Molecular Basis of Cell Signaling
(GS13 1024)
Spring 2020

Guangwei Du, Coordinator

Times: Monday, Wednesday, Friday 1:00-2:30pm; UT-Medical School, Room 4.100

4 credits – 4.5 hrs lecture/wk

Total number of lectures - 37; Total number of exams - 3 (take home)

Signal transduction is one of the most active fields in biomedical research. Precisely controlled activation of signaling molecules is essential for development, normal tissue homeostasis, tissue repair, and immunity. Dysregulation of cellular signaling pathways are responsible for diseases such as cancer, diabetes, cardiovascular disease. Accordingly, therapeutic strategies designed to specifically target altered signaling pathways in disease would achieve better outcomes.

The goal of Molecular Basis of Cell Signaling is to provide graduate students with an in depth understanding of the molecular mechanisms of signaling. The broad purview of signaling provides the fundamentals essential to many fields, and traditionally has served students from multiple disciplines such as cell biology, biochemistry, neurobiology, physiology, pharmacology, cancer and systems biology, and provides fulfillment of the GSBS molecular requirement. The prerequisites are a solid background in cell biology and biochemistry. This course includes the following topics; (1) mechanism of ligand activation and desensitization of G protein coupled receptors, G proteins and second messengers; (2) fundamentals of ion channel structure, activation, function and control by ligands; (3) basic structure, function and localization of protein phosphorylation cascades and their role in growth factor regulation through the "small G protein Ras family; (4) structure and function of membranes including the role of lipid rafts/nanodomains; (5) state of the art studies of the network of transcriptional regulators including the steroid family of ligand-induced transcriptional factors, the complexity of transcriptional complexes, transcriptional control by cAMP/PKA and the circadian clock, and involvement of the cell cycle; (6) systems biology analysis of signaling networks; and (7) fundamentals of computational dynamics for modeling ligand binding/docking to proteins and membrane interactions. Topics covered are introduced by first providing access to a broad perspective with suitable reviews, followed by a focus on the primary literature. Student presentations will involve group discussions of a classic publication in each block in journal club style. Exams are take home which provides a means of minimizing memorization and stimulating creativity, while in the process, driving home important concepts.

Faculty

Block 1**: **Membrane Receptor Signaling

***Faculty**: C. Dessauer, R. Miller, I. Levental**,** M. Zhu, O. Pochynyuk*

Block 2**: **Intracellular Signaling Cascades

***Faculty**: J. Frost, S. Cunha, G. Du, X. Cheng, YP Li, K. Sun, K. Venkatachalam, H-E. Kim, D. Frigo*

Block 3: Nuclear Signaling/Transcription

***Faculty**: W. Li, V. Narkar, R. Berdeaux, C. Denicourt, G. Breton, D. Lee, J Wang*

Block 4**: **Structure and Pathway modeling

***Faculty**: J. Chang; A. Gorfe*

I. ***Membrane Receptor Signaling***

Jan 6	*Structural aspects of G protein signaling Covalent modifications; Oncogenic mutations and disease alpha & βγ subunit structure/function/effectors; adenylyl cyclase*	*C. Dessauer*
Jan 8	*GAPs: regulators of G-protein signaling (RGS) Structures/assays/mechanisms/regulation: GGL domains; RGS9; G protein effectors; structure/regulation*	*C. Dessauer*
Jan 10	*Additional complexities of G protein regulation GDI/Goloco motifs; Downstream effectors*	*C. Dessauer*
Jan 13	*Localization/feedback of cAMP signals PKA anchoring proteins (AKAPs)*	*C. Dessauer*
Jan 15	*Wnt signaling in development and disease*	*R. Miller*
Jan 17	*Ion channels; overview of structure/function/regulation*	*M. Zhu*
Jan 20	***Martin Luther King Day***	
Jan 22	*Regulation of ion channels: 2nd messengers, kinases, ions and G proteins*	*M. Zhu*
Jan 24	*Receptor tyrosine kinases*	*I. Levental*
Jan 27	*Membrane microdomains and signaling*	*I. Levental*
Jan 29	*Ion channels in epithelium*	*O. Pochynyuk*
Jan 31	***Student presentations***	*Drs. Miller & Du, Students*
Feb 3	***Exam I***	

II. ***Intracellular Signaling Cascades***

Feb 5	*Overview of protein kinases and phosphatases*	*J. Frost*
Feb 7	*Rho GTPases*	*J. Frost*
Feb 10	*Lipids as signaling molecules*	*G. Du*
Feb 12	*Lipid regulation of the Ras-MAPK signaling pathway*	*G. Du*
Feb 14	*Ion channel targeting by ankyrin proteins*	*S. Cunha*

Feb 19	*cAMP-mediated cell signaling*	*X. Cheng*
Feb 21	*The unfolded protein response signaling in health and diseases*	*H-E. Kim*
Feb 24	*Intramuscular signaling regulating skeletal muscle proteolysis*	*Y.P. Li*
Feb 26	*Inflammatory signaling*	*K. Sun*
Feb 28	*Ca^{++}compartmentation and signaling*	*K. Venkatachalam*
Mar 2	*mTOR*	*K. Venkatachalam*
Mar 4	*AMPK*	*D. Frigo*
Mar 6	***Student presentations***	*Drs. Kim & Du, Students*
Mar 9	***Exam II***	

III. ***Regulation of Transcription and Translation***

Mar 11	*Overview of transcription regulation and epigenetics*	*W. Li*
Mar 13	*Enhancers: The Ultimate Genomic Executor of Many Signaling Events on Chromatin*	*W. Li*
Mar 16 - 20	***Spring Break***	
Mar 23	*Nuclear Receptors: Steroid Sisters & Orphan Brothers*	*V. Narkar*
Mar 25	*Nuclear Receptors: Steroid Sisters & Orphan Brothers*	*V. Narkar*
Mar 27	*Transcriptional regulation by cAMP*	*R. Berdeaux*
Mar 30	*Transcriptional Mechanisms and Circadian Rhythms I: Basic chronobiology principles established using genetics and genomics.*	*G. Breton*
Apr 1	*Transcriptional Mechanisms and Circadian Rhythms II: Examples of clock control on physiology (outputs).*	*G. Breton*
Apr 3	*p53 signaling in cancers and stem cells*	*D. Lee*
Apr 6	*Growth, cell cycle and transcription*	*C. Denicourt*
Apr 8	*Regulation of gene expression by posttranscriptional modification of cellular RNA*	*C. Denicourt*

Apr 10	*Non-coding RNAs and epigenetic regulation of gene expression*	*J. Wang*
Apr 13	***Student presentations***	*Drs. Denicourt & Du, Students*

IV. ***Structural and Systems Modeling***

Apr 15	*Systems modeling I*	*J. Chang*
Apr 17	*Systems modeling II*	*J. Chang*
Apr 20	*Structure-based modeling: Concepts and Methods*	*A. Gorfe*
Apr 22	*Structure-based modeling: Applications to Ras proteins*	*A. Gorfe*
Apr 24	***Student Presentations***	*Drs. XXX & Du, Students*
Apr 27	*Exam preparation*	
Apr 29	***Exam III***	