IP 805 Essentials of Molecular Biology
Course Syllabus - Spring 2018 Term

Catalog Description

This course covers the essentials of prokaryotic and eukaryotic molecular biology. Topics include DNA and RNA structure; DNA replication, repair, and recombination; the mechanism and regulation of transcription; and protein translation. Fundamental concepts are reinforced by the discussion of human genetic diseases. Credit: 3 (3-0).
Credit hours: 3

Content delivery modes: Lecture-based

Grading Method: Letter Grade

Prerequisites:

Learning Objectives

- Describe the fundamental concepts and applications of modern molecular biology.
- Define the similarities and differences between eukaryotic and prokaryotic organisms as it relates to the processes of transcription, translation, replication, etc.
- Describe the fundamental concepts of the genetic code and the mutagenesis and repair of DNA.
- Describe common mechanisms of gene regulation and the regulation of protein synthesis.

Course Director

Course Director: John Cox

Department: Microbiology, Immunology, and Biochemistry

Email: jcox@uthsc.edu

Phone: (901)448-7080

Class Meetings

Session frequency: 8:30 - 10:00AM

Session duration: Two times per week for 1.5 hours

Location: GEB A315

Faculty

Name: Stephen White
Department: Integrated Program in Biomedical Sciences
Email: stephen.white@stjude.org

Name: Rod Hori
Department: Integrated Program in Biomedical Sciences
Email: rhori@uthsc.edu

Name: Robert Belland

Department: Integrated Program in Biomedical Sciences
Email: rbelland@uthsc.edu

Name: Lorraine Albritton
Department: Integrated Program in Biomedical Sciences
Email: lalbritton@uthsc.edu

Name: Ioannis Dragatsis
Department: Integrated Program in Biomedical Sciences
Email: idragatsis@uthsc.edu

Name: Janet Partridge
Department: Integrated Program in Biomedical Sciences
Email: janet.partridge@stjude.org

Name: Susan Senogles
Department: Integrated Program in Biomedical Sci
Email: sseongles@uthsc.edu

Attendance Policy

Attendance is required. Unexcused absences may adversely affect a student's grade.

Recording Policy

Recording of the lectures or other course materials requires permission of the instructor. By obtaining recording permission, the student agrees that individual recordings of lectures and course materials will be handled according to UTHSC Policy.

Student Evaluation

Honor Code

All students are expected to abide by the UTHSC Honor Code.

Declaration of Disability

Any student wishing to self-disclose a disability for which they require accommodation must register and officially request accommodation through the Disability Coordinator in Student Academic Support Services. All conversations regarding requests for accommodations are confidential.

Evaluation Metrics

Percent: 70
Metric: 70% of the grade will be based on 3 closed book exams, which will be a mix of short answer and essay questions.

Percent: 30
Metric: 6 discussion sessions will account for the 30% of the grade. Students will be asked to evlaue current research articles. Performance will be evaluated based on student participation in the discussion.

Course Content

Jan. 5 Nucleic acid structure Dr. White

- Define the basics of DNA and RNA Structure; sugars, bases, glycosidic and phosphodiester bonds
- Describe the double helical structure of DNA from first principles (Base pairing; major and minor grooves)
- Define the different forms of DNA and RNA: A-, B-, and Z-form DNA; A-form RNA
- Compare and contrast the structures of DNA and RNA
- Describe the structural features of RNA
- Discuss Ribozymes and their uses
- Describe the importance of DNA topology (supercoiling and linkage numbers)
- Discuss the importance of protein-DNA interactions

Jan. 7 Morphology of chromosomes Dr. Partridge

- Describe the structural organization of eukaryotic chromosomes
- Describe how DNA is packaged
- Describe the importance of the nucleosome, chromatin, 30 nm fibers, and scaffold associations in contributing to metaphase and interphase chromosome structure
- Recall the important features of chromosomes (centromere, telomere)
- Describe how chromosomes are localized within nucleus
- Compare the features of transcriptionally active and inactive sequences
- Define chromosomal territories

Jan. 12 Organization of the genome and chromosome structure

Dr. Partridge

- Recall the molecular definition of a gene
- Define monocistronic and polycistronic genes, and gene families
- Describe the chromosomal organization of genes and noncoding DNA
- Describe the organization of protein coding genes
- Define tandemly repeated genes and repetitive DNA sequences
- Discuss the importance and mechanisms to characterize simple repeats
- Recognize interspersed repeats
- Define mobile DNA and transposons
- Discuss the role of retrotransposons (LINEs, SINEs)
- Describe the mechanisms and consequences of transposition

Jan. 14 DNA replication Dr. Hori

- Describe the basic mechanisms of replication
- Describe the structure of replication origins
- Diagram the events that occur during a replication cycle
- Describe the individual steps of DNA replication

Jan. 19 DNA Replication Dr. Hori

- Define the role of proteins involved in replication
- Describe the ORC cycle
- Recall the transcriptional activators in replication
- Define the molecular events associated with licensing

Jan. 21 Recombination Dr. Cox

- Describe the Holliday model of homologous recombination
- Describe the assays used to distinguish the various steps in homologous recombination
- Define the enzymatic machinery involved in homologous recombination in prokaryotes
- Discuss the mechanisms involved in site-specific recombination

Jan. 22 DNA Replication Paper Disc. (1:00-2:00) Dr. Hori

Jan. 26 Recombination Dr. Cox

- Describe the steps involved in homologous recombination in eukaryotes
- Describe the temporal relationship between homologous recombination and the stages of meiosis
- Describe the enzymatic machinery required for homologous recombination in eukaryotes

Jan. 28 Recombination Dr. Cox

- Discuss the steps of immunoglobulin and T cell receptor gene rearrangements
- Describe the role of recombination signal sequences in Ig gene rearrangements
- Diagram the DNA intermediates observed during Ig gene rearrangements
- Recognize the enzymatic machinery involved in Ig gene rearrangements

Feb. 2 DNA repair Dr. Cox

- Describe the steps of base excision repair
- Define the mechanism of nucleotide excision repair
- Define the mechanisms of mismatch repair
- Describe the process and enzymatic machinery required for the post-replication repair of DNA
- Recall the enzymatic machinery involved in the repair of DNA double strand breaks in eukaryotes
- Describe the relationship between DNA repair and cell cycle checkpoint control

Feb. 4 Prokaryotic transcription 1 Dr. Belland

- List the components of E. coli RNA polymerase holoenzyme and recall their functions
- List the protein and DNA elements that are involved in transcription and their roles
- Describe the requirements, enzymology, and steps involved in transcription
- Describe the differences between the properties and functions of #70 and #54
- Diagram the elements of #70 promoters and recall the proteins bound by each

Feb. 5 Recombination Paper Disc. (1:00-2:00) Dr. Cox

Feb. 9 Prokaryotic transcription 2 Dr. Belland

- Describe the major differences between an RNAP closed complex, open complex and elongation complex
- Describe the steps in prokaryotic transcription beginning with binding of RNAP and ending with transcription termination
- Explain the pre-incorporation and post-incorporation mechanisms used by RNAP to maintain the fidelity (accuracy) of the transcript
- Diagram the sequence features in the DNA that contribute to intrinsic (Rho-independent) termination and explain how they lead to termination
- Discuss the role of Rho (#) in transcription termination and natural polarity
- List the protein factors that contribute to anti-termination
- Diagram a generic ribosomal RNA transcript and explain in concept how RNA processing results in the final mature ribosomal RNAs and tRNA
- Name the primary components participating in degradation of *E. coli* mRNA and recall their functions

EXAM I Feb. 10, 1:00-4:00PM in GEB Room A302 (covers material from Jan. 5- Feb. 2)

Feb. 11 Prokaryotic gene regulation 1 Dr. Belland

- List all the targets and mechanisms of regulation that were presented
- Diagram a generic prokaryotic gene and operon, including all the key sites involved in regulation, transcription, and translation
- Explain the differences between genes, operons, regulons and stimulons
- Describe the roles of regulatory proteins and small molecule effectors in carrying out positive and negative regulation, including the concept of allostery
- Describe the three common mechanisms for repression and activation
- Describe how an operon might be regulated by more than one activator

- Explain how the Lac operon is regulated by Lac-specific repression and catabolite repression

Feb. 16 Prokaryotic gene regulation 2 Dr. Belland

- Explain how the Trp operon in *E. coli* is regulated by both a repressor and attenuation
- Explain how the Trp operon in *Bacillus subtilis* is regulated by an RNA-binding protein
- If provided with a diagram of the *E. coli* initiator operon with its regulatory sites, explain how the regulatory processes result in such differing levels of the three protein products
- Describe the key events and molecules that down-regulate rRNA synthesis in the stringent response to amino acid starvation
- Describe how ribosomal protein synthesis is autogenously regulated and coordinated with rRNA levels
- List the types of signals that activate two-component regulatory systems and describe the overall process by which these systems regulate gene expression
- Describe how the heat shock response in *E. coli* is regulated by an alternative sigma factor, an anti-sigma factor and proteolysis

Feb. 18 Prokaryotic translation Dr. Albritton

- Describe prokaryotic translation initiation and the role of the Shine-Delgarno sequence and initiation factors in this process
- Describe elongation and the role of each of the three elongation factors
- Discuss the conformational switch of EF-Tu and its GEF, EF-Ts.
- Describe the peptidyl transferase and the mechanism by which it catalyzes peptide bond formation.
- Discuss the role of chaperones in protein synthesis and describe the three major types of prokaryotic chaperones
- Describe the function of the GroEL-GroES chaperonin

Feb. 23 Eukaryotic transcription Dr. Hori

- Describe the transcription cycle and eukaryotic gene structure
- Describe the general mechanisms eukaryotic gene control
- Describe the eukaryotic RNA polymerases
- Discuss the experimental tools used to analyze the structure of a eukaryotic promoter
- Recall the structure of Pol II promoters

Feb. 25 Eukaryotic transcription Dr. Hori

- Describe how transcriptional activation is measured
- Describe the “modular” design of activators
- Describe gel shift and DNase I footprinting techniques
- Define the basic function and composition of general transcription factors
- Describe the concept of stepwise assembly
- Recall the structures of pol I and pol III promoters

March 1 Eukaryotic gene regulation Dr. Hori

- Describe combinatorial control, cooperative DNA binding and synergistic gene activation
- Describe how transcriptional activators stimulate transcription
- Discuss histones modifications and histone code
- Describe chromatin remodeling complexes
- Describe the role of co-activators in transcription

Exam II March 2, 1:00-4:00PM in GEB Room A302 (covers material from Feb. 4 - Feb. 25)

March 3 Eukaryotic gene regulation Dr. Hori

- Define CpG methylation and its importance
- Discuss the methods used for study of gene regulation
  - In vitro transcription
  - Immobilized template assays
  - Gel shift assays

- Chromatin immunoprecipitation assay (ChIP)

March 8 RNA processing Dr. Dragatsis

- Define the role of the conserved nucleotides in splicing
- Describe the mechanism and importance of RNA editing
- Recognize the importance of RNA splicing
- Describe and identify the components of splicing
- Describe the differences between rRNA and tRNA processing

March 10 Eukaryotic gene regulation (Transgenesis) Dr. Dragatsis

- Understand the steps required for the generation of transgenic mice
- Compare and contrast the generation of knockout vs knockin mice and gene inactivation
- Diagram a conventional gene knockout scheme
- Describe the positive-negative gene knockout scheme

March 11 RNA Processing Paper Disc. (1:00-2:00) Dr. Dragatsis

March 15 Eukaryotic translation Dr. Albritton

- Discuss the implications on translation initiation that result from the difference in the position of the initiator methionine codon in prokaryotic compared to eukaryotic mRNA
- Describe eukaryotic translation initiation and the roles and compositions of the Cap Binding Complex, Kozak consensus sequence and 5' UTR
- Describe elongation and the role of each of the three elongation factors
- Compare cap-dependent with cap-independent (IRES) translation initiation
- Describe polysome analysis by density gradient centrifugation and explain how it reveals which mRNAs are being translated and which are repressed.
- Discuss the basis of diseases of translation initiation and translation repression.

March 17 Eukaryotic translation Dr. Albritton

- Describe microRNAs, their genes and important characteristics.
- Explain the mechanism by which microRNAs regulate translation.
- Describe the use of siRNA, shRNA, and shRNA-miRs as investigational tools.
- Describe global regulation of translation by mTOR & dysregulation in neoplasia.

March 18 Translation Paper Discussion (1:00-2:00) Dr. Albritton

March 21-25 Spring Break

March 29 Eukaryotic translation Dr. Albritton

- Discuss shut-down of cellular translation during poliovirus and diptheria infection.
- Explain the mechanism by which interferon regulates translation initiation.
- Discuss the translational regulation of proteins involved in iron transport.
- Discuss diseases involving loss of iron transport translational regulation.

Mar. 31 Paper Discussion (8:30-9:50) Dr. Senogles

Exam III April 6, 1:00-4:00PM in GEB Room A302 (covers material from March 1 – March 29)