Molecular Basis of Cell Signaling  
(GS13 1024)  
Guangwei Du, Coordinator  
Times: Monday, Wednesday, Friday 1:00-2:30pm; UT-Medical School, Room 4.136  
4 credits – 4.5 hrs lecture/wk  
Total number of lectures - 36; 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  

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

Block 4: Structure and Pathway modeling  
Faculty: J. Chang; A. Gorfe
### I. Membrane Receptor Signaling

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>Jan 14</td>
<td>Structural aspects of G protein signaling Covalent modifications; Oncogenic mutations and disease alpha &amp; βγ subunit structure/function/effectors; adenylyl cyclase</td>
<td>C. Dessauer</td>
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<tr>
<td>Jan 16</td>
<td>GAPs: regulators of G-protein signaling (RGS) Structures/assays/mechanisms/regulation: GGL domains; RGS9; G protein effectors; structure/regulation</td>
<td>C. Dessauer</td>
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<td>Jan 18</td>
<td>Additional complexities of G protein regulation GDI/Goloco motifs; Downstream effectors</td>
<td>C. Dessauer</td>
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<td>Jan 21</td>
<td><strong>Martin Luther King Day</strong></td>
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<td>Jan 23</td>
<td>Localization/feedback of cAMP signals PKA anchoring proteins (AKAPs)</td>
<td>C. Dessauer</td>
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<tr>
<td>Jan 25</td>
<td>Wnt signaling in development and disease</td>
<td>R. Miller</td>
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<tr>
<td>Jan 28</td>
<td>Receptor tyrosine kinases</td>
<td>I. Levental</td>
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<tr>
<td>Jan 30</td>
<td>Membrane microdomains and signaling</td>
<td>I. Levental</td>
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<tr>
<td>Feb  1</td>
<td>Ion channels; overview of structure/function/regulation</td>
<td>M. Zhu</td>
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<td>Feb  4</td>
<td>Regulation of ion channels: 2nd messengers, kinases, ions and G proteins</td>
<td>M. Zhu</td>
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<td>Feb  6</td>
<td>Ion channels in epithelium</td>
<td>O. Pochynyuk</td>
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<td>Feb  8</td>
<td><strong>Student presentations</strong></td>
<td>Drs. Levental &amp; Du, Students</td>
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<tr>
<td>Feb 11</td>
<td><strong>Exam I</strong></td>
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### II. Intracellular Signaling Cascades

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<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Presenter</th>
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</thead>
<tbody>
<tr>
<td>Feb 13</td>
<td>Lipids as signaling molecules</td>
<td>G. Du</td>
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<tr>
<td>Feb 15</td>
<td>Lipid regulation of the Ras-MAPK signaling pathway</td>
<td>G. Du</td>
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<tr>
<td>Feb 18</td>
<td>Overview of protein kinases and phosphatases</td>
<td>J. Frost</td>
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<tr>
<td>Feb 20</td>
<td>Rho GTPases</td>
<td>J. Frost</td>
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<tr>
<td>Feb 22</td>
<td>Ion channel targeting by ankyrin proteins</td>
<td>S. Cunha</td>
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Feb 25 cAMP-mediated cell signaling X. Cheng
Feb 27 Cell death signaling D. Boehning
Mar 1 Intramuscular signaling regulating skeletal muscle proteolysis Y.P. Li
Mar 4 Inflammatory signaling K. Sun
Mar 6 Ca++ compartmentation and signaling K. Venkatachalam
Mar 8 mTOR K. Venkatachalam
Mar 11 The unfolded protein response signaling in health and diseases H-E. Kim
Mar 13 Student presentations Drs. Venkatachalam & Du, Students
Mar 15 Exam II
Mar 18 - 22 Spring Break

III. Nuclear Receptor Signaling/Transcription

Mar 25 Transcription I: Overview of Transcription. PolII Polymerase complexes D. Loose
Mar 27 Transcription II Chromatin structure and remodeling D. Loose
Mar 29 Enhancer: the Genome Executor of Transcription W. Li
Apr 01 Transcriptional regulation by cAMP R. Berdeaux
Apr 03 Nuclear Receptors: Steroid Sisters & Orphan Brothers V. Narkar
Apr 05 Nuclear Receptors: Steroid Sisters & Orphan Brothers V. Narkar
Apr 08 Growth, cell cycle and transcription C. Denicourt
Apr 10 Transcriptional Mechanisms and Circadian Rhythms I: Basic chronobiology principles established using genetics and genomics G. Breton
Apr 12 Transcriptional Mechanisms and Circadian Rhythms II: Examples of clock control on physiology (outputs) G. Breton
Apr 17 p53 signaling in cancers and stem cells D. Lee
Apr 19 Student presentations Drs. Denicourt &
IV. **Structural and Systems Modeling**

- **Apr 22**  
  Systems modeling I  
  *J. Chang*

- **Apr 24**  
  Systems modeling II  
  *J. Chang*

- **Apr 26**  
  Structure-based modeling: Concepts and Methods  
  *A. Gorfe*

- **Apr 29**  
  Structure-based modeling: Applications to Ras proteins  
  *A. Gorfe*

- **May 1**  
  **Student Presentations**  
  *Drs. Chang & Du, Students*

- **May 3**  
  Exam preparation

- **May 6**  
  **Exam III**