Course description

The fourth module of the Foundations in Biomedical Sciences course will focus on the mechanisms of cell communication. This module will begin by discussing overarching concepts before examining the specific types of molecules that initiate and transduce signals. Examples of cell signaling and subsequent cellular responses will then be considered in different contexts to provide a framework on which future learning can be applied. As the module progresses, the complexity of the systems explored will increase from individual cells to multicellular environments such as tissues, organs and organisms. In addition, normal processes as well as the dysregulation of cell-cell communication in disease will be studied.

The course will be aimed towards first year Ph.D. students in the Division of Graduate Medical Sciences. The class will be taught by members of the Division in a variety of Departments utilizing a combination of traditional lectures and discussion sections focusing on primary research. There will be a total of 7 hours of class time per week. Supplementary study materials will be made available using Blackboard (www.blackboard.bu.edu) to aid students in the review of the material. Reading materials will be taken primarily from the scientific literature and will utilize examples of classical studies as well as recent works. Students will be evaluated on their performance on a quiz, problem set, and examination along with active participation in discussion sections.

Course Learning Objectives

At the end of this module students will be able to:

1. Describe the biochemical basis of ligand-receptor interactions
2. Explain in lay language how extracellular signals are interpreted by cells
3. Give examples of how cells communicate with their neighbors to form multicellular structures
4. Compare the mechanisms of tissue maintenance with the breakdown of tissue homeostasis
5. Relate how the dysregulation of normal signaling can lead to disease
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Grading:
Quiz 10%
Final Exam 50%
Problem Set 20%
Breakout Sessions 20%
Total 100%

Recommended reference materials to supplement reading of the literature include:
<table>
<thead>
<tr>
<th>Dates</th>
<th>Class</th>
<th>Instructor</th>
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<tbody>
<tr>
<td>January 10</td>
<td><strong>Lecture 1:</strong> Introduction to basic concepts of cell communication.</td>
<td>Rahimi</td>
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<td></td>
<td>—How do cells signal to one another: extracellular signals, contact-dependent signaling, paracrine signaling, autocrine signaling, gap junctions</td>
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<td>—How are extracellular signals received and processed by cells: ligand-receptor interactions, receptor domains, signaling cascades, feedback loops.</td>
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<td>January 12</td>
<td><strong>Lecture 2:</strong> Introduction to cell signaling – part 1</td>
<td>Kandror</td>
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<td></td>
<td>—The signaling mechanisms of receptor tyrosine kinases (RTKs): receptor dimerization, transautophosphorylation, docking sites and signaling effectors, cytoplasmic tyrosine kinases, Ras superfamily, phosphotases, attenuation of signaling</td>
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<td>—The signaling mechanisms of serine/threonine kinase receptors: TGF-beta receptor, SMADS</td>
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<td>—JAK/STAT: fast track to the nucleus</td>
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<td>January 13</td>
<td><strong>Lecture 3:</strong> Introduction to cell signaling – part 2</td>
<td>Kandror</td>
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<td>—The signaling mechanisms of seven-transmembrane receptors in the context of rhodopsins and olfactory receptors: G-protein-coupled receptors, structure, ligands, G-proteins, signal amplification, desensitization</td>
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**January 13**

**Discussion Session #IV-1**

Two classical receptor tyrosine kinase papers will be discussed in the context of modern technology:


Problem set will be handed out to be reviewed, discussed and returned in #IV-3

**January 17**

**Lecture 4:** Introduction to cell signaling – part 3

—Second messengers: cAMP signaling, phospholipase C signaling, Ca^{2+}, CaM Kinase, direct activation of ion channels, stimulation of transcription


**January 19**

**Lecture 5:** The regulation of cell life and death

—How a loss of cell cycle control can lead to cancer
—Cell death and senescence: Apoptosis pathways, ER stress, Necrosis


**January 20**

**Lecture 6:** Control of cell movement

—How RhoGTPases form the functional link between
extracellular signals and the cytoskeleton
—How cell movements can be directed: Chemotaxis, Dictyostelium, cAMP signaling, Drosophila border cell migration, PDGF/VEGF signaling
—What happens when cell movements are not regulated: Metastasis

1. Wang et al (2011) Signaling mechanisms for chemotaxis


January 20  
**Discussion Session #IV-2**

In class quiz.

Discussion of the research articles assigned for lectures 5 and 6 with emphasis on understanding the big picture in relation to cell communication and also the methodologies used.

January 24  
**Lecture 7:** Creating tissue boundaries and organizing different cell types (Martin)
—How boundaries of different cell types within a tissue are established: Notch signaling and contact inhibition.
—How neurons make connections using repelling and attracting signals: Semaphorin signaling and guidance cues.


January 26  
**Lecture 8:** Epithelial morphogenesis
—How epithelium, the "cover sheet" of all organs, develops during embryonic development: formation and maintenance of cell-cell junctions; establishment of polarity of epithelial cells.
—What happens when the epithelial structure is broken down: Epithelial-to-mesenchymal transition in development and disease.

Martin


January 27

**Lecture 9:** Organizing an embryo
—How different body parts are determined during embryonic development, part 1: Axis determination in invertebrates Drosophila D/V and A/P axis; RNA localization and the concept of the morphogen.
—How different body parts are determined during embryonic development, part 2: Axis determination in vertebrates (wnt signaling and growth factors).


January 27

**Discussion Session #IV-3**

Problem set review.

Papers for #IV-4 will be distributed. Each student will write a lay abstract based on one of the assigned papers.


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<thead>
<tr>
<th>Date</th>
<th>Lecture</th>
<th>Presenter</th>
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| January 31 | Lecture 10: Stem cells  
—What is a stem cell  
—Properties and maintenance of stem cells.  
—The ultimate totipotent cells: Germ cell formation.  

| February 2 | Lecture 11: Cell differentiation  
—How cells diverge from common progenitors: Wnt signaling and hedgehog signaling.  
—How the differentiation process can go wrong: Wnt signaling in cancer progression and the role of hedgehog signaling in basal cell carcinoma.  

| February 3 | Lecture 12: Forming complex structures  
—Organ building: how cells respond to morphogens and signaling pathways to make a three-dimensional structure, the heart  

| February 3 | Discussion Session #IV-4  
In class presentation of lay abstract and critique | |
| February 7 | MODULE IV FINAL EXAM | |