Typically, this is the time of the year that many of us devise new goals to compensate for outcomes that were less than ideal in the past year. I’m proud to claim that the past year in research saw a tremendous growth in all areas and has continued to grow at the first quarter of this new fiscal year. Our previous “new year’s resolutions” to expand the work of research for all departments have surpassed our original goals. This year we are prepared to accelerate the momentum of research further than ever before.

In fiscal year 2013, faculty published 76% more research than in the 2012. Thus far, the College of Dentistry is on track to increase its published research by approximately 20% in fiscal year 2014 after review of its first quarter.

Of course this rise in research has had a trickle-down effect. Students have been encouraged to participate more in research. Twenty-three students were enrolled in the Summer Research Fellowship; up from 18 the previous year. Nineteen of these students presented at the annual Hinman Student Research Symposium which also continues to grow and attract more dental schools across the country.

The new Clinical Research Center, devoted to federal and industry sponsored projects, was completed in the fall of 2012 and has attracted industry sponsors to select UTHSC as the site of their clinical research trials. The center offers a private setting with four fully equipped operatories, a separate office for confidential patient-subject consultation, a group workspace outfitted with four computers where research personnel can collaborate, and a supply and service room where research coordinators prepare clinical research materials.

This year we have strategized plans underway to further develop the scope of stem cell research, erosion: demineralization/remineralization studies, and plaque glycolysis and regrowth methods.
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Take a look at the published work of our Research Faculty!

Dr. Franklin Garcia-Godoy co-authored Primary Preventive Dentistry in its 8th edition.

Dr. Martha Wells published a chapter in Pediatric Dentistry: Infancy through adolescence.
# Department of Bioscience Research

875 Union Avenue, Memphis, TN 38163 | (901) 448-6333 | [www.uthsc.edu/dentistry/research](http://www.uthsc.edu/dentistry/research)

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## Senior Executive Associate Dean for Research

**Franklin Garcia-Godoy, D.D.S., M.S., Ph.D., Ph.D.**

Chair, Department of Bioscience Research  
Director, Bioscience Research Center  
Professor, Department of Physiology, University of Tennessee Health Science Center  
Adjunct Professor, Department of Biomedical Engineering, University of Memphis  
Adjunct Professor, Department of Biomedical Engineering, Florida International University  
Senior Clinical Investigator, The Forsyth Institute, Boston, Massachusetts  
Adjunct Professor, Department of Conservative Dentistry and Periodontology, University of Munich

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### Faculty

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<tr>
<td>Jegdish Babu, B.S., M.S., Ph.D.</td>
<td>Associate Professor</td>
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<td>Melody Barron, D.D.S.</td>
<td>Assistant Professor</td>
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<td>Professor</td>
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<td>Chris Ivanoff, D.D.S.</td>
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<td>George T.J. Huang, D.D.S., M.S.D., D.Sc.</td>
<td>Professor &amp; Director for Stem Cells &amp; Regenerative Therapies</td>
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<td>Mark Scarbecz, Ph.D.</td>
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<td>Assistant Dean of Institutional Affairs</td>
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<td>Edwin Thomas, M.S., Ph.D.</td>
<td>Professor</td>
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<td>David Tipton, D.D.S., Ph.D.</td>
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<td>Antheunis Versluis, Ph.D.</td>
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<td>Director of Biomaterials</td>
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<td>Yanhui Zhang, B.S., M.S., Ph.D.</td>
<td>Assistant Professor</td>
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### Staff

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<tr>
<td>Brandy Clark, CDA, R.D.A</td>
<td>Clinical Dental Assistant</td>
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<td>Margaret Jefferson</td>
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<td>Admin Service Assistant</td>
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<td>Nancy Turner</td>
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<tr>
<td>Laura Young, B.A., M.P.H.</td>
<td>Grants &amp; Clinical Research Manager</td>
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The CLINICAL RESEARCH CENTER

A year after its completion, the Clinical Research Center in the Dental Building is bustling with activity and attracting new clinical research in both the public and private arenas. The center was introduced in September 2012 in order to accommodate the request for UTHSC to facilitate industry clinical trials and to attract faculty and private organizations alike to lead academia in clinical research and the advancement of dental best practices.

The Clinical Research Center (CRC) is under the direction of Dr. Franklin Garcia-Godoy, Senior Executive Associate Dean for Research. It is designated solely for clinical research projects. The facility consists of approximately 300 square feet of clinic space, with four dental units, a consultation room, a dispensing/storage room, and a separate office. Research at the Clinical Research Center include but not limited to dental instruments, devices and technique testing, medicinal clinical trials, whitening kit testing, toothpaste, toothbrush and mouth rinse testing. Five industrial sponsored clinical trials have been successfully completed; six more clinical trials and pilot study projects are actively ongoing currently.

DEPARTMENT OF BIOSCIENCE RESEARCH – CURRENT FACULTY & STAFF

Back row: Geraldine Moore, Iva Pendleton, Jegdish Babu, Brian Morrow, Anastasios Karydis, Mark Scarbecz, Franklin Garcia-Godoy, Middle row: Qian Zheng, Melody Barron, George Huang, David Tipton, Camille Brown, Edwin Thomas, Front row: Laura Young, Yanhui Zhang, Colette Stewart, Margaret Jefferson
Research Spotlight

DR. DAVID TIPTON

Inhibition of IL-17-stimulated IL-6 and IL-8 Production by Cranberry Components in Human Gingival Fibroblasts and Epithelial Cells. *Journal of Periodontal Research* 2013; 48:638-646.

Abstract Presentations and Awards:

Dr. David Tipton recently published research with the help of student researchers. Sueellen Cho and Nia Zacharia contributed to this study, as recipients of Dental Student Research Fellowships from the University of Tennessee College of Dentistry Alumni Endowment Fund, and both were awarded with James C. Ragain Awards for Excellence in Research.

Presentations

They presented aspects of this work at the 2010 and 2011 Hinman Student Research Symposium, the 2011 and 2012 College of Dentistry Research Day and Table Clinics, and at the 2011 and 2012 meetings of the American Association for Dental Research.

Publication

Periodontal disease is an inflammatory disease that involves the gingiva, periodontal ligament, and alveolar bone. It is characterized by dense infiltrations of immune cells including various T helper (Th) cell populations. Th17 cells produce the cytokine interleukin (IL)-17, and both have been detected in gingival crevicular fluid and in gingival tissue biopsies of chronic periodontitis lesions. IL-17 can stimulate many types of cells, including fibroblasts and epithelial cells, to produce inflammatory cytokines. These include IL-8, which promotes inflammation by acting as a chemoattractant for neutrophils, and IL-6, which among many other activities stimulates bone resorption, possibly through stimulating osteoclast formation. Through its effects on gingival fibroblasts (the most abundant cells in the periodontal connective tissue) and epithelial cells, IL-17 may promote local tissue inflammation and destruction in periodontal diseases.

Regulation of fibroblast/epithelial cell inflammatory responses has been suggested to be one way of preventing/controlling the progression of periodontitis. Used adjunctively to conventional periodontal treatment, host modulatory therapy (HMT) comprises systemically or locally delivered substances which can reduce tissue destruction by downregulating destructive host inflammatory responses, including those of fibroblasts and epithelial cells in the periodontium. Natural plant products and essential oils can act as HMT agents and have beneficial effects because they can rupture bacterial cell walls, inhibit bacterial enzymes, and reduce prostaglandin and pro-inflammatory cytokines. The focus of this research was the cranberry (*Vaccinium macrocarpon*), a native North American polyphenolic-rich fruit. Cranberry polyphenols have diverse activities such as inhibiting human cancer cell proliferation, anti-inflammatory effects, and preventing adherence of urinary tract pathogens. Earlier studies in our laboratory have shown that cranberry polyphenols inhibit production of several pro-inflammatory molecules and proteases by gingival cells in response to several different stimulators, including IL-1β, LPS from periodontopathogens, and advanced glycation endproducts.
The long-term purpose of this line of investigation is to continue to determine whether cranberry polyphenols, by attenuating the inflammatory response of major cell types in periodontal tissues, may have a beneficial effect on slowing periodontal disease progression in combination with conventional therapy. The objective of the present study was to determine whether cranberry polyphenol treatment of human gingival fibroblasts and epithelial cells stimulated with IL-17 reduces their contribution to periodontal inflammation, specifically via production of IL-6 and IL-8.

Human gingival epithelial cells and normal human gingival fibroblasts were exposed to cranberry polyphenols (a high molecular weight, non-dialyzable material, NDM) derived from cranberry juice, IL-17, or NDM + IL-17. Toxic effects of NDM (membrane damage and decreased viability) were assessed by lactate dehydrogenase activity released into cell supernatants and by measuring activity of a mitochondrial enzyme, respectively. IL-6 and IL-8 in cell culture supernatants were measured by enzyme-linked immunosorbent assays. Data were analyzed using one-way analysis of variance and Scheffe’s F procedure for post hoc comparisons. Short term exposure to NDM caused no cell membrane damage in either cell line. Measured by effects on viability, epithelial cells were more sensitive than the fibroblasts to longer NDM exposure (IC\textsubscript{50} values of ~ 60 µg/ml and ~ 275 µg/ml NDM, respectively). In both cell lines, IL-17 significantly stimulated production of IL-6 and IL-8. Non-toxic levels of NDM inhibited IL-6 and IL-8 production by epithelial cells and fibroblasts in the presence or absence of IL-17 by as much as ~90%.

The results of the present study support the concept of a role for Th17 cells and IL-17 in periodontal disease, via stimulation of IL-6 and IL-8 production by both gingival fibroblasts and epithelial cells. The inhibition of both cytokines by cranberry NDM suggests that cranberry polyphenols may have potential to be developed as a preventive/therapeutic agent for periodontitis, perhaps in the form of a mouthrinse or subgingival medicament.

**DR. GEORGE HUANG**

Dr. George T.-J. Huang, D.D.S, M.S.D., D.Sc. is a Professor in the Department of Bioscience Research. He joined the UTHSC dental faculty in 2012 and assumed the position as Director for Stem Cells and Regenerative Therapies. Prior to joining UTHSC, Dr. Huang had been the Herbert Schilder Professor and Chair in the Department of Endodontics at Boston University and Chair of the Department of Endodontics at Columbia University. He has been working on stem cell research for more than ten years and here at UTHSC continues this endeavor in the areas of stem cell characterization and stem cell-based tissue regeneration. Below is an overview of his latest research.

**Stem cell-based dental tissue regeneration**

The goal of this project is to utilize adult stem cells and tissue engineering methods to regenerate lost tooth structure. We focus on characterizing dental stem cells including dental pulp stem cell (DPSCs), stem cells from apical papilla (SCAP), stem cells from human exfoliated teeth (SHED), and periodontal ligament stem cells (PDLSCs) and utilizing these stem/progenitor cells to regenerate dental tissues including dental pulp, dentin, cementum and periodontal ligament using animal models.

In the case of pulp and dentin regeneration, Dr. Huang’s group was the first to show that by using a small animal study model, pulp tissue can be generated de novo, meaning the regenerated pulp can repopulated in the emptied root canal space as well as newly deposited layers of dentin on the root canal walls. The study has been published in the journal *Tissue Engineering* in 2009 (Stem/progenitor cell-mediated de novo regeneration of dental pulp with newly deposited continuous layer of dentin in an in vivo model. Huang GT, Yamaza T, Shea LD, Djouad F, Kuhn NZ, Tuan RS, Shi S. Tissue Eng Part A. 2010 Feb;16(2):605-15. doi: 10.1089/ten.TEA.2009.0518.). This animal model is a combination of ectopic and orthotopic approach to test the regeneration of pulp and dentin. The pulp and dentin are regenerated in the root canal space of a human tooth fragment, which presents an
Figure 1 Blue arrow in (A) indicates the blood supply entrance; green arrows in (B) and (C) indicate continuous layer of uniformed thickness of regenerated dentin next to the regenerated pulp (rP); Scale Bars: (A) 1mm; (B and C) 500 µm.

By the orthotopic method, whereas the entire tooth construct that carries the stem cells to regenerate pulp and dentin is transplanted into the subcutaneous space of mice, which represents an ectopic method. The mouse provides an in vivo environment as the source of blood supply to allow the stem cells to regenerate pulp. As shown in Fig. 1, the root canal space was filled entirely by pulp-like tissue accompanied by mature vascularization. The composed dentin structure insinuated that it was produced by a new layer of odontoblast-like cells expressing dentin sialophosphoprotein, bone sialoprotein, alkaline phosphatase, and CD105. This study provides the first evidence of regeneration of vascularized pulp-like tissue and its formation of dentin-like mineral structures diffusing onto existing dentin walls in the root canal space. Most impressive was the formation of a continuous layer of dentin-like tissue on existing dentinal walls and on MTA cement surface.

Currently Dr. Huang's lab is working on this regenerating pulp as well as periodontal ligament using a large animal, minipigs, for the orthotopic regeneration of these dental tissues. The ultimate goal is to mount human clinical trials to test this pulp-dentin regeneration new technology.

Generation and utilization of induced pluripotent stem (iPS) cells for neural regeneration

The goal of this study is to generate and characterize iPS cells from dental stem/progenitor cells. Various approaches are being used to generate iPS cells including viral and non-viral methods. The generated iPS cells are pluripotent and are capable of becoming cells of all three germ layers. iPS cells are being tested to differentiate into various cell types in vitro and in vivo. These cells may become an indefinite cell source for tissue regeneration.

Dr. Huang's lab was the first to report that dental stem cells can be reprogrammed from dental stem cells. This work was published in Stem Cells and Development in 2010 (iPS cells reprogrammed from human mesenchymal-like stem/progenitor cells of dental tissue origin. Yan X, Qin H, Qu C, Tuan RS, Shi S, Huang GT. Stem Cells Dev. 2010 Apr;19(4):469-80. doi: 10.1089/scd.2009.0314.). These iPS cells carry transgenes that are needed to reprogram the cells. Subsequently, Dr. Huang's lab generated Transgene-Free (TF) iPS cells that the transgenes were removed from the reprogrammed iPS cells and this gene removal does not affect the reprogramming status of the iPS cells. Neurogenic capacity was tested in TF iPS cells reprogrammed from stem cells of apical papilla (SCAP) and the work was published in Stem Cell Research and Therapy in 2012 (Establishment of transgene-free induced pluripotent stem cells reprogrammed from human stem cells of apical papilla for neural differentiation. Zou XY, Yang HY, Yu Z, Tan XB, Yan X, Huang GT. Stem Cell Res Ther. 2012 Oct 24;3(5):43.).

As shown in Fig 2, TF SCAP iPSCs underwent neural differentiation formed neural rosettes and neural tube-like structures which are made up of neural precursor cells. Some cells have further differentiated into neural-like cells expressing neural markers. Currently, further investigation is underway to differentiate functional neurons derived from these iPSCs. Dr. Huang has been collaborating with Dr. Kristen O’Connell at the UTHSC Department of Physiology to determine the functional aspects of the neuron-like cells from iPSCs. The long-term goal of the project will be to test whether these cells can enhance neural regeneration after traumas or diseases using animal study models.

To learn more about Dr. Huang's research here at the University of Tennessee Health Science Center, please contact him by email at ghuang4@uthsc.edu or by phone at (901) 448-1490.
The surge in faculty research has had a favorable impact on student research. On October 25th through October 27th, the College of Dentistry hosted its largest Hinman Student Research Symposium yet. UTHSC dental students represented 19 of 103 students from 46 dental schools from across the U.S. and Canada at the famous Peabody Hotel.

Each year, the symposium provides students the opportunity for international and national recognition awards for their excellence in dental research. Three UTHSC students were selected to give oral presentations to the symposium attendees while the other 16 students presented amongst all of their peers at the poster presentation.

Are you a faculty or student member of the American Association for Dental Research (AADR)/International Association for Dental Research (IADR)? Or new to research and would like to immerse within the dental research community at UTHSC? If so, now is the time to join the AADR Memphis Section to become more involved in dental research on the local level.

Membership in the AADR Memphis Section will include invitation and attendance at the quarterly guest lectures, lunch-and-learn sessions, and review/assistance with research proposals.

In November 2013, over thirty faculty and staff came out to the AADR Memphis Section quarterly seminar. Dr. George Huang presented his study: Dental stem cells for tissue regeneration.

**Elected AADR Memphis Section Officers for 2014**

- **President:** Dr. George Huang (Professor | Director of Stem Cells and Regenerative Therapies)
- **President-Elect:** Dr. Anastasios Karydis (Assistant Professor, Dept. of Periodontology)
- **Vice-President:** Dr. Antheunis Versluis (Professor | Director of Biomaterials)
- **Secretary:** Dr. Yanhui Zhang (Assistant Professor, Dept. of Bioscience Research)
- **Treasurer:** Dr. Edwin Thomas (Professor, Dept. of Bioscience Research)
**Technology Spotlight**

**EVO HD LS15 Scanning Electron Microscope (SEM)**

**Location**
Bioscience Research Center

**Description**
Carl Zeiss (Oberkochen, Germany) – life science SEM with Peltier cooling stage (wet imaging), variable pressure (VPSE), back scatter (BSD), EDS by Oxford, and Deben low range Transmission Electron Microscope (STEM) detectors.

**Applications**
The SEM can be used to analyze life science and material samples at different temperatures, pressures and humidity. Imaging can be done with relatively wet samples by controlling the environmentally conditions to avoid dehydration.

One can explore biological or material composition samples without sputter coating samples.

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**Calendars**

**As you fill in your day-planner with all your spring events,**

**Student Research Day – February 18th, 2014**
Student Activities Center

**AADR Annual Meeting – March 19-22, 2014 in Charlotte, NC**
Early registration ends February 3rd

**Hinman Dental Meeting – March 27-29, 2014 in Atlanta, GA**

**Alumni Endowment for Research Grant Deadline**
Friday, April 28th at 5:00 pm CST
The following is a list of clinical research studies conducted by UT College of Dentistry faculty in Fiscal Year 2013 to present. The title, investigators, and study objective are listed for each project.

A clinical evaluation of NobelProcera™ implant bar overdenture in the mandible or maxilla on 4 NobelProcera™ CC implants

**Study Objective:** To determine the bone behavior and survival rates of the NobelProcera™ implants, the bar, and the overdenture evaluating its clinical behavior.

**Principal Investigator:** Dr. Jain Vinay and Dr. Audrey Selecman

**Co-Investigators:** Dr. David Cagna, Dr. Pradeep Adatrow

Multi-center phase 3 trial of minocycline hcl1 mg microspheres for use in subjects with peri-implantitis: clinical and microbiological evaluations.

**Study Objective:** To demonstrate the ability of Minocycline HCl Microspheres, 1mg to improve peri-implantitis, following mechanical debridement, when compared to debridement alone.

**Principal Investigators:** Dr. Paul Bland

**Co-Investigators:** Dr. Anastasios Karydis, Dr. Rania Livada

**Research Staff:** Colette Stewart, Laura Young (Coordinator/Research Associate)


**Study Objective:** To determine the effectiveness of fluoride varnish in treating white spot lesions as compared to fluoride gel.

**Principal Investigators:** Dr. Franklin Garcia-Godoy

Dr. Terry Trojan

Dr. Floyd Trammell (Orthodontic Resident),

**Research Staff:** Colette Stewart (Coordinator/Research Associate)

Influence of Maternal Factors on Caries Development during Early Childhood. A Pilot Study (Ancillary to the CANDLE Study)

**Study Objective:** The purpose of this study is to investigate the impact of maternal factors on the development of dental cavities among 3-year-old children.

**Principal Investigators:** Dr. Liang Hong and Dr. Franklin Garcia-Godoy

**Co-Investigators:** Dr. Frances Tylavsky (Department of Preventive Medicine – CANDLE Study), Dr. Martha Wells, Dr. Daranee Versluis-Tantbirojn

**Research Staff:** Shantel Jeffries (Coordinator/Research Associate)
Assessment of oral health in a population from the Memphis area.

Study Objective: The purpose of this study was to assess prevalence of caries, plaque acidogenicity in a population of adult subjects (18-60 years of age) from the Memphis, TN area.

Principal Investigator: Dr. Franklin Garcia-Godoy
Co-Investigators: Dr. Yanhui Zhang
Research Staff: Colette Stewart (Coordinator/Research Associate)

Assessment of chronic plaque stability during the use of a non-antibacterial fluoride dentrifice.

Study Objective:

Principal Investigator: Dr. Franklin Garcia-Godoy
Co-investigator: Dr. Yanhui Zhang
Research Staff: Colette Stewart (Coordinator/Research Associate), Marissa Arriaga (Hygienist)

Assessment of experimental dentrifices on chronic plaque acidogenicity as compared to a marketed dentrifice over 3 months.

Study Objective: To assess plaque acidogenicity for experimental dentrifrices as compared to a marketed dentrifice over three months after chronic use and immediately after acute treatment.

Principal Investigator: Dr. Franklin Garcia-Godoy
Co-Investigators: Dr. Yanhui Zhang
Research Staff: Colette Stewart, Laura Young (Coordinator/Research Associate), Marissa Arriaga (Hygienist)

A study to assess the effects on plaque glycolysis of a test mouth rinse as compared to marketed control.

Study Objective: To evaluate the anti-glycolytic activity of a marketed 0.075% cetylpyridinium chloride (CPC) mouth rinse on dental plaque bacteria, relative to a 0.07% CPC positive control.

Principal Investigator: Dr. Franklin Garcia-Godoy
Co-Investigator: Dr. Yanhui Zhang
Research Staff: Colette Stewart, Laura Young (Coordinator/Research Associate), Marissa Arriaga (Hygienist)

Evaluation of the relationship between contact time and treatment duration on whitening effectiveness and safety of a 5.25% H2O2 high adhesion whitening strip.

Study Objective: To evaluate the relationship between contact time and treatment duration on whitening effectiveness and safety of a 5.25% H2O2 high adhesion whitening strip.

Principal Investigator: Dr. Franklin Garcia-Godoy
Co-Investigator: Colette Stewart
Research Staff: Laura Young (Coordinator/Research Associate), Marissa Arriaga (Hygienist)
PUBLICATIONS


Bicalho AA, Valdivia ADCM, Barreto BCF, Tantbirojn D, Versluis A. Soares CJ. Incremental filling technique and composite material – Part II - Shrinkage and shrinkage stresses. *Operative Dentistry*, accepted for publication.


Wells, M. *Beyond the guidelines: factors affecting behavior guidance.* Presentation at the American Academy of Pediatric Dentistry Conference, November 15-16, Chicago, IL.


DeSchepper E. Development of a preclinical radiographic shielded alignment device. Abstract for the 2014 American Dental Education Association Annual Session, March 15-18, San Antonio, TX.


The following is a list of current grants held by UT College of Dentistry faculty.

**FEDERAL/FOUNDATION GRANTS**

- **Stem cell-based therapy for regenerative endodontics**
  - PI: Dr. George Huang (Bioscience Research)
  - NIH/NIDCR R01

- **Hinman Student Research Symposium**
  - PI: Dr. Franklin Garcia-Godoy
  - NIH/NIDCR (R13)

- **Plaque glycolysis analysis**
  - PI: Dr. Franklin Garcia-Godoy
  - Procter & Gamble

- **Osteonecrosis of the jaw (ONJ) case registry**
  - PI: Dr. Cesar Migliorati
  - Amgen

- **Effects of non-thermal plasma treatment on composite restoration and caries prevention**
  - PI: Dr. Liang Hong
  - NIH

- **Stem cell-mediated periodontal ligament regeneration for avulsed teeth**
  - PI: Dr. George Huang
  - American Association of Endodontics

- **Evaluation: NobelProcera implant bar overdenture in the mandible/maxilla on NobelReplace implants**
  - PI: Dr. David Cagna
  - Co-PIs: Dr. Vinay Jain and Dr. Audrey Selecman
  - Nobel Biocare

- **Advanced nursing Education (ANE) Grant**
  - Co-I: Drs Cesaeer Migliorati, Timothy Hottel, Cassandra Ballard-Holder
  - HRSA

- **Whitening system evaluation**
  - PI: Dr. Franklin Garcia-Godoy
  - Co-PI: Colette Stewart
  - Procter & Gamble

- **Plaque pH analysis project**
  - PI: Dr. Franklin Garcia-Godoy
  - Procter & Gamble
The UTHSC College of Dentistry was founded in 1878 making it the oldest dental college in the South, and the third oldest public college of dentistry in the United States.

The College contains a 4-year dental program, totaling approximately 320 students. In addition, students in the Postgraduate dental programs and Dental Hygiene are included.

The College is dedicated to providing professional, graduate, and postgraduate education; conducting dental research; and, delivering state-of-the-art patient care and public service.