Molecular Basis of Cell Signaling
(GS13 1024)

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 - 36; Total number of exams - 4 (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) basic structure, function and localization of protein phosphorylation cascades and their role in growth factor regulation through the "small G protein Ras family; (3) structure and function of membranes including the role of lipid rafts/nanodomains; (4) systems biology analysis of signaling networks; (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) fundamentals of ion channel structure, activation, function and control by ligands; 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**: R. Clark, C. Dessauer, R. Miller, I. Levental*

Block 2**: **Intracellular Signaling Cascades
***Faculty**: J. Frost, G. Du, X. Cheng, K. Venkatachalam, D. Boehning, YP Li*

Block 3: Nuclear Signaling/Transcription
***Faculty**: D. Loose, R. Berdeaux, V. Narkar, G. Breton, C. Denicourt, D. Lee*

Block 4**: **Ion Channel Signaling
***Faculty**: M. Zhu, O. Pochynyuk, S. Cunha*

Block 5**: **Structure and Pathway modeling
***Faculty**: J. Chang; A. Gorfe*

I. ***Membrane Receptor Signaling***

Jan 08	*GPCR Structure and Function; ligand binding and activation; amplification; weak and strong agonists, antagonists, inverse and biased agonists*	*R. Clark*
Jan 10	*Structural aspects of G protein signaling Covalent modifications; Oncogenic mutations and disease alpha & βγ subunit structure/function/effectors; adenylyl cyclase*	*C. Dessauer*
Jan 12	*GAPs: Regulators of G-protein signaling (RGS)Structures/assays/mechanisms/regulation: GGL domains; RGS9; G protein effectors; structure/regulation*	*C. Dessauer*
Jan 15	***Martin Luther King Day***	
Jan 17	*Additional Complexities of G protein regulation GDI/Goloco motifs; Downstream effectors*	*C. Dessauer*
Jan 19	*Discovery of Some Key Developmental Signaling Pathways*	*R. Miller*
Jan 22	*Localization/feedback of cAMP signals PKA anchoring proteins (AKAPs)*	*C. Dessauer*
Jan 24	*Wnt Signaling in Development and Disease*	*R. Miller*
Jan 26	*Receptor tyrosine kinases*	*I. Levental*
Jan 29	*Membrane microdomains and signaling*	*I. Levental*
Jan 31	***Student presentations***	*Drs. Levental & Du, Students*
Feb 2	***Exam I***	

II. ***Intracellular Signaling Cascades***

Feb 5	*Overview of Protein Kinases and Phosphatases*	*J. Frost*
Feb 7	*Rho GTPases*	*J. Frost*
Feb 9	*Rho GEFs and GAPs*	*J. Frost*
Feb 12	*Lipids as signaling molecules*	*G. Du*
Feb 14	*Lipid regulation of the Ras-MAPK signaling pathway*	*G. Du*

Feb 16	*cAMP-mediated cell signaling*	*X. Cheng*
Feb 19	***Holiday – President's Day***	
Feb 21	*Cell death signaling*	*D. Boehning*
Feb 23	*Intramuscular signaling regulating skeletal muscle proteolysis*	*Y.P. Li*
Feb 26	*Ca^{++}compartmentation and signaling*	*K. Venkatachalam*
Feb 28	*mTOR*	*K. Venkatachalam*
Mar 2	***Students presentations***	*Drs. Venkatachalam & Du, Students*
Mar 5	***Exam II***	

III. ***Nuclear Receptor Signaling/Transcription***

Mar 7	*Transcription I; Overview of Transcription. PolII Polymerase complexes*	*D. Loose*
Mar 9	*Transcription II Chromatin structure and remodeling*	*D. Loose*
Mar 12 - 16	***Spring Break***	
Mar 19	*Transcriptional regulation by cAMP*	*R. Berdeaux*
Mar 21	*Nuclear Receptors: Steroid Sisters & Orphan Brothers*	*V. Narkar*
Mar 23	*Growth, cell cycle and transcription*	*C. Denicourt*
Mar 26	*Transcriptional Mechanisms and Circadian Rhythms I: Basic chronobiology principles established using genetics and genomics.*	*G. Breton*
Mar 28	*Transcriptional Mechanisms and Circadian Rhythms II: Examples of clock control on physiology (outputs).*	*G. Breton*
Mar 30	*p53 signaling in cancers and stem cells*	*D. Lee*
Apr 2	*Integration of signaling at the level of transcription*	*D. Loose*
Apr 4	***Students presentations***	*Drs. Narkar & Du, Students*
Apr 6	***EXAM III***	

IV. ***Ion channel Signaling***

Apr 9	*Ion channels; overview of structure/function/regulation*	*M. Zhu*
Apr 11	*Regulation of ion channels: 2nd messengers, kinases, ions and G proteins*	*M. Zhu*
Apr 13	*Ion channels in epithelium*	*O. Pochynyuk*
Apr 16	*Ion channel targeting by ankyrin proteins*	*S. Cunha*
Apr 18	***No Student Presentations***	

V. ***Structural and Systems Modeling***

Apr 20	*Systems modeling I*	*J. Chang*
Apr 23	*Systems modeling II*	*J. Chang*
Apr 25	*Structure-based modeling: Concepts and Methods*	*A. Gorfe*
Apr 27	*Structure-based modeling: Applications to Ras proteins*	*A. Gorfe*
April 30	***Student Presentations***	*Drs. Chang & Du, Students*
May 2	*Exam preparation*	
May 4	***Exam IV***	