MCDB 5230 Gene Expression Fall 2019

Gold A350
Tue: 4-5:15PM: Friday1:00-2:15PM
Course Organizer: Ken Krauter krauter@colorado.edu 2-6693

Fall semester of Core is divided into two sections:
A) Fall1 - Protein Structure/function Aug 27-Oct 15

B) Fall2 - Genome Organization and Gene expression Oct 17– Dec 12

They will be taught by faculty in blocks of 4-5 lectures per topic. The class meets Tues 4-5:15 and Fri- day 1-2:15 in room Gold A150. **First class is August 27**. There will be a total of ~28 classes in the fall. Like all graduate classes you take, you need to achieve a grade of B or better in order for the course to count toward your Ph.D. In addition you **MUST** pass this course to advance in the program.

Grading will be based on classroom attendance and participation as well as your scores on the two take-home at the ends of Fall1 and Fall2. Exams will be designed as problem solving exercises graded by the instructors. Classes are expected to be highly interactive alternating "lecture style" and paper discussion. Formats for the paper discussions are discretionary but will involve some sort of required oral discussion of specific data/figures in the assigned papers.

Below are the topics to be covered:

Protein Structure and Function

Class 1 Aug 27 (Copley) Review of general protein structure with an in-class lab using molecular modeling software, Chimera.
Assignment
download Chimera
Readings
Directed evolution of genetic parts.pdf
Visualizing Protein Structures Using Chimera v2.dotx

Class 2 Aug 30 (Copley) Evolution of protein function, especially how new functions can arise from existing proteins with either structural or functional similarity.
PowerPoint for class
Catalysis 2019.pptx
Modulation of protein function by small molecules 2019.pptx
Protein evolution 2019.pptx

Class 3 - 4 Sep 3,6 (Copley) Characterization of small molecule interactions, modulation of protein function by small molecules and control of transcriptional regulators – e.g. AraC, the transcriptional regulator used to control the pBAD promoter. Enzyme inhibition/activation, competitive, non-competitive and uncompetitive inhibition, allosteric regulation, and receptors.
Guidelines for Paper Discussions Paper presentations for Class 4.docx

Class 5 - 8 Sep 10,13,17,20 (Old) a) Non-covalent interactions; b) Enzymes, catalysis (kinetics review), enzyme classes (polymerases, kinases, proteases, ATPases, etc); c) Macromolecular machines, covalent modifications (phosphorylation & ubiquitin signaling) and compartmentalization. Combinatorial post-translational modifications, regulation through multi-site modification. d) Bioenergetics, metabolism, metabolic flux, and metabolomics. Methodologies involving spectroscopy will be covered using both lecture and relevant papers.

Readings
Knight and Shokat 2005 - Features of selective kinase inhibitors.pdf

Knight and Shokat 2007 - Chemical genetics - where genetics and pharmacology meet.pdf

Taylor and Kornev - 2011 - Protein kinases evolution of dynamic regulatory p.pdf
Wang et al. 2014 - MELK is an oncogenic kinase essential for mitotic progression in basal-like breast cancer cells.pdf

Lin et al. - 2019 - Off-target toxicity is a common mechanism of actio.pdf
Outline_WOld_Class5to8.docx

Class 9-11 Sep 24-27 (Park) Specific protein degradation, including degradation machinery, the role of proteolysis in fundamental cellular processes, and their relationship to several pathogenic conditions (e.g. Neurodegenerative diseases, including Alzheimer's and Parkinson's syndrome)

Readings
Sept24 Dual Role of Ribosome-Binding Domain of NAC as a Potent Suppressor of Protein Aggregation and Aging-Related Proteinopathies.pdf

Sept27 Distinct proteostasis circuits cooperate in nuclear and cytoplasmic protein quality control.pdf

Class 12-13 Oct 1-4 (Park) Protein translational control including lecture and paper discussion.
Readings
Oct1 Tau-driven 26S proteasome impairment and cognitive dysfunction can be prevented early in disease by activating cAMP-PKA signaling.pdf

Oct4 The proteasome biogenesis regulator Rpn4 cooperates with the unfolded protein response to promote ER stress resistance.pdf

Class 14,15 Oct 8,15 (Stowell) Function/regulation of the axonal synapse.
Readings
2019_slides.pdf

EXAM ON FALL1 WILL BE GIVEN OVER THE WEEKEND OF OCT 20

Class 16 - 17 Oct. 18 – Oct. 22 (Singh) Series will cover elements of mRNA synthesis including transcription, nuclear RNA processing, cytoplasmic RNA fates and functions, and RNA degradation. An understanding of the dynamic nature of mRNA expression vis-à-vis cell function will be covered.
Course material for Fri and Tue (4 pdfs) can be found below.
1. On Friday, I will present Singh_TranscriptionLecture2019.pptx.
2. On Tuesday, There will be 8-10 min each student presentations as follows (come prepared with a ppt presentation for your group).
Students with last names (A-D) will present Levine...pdf
Students with last names (F-M) will present Salisbury ...pdf
Students with last names (N-W) will present Hnisz...pdf
I will wrap up transcription and transcriptional control.

Singh_Hnisz-Sharp-Cell2017PIIS009286741730185X.pdf
Singh_Levine-TjianPIIS0092867414002013.pdf
Singh_Salisbury-Cramer-NatSt-2015nrm3952.pdf
Singh_TranscriptionLecture2019.pptx

Class 18 - 19 Oct 29- Nov 1 (Chuong) Chromosomal organization of chromosomes and the DNA within them. Emphasis on human diseases related to changes in DNA organization.
Readings

Heinz2018Cell.pdf
Class 20-23 Nov 5-15 (Yi) Roles of ncRNA in gene regulation and development. Cellular/tissue-specific transcriptional gene regulation, especially as it pertains to the "alternative genetic code" histone modifications. This section will provide clinically relevant phenotypes associated with this regulatory mechanisms.

Readings
Crispr screen_Ago_Mendell.pdf
In vivo reprogramming_Belmonte.pdf

Class 24-25 Nov.19,22 (Arnoult) DNA Replication and repair especially related to cancer and disease.

THANKSGIVING WEEK – NO CLASS Nov. 26-29

Class 26 - 28 Dec 3 – 10 (Singh) Series will cover elements of mRNA synthesis including transcription, nuclear RNA processing, cytoplasmic RNA fates and functions, and RNA degradation. An understanding of the dynamic nature of mRNA expression vis-à-vis cell function will be covered.

Readings
Singh_RNAProcessLect2019.ppt
Singh_BentleyReview-nrg3662.pdf
Singh_CramerPromoterswapRNAProcPNAS-1997.pdf
Singh_NMDLykke-Andersen_Steitz2000.pdf
Singh_RNA_QualityControlReview.pdf

EXAM ON FALL2 WILL BE GIVEN DEC. 11 DUE DEC 14 9AM