with core customers during sample drop-off and pickup. She is also available for consultation regarding experimental design for preparing specimens for routine histology services.

Administrative Manager: Mr. Tim Hodge supervises the personnel and the operating budget related to clinical pathology services for University Clinical Health (UCH). He is a full-time employee of UCH.

Histotechnician: The equivalent of one half-time (50% effort) UCH employee is provided by the Office of Research to support research services for the RHC services within the UCH pathology clinical laboratory. Several histotechnicians rotate to complete research projects.

B. Oversight Committee

The following faculty were members of the FY22 Research Histology Core Internal Advisory Board:

Gustavo Miranda-Carboni (Medicine)
Elena Parfenova (Physiology)
RK Rao (Physiology)

C. Equipment and Service Contracts

All equipment maintained by the core is owned by UCH. Per the current contract agreement with UCH, UTHSC shares the costs of equipment maintenance agreements in a 50:50 split with UCH, after maintenance costs are first pro-rated for the fraction of completed research-based projects.

D. Usage Volumes by service request type

Service	FY18*	FY19**	FY20**	FY21**	FY22**
Blocks/Embed, paraffin	550	1,623	2,267	1,982	1,104
Sectioned slides, paraffin	3,091	2,773	3,628	4,467	1,856
H&E stain, paraffin	802	627	1,241	911	672
Sectioned slides, cryosection	383	1,062	0	0	60
H&E stain, cryosection	N.R.	22	0	0	0
Level I-II special stains	N.R.	118	88	47	51

N.R.: not previously reported
*Data collected from paper submission forms
**Data collected from the iLab core management software system

In addition to these fee-for-service options, the core trains researchers to properly employ histology and molecular pathology approaches through consultation. The following services are provided at no charge:

A) Consultation with investigators and their staff on proposed experimental design for histopathology services
B) Boilerplate language for histology core facilities and resources for grant applications
C) Letters of support, including estimated costs of core usage for grant submissions

Overall usage of the core lab:

The core processed 3,750 service units on behalf of 23 total UTHSC laboratories across eight departments and three colleges in FY22 (COM, COP, COD).

UTHSC departments that requested services FY22:

College of Medicine:

Medicine:	1 investigator
MIB:	1 investigator
Ophthalmology:	1 investigator
Orthopaedic Surgery:	2 investigators
Pediatrics:	5 investigators
Pathology:	1 investigator
Physiology:	5 investigators
Transplant Biology:	1

COP:
Pharmaceutical Sciences: 5 investigators

COD:
Biosciences Research: 1 investigator

E. Fee Structure, FY22

The RHC core offers the following services, which are priced in the bottom-quarter to bottom-third relative to peer academic institutions that offer similar histopathology services.

Paraffin Blocks and Slides:	
Processing without paraffin embedding:	$2.82/cassette
Processing and paraffin embedding:	$3.38/block
Unstained slides, paraffin block:	$2.82/slide
Recut of previously faced paraffin block:	$2.82/slide
H&E-staining of cut slides:	$3.94/slide
Frozen Embedded Sections:	
Unstained, cryosectioned slide:	$5.62/slide
H&E-staining of cryosectioned slide:	$3.94/slide
Special Stains:	Begin at $16.88/slide
Extended consult with core manager:	Please inquire

Applies to non-routine, continuing consultations or to special projects consultation to prepare histology projects. Consultation related to experimental design should occur by appointment with the core manager prior to sample submission; the initial consultation is available at no charge.

Referrals for histopathology:
Consultation for histopathology analysis of prepared samples should be arranged by contacting the Department of Pathology and requesting a referral to a pathologist through the department chair. The Department of Pathology also maintains a digital slide scanner for archiving slide images.

IV. GRANTS SUPPORTED BY THE CORE, FY22

Adebiyi, Adebowale
USPHS NIH Grant R01 DK-120595, Vascular ion channels and microcirculation in neonatal urinary tract obstruction

Chen, Guoyun
USPHS NIH Grant AI-137255, Targeting Siglec-9/E for therapy of sepsis

Gu, Weikuan
Tiantan Hospital Agreement, Center of Integrating Genomics and Bioinformatics for International Study of Stroke (CIGB-ISS)

Kassan, Modar
USPHS NIH Grant HI-150360, MiR-204 regulates type 1 IP3R/Ca2+ axis to control

vascular smooth muscle cell contractility and blood pressure: Potential role of the gut microbiome

Johnson, Rajasingh
USPHS NIH Grant HL-141345, scaRNA Modified Induced Pluripotent Stem Cell-Derived Cardiomyocytes or Exosomes Therapy for Chronic Ischemic Cardiomyopathy Patient

Jonsson, Colleen
USPHS NIH Grant AI-142762, Center of Excellence for Encephalitic Alphavirus Therapeutics [CEEAT]

Makowski, Liza
USPHS NIH Grant CA-253329, Role of microbial-modulated bile acid receptor signaling in breast cancer

Seagroves, Tiffany
Army Grant W81XWH2010019, Discovery of Orally Bioavailable Tubulin Inhibitors to Overcome Taxane Resistance in Metastatic Breast Cancer

Singh, Udai
USPHS NIH Grant AI-140405, Adipose T cell microRNAs (miRs) regulate macrophage function during obesity

Sun, Zhongjie
USPHS NIH Grant AG-049780, Investigation into Heart Aging

USPHS NIH Grant AG-062375, Epigenetic Regulation of Kidney Function and Blood Pressure

Tigyi, Gabor

University of Maryland Subcontract to USPHS NIH Grant AI-150574, Intercollaborative Radiation Countermeasure (INTERACT) Consortium for Advanced Development of Medical Countermeasures to Mitigate/Treat Acute and Delayed Radiation Syndromes

USPHS NIH Grant CA-092160, Anticancer Strategies Targeting the Autotaxin-LPA Receptor Axis

Xu, Junwang
USPHS NIH Grant GM-128660, The role of long non-coding RNA GAS5 in diabetic wounds

V. BUSINESS DEVELOPMENT

A. Market Assessment

The market for core services includes investigators who use research animals at UTHSC, Le Bonheur and the surrounding Memphis area. Investigators who currently do not use the RHC either pay for their own staff to prepare histology specimens, they use outside vendors such as LabCorp, or they use services offered by Methodist University Hospital pathology unit, which directly negotiates with investigators to provide research pathology services at a higher discounted rate than available at the RHC institutional core.

B. Marketing Plans to Obtain New Business

The focus of marketing for the RHC core in FY23 will be to continue to expand the core customer base throughout Memphis and the UTHSC system. The core will continue to participate in events sponsored by the Office of Research, and will develop marketing materials with Lee Ferguson. Dr. Seagroves will also work with Lee to create the RHC core website and to point to the RHC from the Department of Pathology website.

C. Forecasted Volumes for New Business

The core increased pricing for all services by 3% for the FY22 period. The rate structure, effective July 1, 2019, continued to place UTHSC in the bottom-quarter to bottom-third of peer institutions that offer histology services. Overall, FY22 total revenues ($13,261) decreased relative to FY21 ($23,568) because fewer total specimens were paraffin-embedded and sectioned (~50% decrease in services in FY22 vs. FY21). However, the number of laboratories served increased from 20 in FY21 to 23 in FY22. Notably, several key users return to the RHC FY over FY, such as Dr. Bajwa. In FY23, it is projected that core use will increase relative to FY22 levels due to the increase in the number of awarded grants and contracts, and the record number of mouse cages housed in the LACU in FY22 (since animal specimens are the bulk of research samples processed).

VI. Actual Budget – FY22: (July 1, 2021 to June 30, 2022)

FY2022	DEBITS	CREDITS
Salaries	47,964	
Supplies	19,409	
Service Contracts	0	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***67,373***	
FY22 Internal Recoveries		13,261
FY22 External Recoveries		0
TOTAL CREDITS		***13,261***
Income / (Subsidy)	(54,112)	
State Appropriation	16,646	
Net Income / (Subsidy)	**(37,466)**	

*After cost-sharing of expenses (50:50) and crediting of shared recoveries (50:50) with UCH, applied to the supplies budget category.

Subsidy, before state appropriation, %	80
Subsidy, after state appropriation, %	56

Advanced Imaging Core (AIC) Institutional Research Core Facility Analysis Report FY22

Written by Rachel Escue Helms, PhD; Natalie Smith, MS; and Tiffany N. Seagroves, PhD

1. Relative to a specific core's mission, is the designation as an "institutional core" appropriate?
The Advanced Imaging Core designation as an institutional core is appropriate since it served five labs within two departments (Physiology and Pharmacology). However, only one college was served by the AIC, the College of Medicine.

2. Does the core pass the multi-departmental, multi-investigator litmus test?
Yes. In FY22, the AIC completed over 200 hours of training, consultations, and imaging for seven unique users across two departments on campus. However, six of seven users are affiliated with the Department of Physiology and all users are affiliated with the College of Medicine.

3. Is there sufficient intra- and inter-departmental use and if not, why?
No. The current revenues for AIC indicate that 90% of core revenue is attributed to a single department, Physiology. Word of mouth from Physiology users has increased use in FY22 over FY21 levels. There were several technical issues with the instruments/software over FY22. The Elyra has experienced recurring issues with laser attenuation and image resolution that were recently resolved. To take advantage of on-site Zeiss field support to diagnose equipment issues, Dr. Helms had invited multiple confocal users on campus to test their samples on the Elyra at no charge during equipment testing.

4. Can the services for the core be outsourced more economically?
No. AIC service fees are already within the bottom-half to bottom-third of average pricing for similar services at peer institutions, and the AIC is the only facility in the Memphis area offering these single molecule resolution microscopy with the Elyra 7 equipment.

5. Are there unaccounted benefits beyond fiscal consideration to warrant continued institutional underwriting? (e.g., grants funded through investigator use, publications, etc.)?
Yes. Since opening in January of 2021, images and data generated by the core have led to the funding of two grant applications and the publication of one manuscript for the Jaggar laboratory. The core has also submitted letters of support for pending grant applications.

6. Is the core currently self-sufficient or is it subsidized by the Institution?
In FY22, the AIC was subsidized by the institution. The subsidy required was 90%.

Accomplishments this past year:

- Dr. Rachel Helms traveled to the ABRF annual conference to represent the AIC.
- Four new users were trained to independently use the Elyra 7 and associated software.
- Two grant applications including data generated in the AIC were funded.

Financial Overview – FY22:

TOTALS	FY21*	FY22
Revenues	5,080	11,785
Expenses	(481,567)	(120,922)
Income (Subsidy)	(476,487)	(109,137)
Other Costs	0	0
Income (Subsidy)	(476,487)	(109,137)
State Appropriation	18,586	2,418
Net Income (Subsidy)	(457,901)	(106,719)
Subsidy, % before State Appropriation	99%	90%
Subsidy, % after State Appropriation	95%	88%

*The AIC opened in Q2 of FY21.

7. Suggested outcomes:

It is recommended that the AIC continue as an institutional core in FY23. It is also recommended that the budget for the AIC be adjusted to account for the actual operating expenses, since the FY22 state appropriation ($2,418) was grossly insufficient to subsidize recurring operating expenses. However, if use of the core does not continue to increase in FY23/FY24, it may be more appropriate to designate the AIC as a college- or department-based core facility.

Advanced Imaging Core (AIC) Institutional Core Facility
Summary of Institutional Core Activities for FY 2022

Written by Rachel Escue Helms, PhD; Natalie Smith, MS; and Tiffany N. Seagroves, PhD

I. PUBLICATIONS

MacKay CE, Floen M, Leo MD, Hasan R, Garrud TAC, Fernández-Peña C, Singh, P, Malik, KU and **Jaggar JH**. **2022.** A plasma membrane-localized polycystin-1/polycystin-2 complex in endothelial cells elicits vasodilation. eLife 2022 Mar 1;11:e74765. doi: 10.7554/eLife.74765. PMID: 35229718.

II. SUMMARY OF ACTIVITIES

A. Personnel

Microscopy Manager: Rachel Escue Helms, PhD, staff (100% effort)
Dr. Helms supervises all core activities, including consultations with new users and experimental design, training on the microscope systems, imaging of user samples, data analysis, equipment maintenance, SOP and guide writing, and service request scheduling and billing.

B. AIC Internal Advisory Board

The following faculty were members of the FY22 Advanced Imaging Core Internal Advisory Board (IAB):

John Cox (Microbiology, Immunology &l Biochemistry)
TJ Hollingsworth (Opthalmology)
Jonathan Jaggar (Physiology)
Tony Marion (Microbiology, Immunology & Biochemistry)
Wen Lin Sun (Pharmacology)

C. Equipment

FY22 equipment located in the AIC lab space

Equipment	Cost	Funding Source/Purchase FY
Zeiss Elyra 7 (LS)/ Axio Observer	$644,023	Office of Research funding/ FY21
Miltenyi Biotec Ultramicroscope II, Light Sheet Fluorescence Microscopy (LSFM)	$194,159	VCR startup funding/ FY18

D. Service Contracts

The Elyra system is maintained by a service contract with Carl Zeiss Microscopy, ($39,054.12). The LSFM system is not currently under service contract due to low volume of use.

E. Usage Volumes by Service Request Type

Service	Revenue	Service Requests	Units (hrs)
Unassisted Imaging by Trained Users	$ 7,380.00	54	135.25
Assisted Imaging	$ 1,560.00	7	19.50
Workstation – Trained Users	$ 1.065.00	28	39.50
Assisted Workstation Use	$ 140.00	1	1.75
Consultation	$ 200.00	2	4
Training	$ 1,440.00	7	18.00
TOTAL	**$ 11,785.00**	**99**	**216**

*Consultation fees are initially paid by the user at the time of consultation and then credited back towards future imaging experiments.

Usage by Lab

Lab	Total Revenue	Percent of Total Use
Jaggar, Jonathan (UTHSC) Lab	$11,015	93.5%
Adebiyi, Adebowale (UTHSC) Lab	$ 350	3.0%
Sun, Zhongjie (UTHSC) Lab	$ 220	1.9%
Mancarella, Salvatore (UTHSC) Lab	$ 100	0.8%
Vaithianathan, Thirumalini (UTHSC) Lab	$ 100	0.8%

F. Multi-year Trends

PI	(Department, College)	FY21 (Q2-Q4)	FY22
Zhou, Q.	Medicine, COM	$1,070.00	
Cox, J.	MIB, COM	$ 480.00	
Vaithianathan, T.	Pharmacology, COM		$ 100.00
Adebiyi, A.	Physiology, COM		$ 350.00
Jaggar, J.	Physiology, COM	$3,130.00	$11,015.00
Mancarella, S.	Physiology, COM		$ 100.00
Parfenova, E.	Physiology, COM	$ 80.00	
Sun, Z.	Physiology, COM	$ 320.00	$ 220.00
	TOTAL	**$5,080.00**	**$11,785.00**

G. Fee Structure FY22

Note: As the AIC opened during Q2 of FY21, prices were not increased for FY22.

Zeiss Elyra 7 Super Resolution Microscopy (SRM) Unit

Initial consultation*:	$100.00/consult
Follow-up extended consultations:	$125.00/hour
Initial training:	$80.00/hour/user
Imaging:	
Imaging of fixed specimens by trained users:	$40.00/hour
Live-imaging of specimens by trained users:	$50.00/hour
Imaging of fixed specimens by core manager:	$80.00/hour
Live-imaging of prepared specimens by core manager:	$100.00/hour
Data analysis on dedicated workstations (ZEN Black software):	
Unassisted data analysis on the workstation:	$15/hour
Assisted data analysis on the workstation:	$80/hour

LaVision Ultramicroscope II Light Sheet Fluorescence Microscopy (LSFM) Unit

Initial consultation:	$150.00/consult
Follow-up consultations:	$125.00/hour
Initial training:	$250.00/new user
Imaging:	
Imaging of prepared specimens by trained users:	$30.00/hour
Imaging of prepared specimens with core assistance:	$80.00/hour
Data analysis:	
Assisted data analysis with core staff:	$100.00/hour

III. GRANTS SUPPORTED BY THE CORE, FY22

Adebiyi, Adebowale

USPHS NIH Grant DK-127626, Urotensin II and renal insufficiency in growth-restricted infants.

Jaggar, Jonathan
USPHS NIH Grant HL-133256, Blood pressure regulation by smooth muscle cell ion channels

Mancarella, Salvatore
USPHS NIH Grant HL-153638, Defining the roles of Orai3 channel in cardiomyocytes and cardiomyopathy.

Mata Daboin, Alejandro
American Heart Association, HA834834, Blood pressure regulation by endothelial cell TMEM16A channels

Sun, Zhongjie
USPHS NIH Grant AG-062375, Epigenetic Regulation of Kidney Function and Blood Pressure

Vaithianathan, Thirumalini
USPHS NIH Grant EY-030863, Dynamics of calcium signals control neurotransmitter release in retinal ribbon synapses

IV. BUSINESS DEVELOPMENT

A. AIC History

Planning for the AIC began in FY17 to address the need for more advanced microscopy and imaging services on campus. To that end, a LaVision Biotec (now Miltenyi Biotec) Ultramicroscope II light-sheet fluorescence microscope (LSFM) was purchased in FY2018 and installed in the TSRB. In FY20, the Zeiss Elyra 7 LS super-resolution microscope (SRM) was purchased, but due to the COVID-19 panedmic, installation in the Johnson building was delayed until September 2020. Following the hiring of Dr. Helms as microscopy manager for the AIC in November of 2020, the core officially opened for business in Q3 of FY21 in January of 2021.

B. Market Assessment

The market for AIC services includes any investigators within UTHSC and surrounding institutions who use imaging experiments to support their research. Investigators who do not currently use the AIC for imaging services rely on departmental imaging systems, typically using confocal microscope technology, with a high number of users relying on the imaging center within the UTHSC Neuroscience Institute. However, the AIC is the only location on campus, or in the Memphis area, offering super-resolution microscopy technologies, including single molecule localization microscopy (SMLM), to internal and external customers.

C. Competitive Analysis

While planning for the AIC, Dr. Seagroves compared service fees across 14 research institutions housing similar imaging instruments in core facilities. As a result, AIC prices have been set such that UTHSC ranks in the bottom-half to bottom-third of peer institutions, consistent with pricing policies of other UTHSC institutional cores. In

addition, local competition is minimal as there are no facilities in the Memphis area that offer the same services the AIC does. Although St. Jude Children's Research Hospital maintains an older Elyra model, the microscopy core does not accept external specimens for imaging.

D. Marketing Plans to Obtain New Business

The current goal for marketing the AIC is to expand the user base on the UTHSC campus. The AIC will continue to work with Lee Ferguson in the Office of Research to update the AIC website with training materials and guides as well as to develop a gallery of user images provided by UTHSC investigators. Dr. Helms will also give a presentation about the imaging methodologies offered by the core as part of the Office of Research Hot Topics in Research series.

E. Forecasted Volumes for New Business

In July of 2022, the AIC began offering two different imaging services for trained users: one for users performing SMLM and one for users performing SIM. While the SMLM imaging service price increased with the new fiscal year, the SIM imaging service was introduced at a reduced price of $25/hr. The SIM service is most comparable to confocal imaging, and it is anticipated that the reduced price will increase the accessibility of the core to those users.

V. ACTUAL BUDGET FY22 (July 1, 2021 to June 30, 2022)

FY2022	DEBITS	CREDITS
Salaries	72,799	
Supplies	9,069	
Service Contracts*	39,054	
Equipment (> $5,000)	0	
Other Expenses	0	
TOTAL EXPENSES	***120,922***	
FY22 Internal Recoveries		11,785
FY22 External Recoveries		0
TOTAL CREDITS		***11,785***
Income / (Subsidy)	(109,137)	
State Appropriation	2,418	
Net Income / (Subsidy)	**(106,719)**	

*Service Contracts/Maintenance expenditures included a Carl Zeiss Microscopy, LLC invoice, which totaled $39,054 for FY22.

Subsidy, % before State Appropriation 90%
Subsidy, % after State Appropriation 88%

Conclusions and Global Recommendations Impacting All Cores

Strong support of research cores and shared facilities is essential to maintaining international recognition of research programs, increasing extramural funding, recruiting, and retaining outstanding research faculty and generating high-impact data for publications.

Institutional cores are currently defined as shared resources that are, or will be, widely used among UTHSC faculty from multiple departments, colleges and, in the future, campuses. The institutional research cores currently receive their budget from the state of Tennessee, including the Tennessee Higher Education Commission (the Molecular Resource Center of Excellence) and the institution, which then receives all fees for service. The fees are set based upon market evaluation. Since FY16, institutional cores have been expected to sit on their financial bottom, to be managed with a business model using business plans to develop budgets and to employ data-based metrics to measure core success. Investment in core facilities is a priority of the Office of Research. Overall, during FY16-FY18, ~$2.5M of the $5M in funds distributed to the VC for research startup fund were used to subsidize core facilities, including large equipment purchases. In FY19, there were also substantial investments in animal caging and core equipment for the LACU and the RBL cores. In FY21, there was investment in the newly launched Advanced Imaging Core, including the purchase of a Zeiss Elyra 7 lattice SIM super resolution microscope system.

Detailed core activity and core analysis reports have been provided annually to the campus since FY16. Complete copies of the reports are available for direct download from the UTHSC institutional cores website. Not only do the reports highlight the financial performance of each core, but they also review in detail how the cores serve the campus across colleges and departments, by reporting on the volume of use of services, the extramural grants/awards supported by the core and overall core productivity (such as publications produced, core support of grant awards, core service to the campus, etc.).

Since FY16, the cores have increased their promotional efforts through more frequent presentations to individual departments, through the Office of Research Hot Topics seminar series and through invitation of special guest speakers sponsored by the cores focused on emerging technologies (“Shared Resources Technology Talks”). The cores also update their websites and develop new marketing materials on a bi-annual basis, including the one-page core brochures and color printed core booklets, which are distributed in print as part of Office of Research-sponsored campus events. Boilerplate facilities and resources pages describing each institutional core are updated at least once per year. These are provided to the Office of Sponsored Programs and posted on the research cores website to support grant submissions. Due to the COVID-19 pandemic, the Hot Topics in Research and Shared Resources Technology Talks seminar series were suspended beginning in Q3/Q4 of FY20 until Fall of 2021. Between October 2021 and May 2022, five institutional cores presented in the Hot Topics in Research series on their service offerings (the MPMS unit of PMC, the MedChem Core, the MRC, the mBIO Core, and the PMC).

Although rates for core services have been routinely increased by 3% over prior fiscal year levels during FY16-FY20, these increases were insufficient to offset the increased operating expenses associated with personnel and with service agreements or supplies. For example, the total budget necessary to operate the core facilities increased from $6,272,412 in FY19 to $7,772,001 in FY21 (23.9%). The influx of additional institutional support for the core facilities over the FY21- FY22 periods resulted in a non-deficit budget for the first time in FY22 since these reports were first generated. To proactively project the budgets needed to operate the

institutional core facilities, every year in the spring, three year rolling business plans are prepared by the Office of Research for each core facility based on recent historical data, knowledge of future needs and current financial data (e.g., the first six months of the current FY period).

Total recoveries increased in FY22 relative to FY21 for the LACU, MRC, PMC, and AIC cores. Recoveries were similar to FY21 levels for the FCCS Core. Recoveries decreased slightly in the mBIO Core in FY22, whereas recoveries decreased by 42% for the MedChem Core; however, total expenses were offset by grant-funded salary support for the director (operating expenses decreased in FY22 to $71,943 from $96,384 in FY21). Recoveries also decreased by 32% for the RBL, by~50% for the MPMS Unit of the PMC and by 56% for the RHC. After accounting for subsidies ("income") from the state of Tennessee, from the THEC, and from the cost-savings realized due to unfilled vacant positions, the total subsidy for all UTHSC institutional cores in FY22 was a net surplus of $179,679. In comparison, the total year end net subsidy in FY20 was $560,140, and the net subsidy in FY21 was $172,357. With the right-sizing of the operating budget, there is renewed focus on obtaining dedicated, recurring budgets for: 1) the cores to replace broken and outdated equipment and 2) to purchase new equipment or to develop new institutional core facilities.

There remain opportunities for further improvements in managing core operations, including enhancing internal and system-level marketing efforts to increase demand for core services, and enhancing communication efforts to spread awareness about core services and the expertise of our core directors on a statewide level. All of these efforts will lead to increased demand for core services and thereby, service fee recoveries, while supporting our researchers as they compete nationally/internationally for extramural support. In addition, there is momentum to continue to apply for extramural support for core equipment (for example, through the S10 grant or other infrastructure mechanisms) and to secure philanthropic support. Together, these steps will allow the Office of Research to achieve our long-term goal to reduce additional core subsidies needed at fiscal year-end to "backfill" the operational budgets, while investing in launching one new institutional core every one-two years, as outlined in the Operational Strategic Plan for Research.

Across the board, the specific recommendations for all institutional cores are outlined below:

- The highest priority is to secure an annual budget to replace aging/outdated equipment in the institutional cores. This investment will result in increased extramural funding and will support the recruitment of new faculty and retention of current faculty.
- The second highest priority is to secure an annual, recurring budget to purchase new, high-end instrumentation for the institutional cores so that our campus can invest in cutting-edge technologies that lead to innovative, high impact research programs, increasing the likelihood of grant proposal funding and increasing each health science center campus' national reputation.
- The third highest priority is to ensure continuation of an annual operational budget that is sufficient to meet the budgetary needs of the institutional cores, preventing the recurring need to identify sources to "zero out" net deficits across cores at the end of each fiscal year.
- All institutional cores should continue to incorporate an annual inflationary increase of 3% in user fees to match the 3% inflationary increase that can typically be requested on extramural funding sources. Throughout FY22, the inflation rate remained high, and the costs of supplies and equipment service agreements often far exceeded 3%.

- The Office of Research will continue to promote core capabilities and expertise to internal users, and to expand marketing of core capacities to external users, including commercial users who pay higher service fees. The cores will also continue to participate in the Hot Topics in Research seminar series, Shared Resources Technology Talks and in new faculty fair events when sponsored by the Office of Academic, Faculty and Student Affairs and/or the Office of Research. The next research fair is tentatively scheduled for September of 2023 (Q1 FY24).
- The Office of Research will continue to strive to eliminate redundant, underutilized core resources or to outsource commodity services in order to invest in emerging technologies in the core facilities.
- The Office of Research will increase efforts to coordinate with individual colleges to assist with start-up packages that include capital equipment, including discussions to determine whether individual instrumentation would be utilized more efficiently within a shared resource than in an individual laboratory. We will also work with colleges to reduce or to eliminate the redundant purchases of new equipment during faculty recruitment that may already exist in institutional cores and/or that may compete with the institutional cores. An alternative approach to address this issue may be to offer institutional dollars as part of startup packages that can only be spent in the cores.
- Continue to support distribution of boilerplate facilities and resources language for grant and contracts related to institutional core resources and to update these documents at least bi-annually.
- Survey core users more frequently to receive up-to-date feedback about the quality of core services, the perceived value of core services, turnaround time for sample processing and customer service quality, in order to further improve core operations.
- When feasible, work with centers and institutes to cost-share core capital equipment to be utilized by a broad group of member investigators, such as a rodent MRI system.
- To provide sufficient administrative support for core directors in preparation of NIH S10 equipment or other infrastructure-based proposals, to acquire high-end instrumentation.
- Enhance the number of Shared Resources Technology Talks organized by the institutional cores to spread awareness of new technologies and to remind the research community of the breadth of expertise of our core directors.
- Ensure that the IABs for each core meet at least once per year to advise on core operations and to learn about core achievements and challenges.
- Continue to work with the Office of Development and Alumni Affairs to develop relationships with new philanthropic sources and to build relationships with equipment vendors, who may provide discounted or gift-in-kind equipment for the cores. As part of this ongoing effort, Greg Harris became a member of the VCR research cabinet in FY18. Current projects organized by Greg include the acquisition of functional equipment donated by Glaxo Smith Kline and establishing a Dell-supported artificial intelligence server cluster in collaboration with the mBIO Core.
- If investigators are using the time of core directors and/or core personnel for development of grant proposals, protocol development to provide preliminary data, or in-depth consultation related to experiment, including data analysis and troubleshooting, then it is fair, reasonable, and expected that they should be added on the faculty member’s grant application for the percentage of time utilized. We will continue to engage with the associate vice chancellor for Research-Office of Sponsored Programs and with the assistant/associate deans of Research within the colleges to develop guidelines that are enforceable during pre- and post-award review.

UTHSC
RESEARCH

910 Madison Avenue | Suite 608 | Memphis, TN 38103 | 901.448.7125 | research@uthsc.edu | UTHSC.edu/research