Proposed Syllabus, Spring 2016

COURSE INFO:
Course Organizer: Pam Cowin, Professor <cowinp01@nyumc.org>

COURSE GOALS:
Modern cell biology is an exciting discipline relevant to all biologists. In addition, cell biological techniques are essential for mechanistic analysis and preclinical drug validation and hence the study of cell biology is also relevant to the fields of translational and regenerative medicine and drug discovery. Cell biology has played a critical role in the discovery of adult tissue stem cells and reprogramming. Cell biology covers a broad spectrum ranging from subcellular analysis of organelles, cytoskeletal complexes and protein trafficking to studies of complex cell interactions and behaviors. Thus cell biology intersects with and complements the fields of developmental biology, illuminating mechanisms essential for the formation and maintenance of tissues. It has provided critical insight into understanding the inappropriate proliferative states and metastatic behavior of tumor cells in cancer biology and the disintegration of tissues in degenerative pathologies. This course aims to stimulate exploration of concepts and current approaches in modern cell biology and offers a range of active learning and participatory modules to achieve this.

COURSE DESCRIPTION:
The course will cover a broad range of topics relevant to cell biology. It emphasizes basic fundamental cell biology and highlights translational medical applications. The course will cover the following concepts and themes: cell and molecular interactions governing potency, differentiation and plasticity among cellular hierarchies, mechanisms of cell adhesion, migration, communication and dynamic cytoskeletal reorganization in the construction of tissues, regulation of cell proliferation and cell death, and subcellular protein trafficking and signaling. The aberration of these processes in relevant pathological situations will also be discussed throughout the course. The lecture/tutorial format will give students a broad background and the opportunity to engage in discussion on exciting recent data in the field.

COURSE LOGISTICS:
3 credits.
Two 90-minute lectures/week in SK3 9-10:30am Tuesdays and Thursdays.
One 90-minute small group tutorials on Friday morning. Each group explores a different paper along a common theme and this is to stimulate a greater breadth of knowledge as a whole by stimulating “after class” discussion among the student body. There will be two weeks when in place of the above format students will be divided into 3 research groups and given free rein to explore present a 30 minute ppt on a set topic to the class.

GRADING:
In this course we focus on achieving education through preparation and active participation by the students. They are expected to come to class having read set current reviews prior to each of the two weekly lectures. They are encouraged to bring questions and actively engage with the lecturer in order to reach a conceptual understanding of the topic. Small group tutorials are an important aspect of this course where students meet with different faculty in groups of three or four to discuss the concepts raised by a current paper within a tutorial setting. Students are given a choice of tutorial group assignment at the beginning of the course so that they can build this in depth aspect of the curriculum in accord with their own particular research interests.
There will be a take home essay at the end of the course. Students are allowed to choose from a sign up list of topics and are also encouraged to suggest a topic to explore in this manner to a faculty lecturer in the course.

Grading is de-emphasized. The goal is that all students will work actively throughout the course to acquire their own education rather than be tested. This is emphasized at the opening of the course. Grades are based on preparation for class as judged by their active participation in lectures, ppt presentations and tutorial discussion, as well as on their take home essay. Lecturers will be asked to provide feedback on the essay and students may seek guidance while writing it so that the “exam” becomes an education in itself.

**Relevant programs:** Stem Cell Biology, Cellular and Molecular Biology, Developmental Genetics, Molecular Oncology and Immunology, Molecular Pharmacology, Pathobiology, Biomedical imaging and informatics
Week 1: Stem Cells, Lineage and Plasticity

Goal: To introduce students to the concepts and mechanisms by which cell diversity is generated, maintained and/or reprogrammed. The first lecture covers the development of ES cells from prior work on teratomas emphasizing the concepts of niche and potency. Through learning about iPS cells students gain insight into the control of potency and differentiation and the plasticity of the cellular state. The second lecture uses intestine to discuss concepts of the stem cell hierarchy and the niche in generating reserved quiescent as well as activated zones of stem cell activity. It discusses how the stem cells generate the niche and are regulated by the niche. It introduces the role of Wnt Hh and Notch signaling in these processes. Colon cancer is discussed as an example of how deregulated stem cell activity predisposes to cancer and is presented as a careful parsing of the distinction between stem and cancer stem cells.

Tutorials: Recent primary literature will be selected to build upon themes of iPS manipulation, lineage tracing, in vitro models of stem cell and cancer stem cell activity.

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<th>Day</th>
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<th>Room</th>
<th>Lecturer info</th>
<th>Topic</th>
<th>Time</th>
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<tbody>
<tr>
<td>Tues</td>
<td>Jan. 12</td>
<td>SK-3</td>
<td>Dr. Matthias Stadtfeld <a href="mailto:matthias.stadtfeld@med.nyu.edu">matthias.stadtfeld@med.nyu.edu</a> (646) 501-6750 SK4 lab 1</td>
<td>ES and IPS Cells</td>
<td>9:00-10:30am</td>
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<tr>
<td>Thurs</td>
<td>Jan. 14</td>
<td>SK-3</td>
<td>Dr. Pam Cowin. <a href="mailto:Cowinp01@nyumc.org">Cowinp01@nyumc.org</a> x38715 MSB 621</td>
<td>Adult Tissue Stem Cells</td>
<td>9:00-10:30am</td>
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<tr>
<td>Fri</td>
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<td>TUTORIALS</td>
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<td>MSB424</td>
<td>Matthias Stadtfeld <a href="mailto:matthias.stadtfeld@med.nyu.edu">matthias.stadtfeld@med.nyu.edu</a></td>
<td>ES and IPS Cells</td>
<td>9:00-10:30am</td>
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<td>MSB659</td>
<td>Pam Cowin <a href="mailto:Cowninp01@nyumc.org">Cowninp01@nyumc.org</a></td>
<td>Adult Tissue Stem Cells</td>
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<td>MSB424</td>
<td>Markus Schober <a href="mailto:Markus.Schober@nyumc.org">Markus.Schober@nyumc.org</a></td>
<td>ES and IPS Cells</td>
<td>10:30-12:00am</td>
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<td>MSB659</td>
<td>Mayumi Ito <a href="mailto:Mayumi.Ito@nyumc.org">Mayumi.Ito@nyumc.org</a></td>
<td>Adult Tissue Stem Cells</td>
<td>10:30-12:00am</td>
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</table>

Readings for lectures:
Alberts et. al., Molecular Biology of the Cell, 6th edition Chapter 22, pp 1251-1262
Stem cells, the molecular circuitry of pluripotency and nuclear reprogramming. Jaenisch R1, Young R.

Alberts et. al., Molecular Biology of the Cell, 6th edition Chapter 22, pp 1217-1227
The intestinal crypt, a prototype stem cell compartment. Clevers H1.

Tutorial Papers:


Cell. 2006 Aug 25;126(4):663-76. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Takahashi K1, Yamanaka S.
Week 2: Actin Cytoskeleton and Migration

The first lecture covers actin filament structure as revealed by crystallography and EM and biochemical analyses, assembly characteristics, treadmilling, interactions with myosin, regulation by bundling, severing and capping proteins, cellular functions in cortical and filamentous cytoskeleton, role at adherens and focal contact cell junctions, axons, dendrites and in contractile rings during cell division. The second lecture concentrates on cell migration and the role of the GTPases Rho Rac and Cdc42 in lamellipodia, filopodia and cytoskeletal dynamics. Contact guidance, directed individual and collective cell migrations and response to gradients will be covered.

Tues Jan 19  SK-3     Ed Ziff Actin Dynamics 9:00-10:30am
                edward.ziff@nyumc.org
                x35774 SK5-1

Thurs Jan 21  SK-3     Holger Knaut Collective Migration EMT &
                      Holger.Knaut@med.nyu.edu Motility
                      x37227 SK4-15

Fri Jan. 22  TUTORIALS
MSB 424     Holger Knaut. Holger.Knaut@med.nyu.edu 9:00-10:30am
MSB659      Ed Ziff    edward.ziff@nyumc.org 9:00-10:30am
MSB424      Holger Knaut. Holger.Knaut@med.nyu.edu 10:30-12:00am
MSB659      Ed Ziff    edward.ziff@nyumc.org 10:30-12:00am

Lecture Readings
Alberts et. al., Molecular Biology of the Cell, 6th edition Chapter 16, pp 889-965

Science 326, 1208 (2009); Actin, a Central Player in Cell Shape and Movement Thomas D. Pollard and John A. Cooper


Development. 2014 May;141(10):1999-2013. Cell migration: from tissue culture to embryos. Reig G1, Pulgar E, Concha ML.

Tutorials

Dev Cell. 2006 May;10(5):673-80. Chemokine signaling mediates self-organizing tissue migration in the zebrafish lateral line. Haas P1, Gilmour D.

The first lecture will cover the large integrin family and the diverse roles of its members in cell-matrix, cell-cell and clotting interactions. Signaling from kinases and adaptors localized at focal contacts will be covered and the mechanisms of inside out and outside in signaling at these sites. Structural changes in integrin shape and clustering that lead to activation will be discussed. The recently emerging role of specific integrins as mechanotransducers essential for stretch-mediated TGF-beta activation and the consequence of this for cell motility, EMT and feedback loop to matrix synthesis will be introduced. The second lecture will briefly review matrix composition and the role of fibroblasts in its synthesis and then build upon the first lecture through the paradigm of Marfan syndrome, which was initially viewed as a genetic disease in which mutations compromised elastic fibers. More recent work has shown that the elastic fiber defect produces results in loss of docking sites for latent TGF-beta and BMP and when compromised results in excessive signaling due to failure to sequester and locally activate these signaling molecules. This illustrates the interconnection and feedback between the matrix surroundings of cells and signaling that affects their motility and matrix production with pathological ramifications for multiple genetic syndromes as well as EMT induction in cancer and distortion of niche-induced stem cell quiescence in other settings.

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<tr>
<td>Tues</td>
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<td>SK-3</td>
<td>John Munger</td>
<td>Integrins as mechanosensors</td>
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<td>Thurs</td>
<td>Jan. 28</td>
<td>SK-3</td>
<td>Dan Rifkin</td>
<td>Extracellular Matrix</td>
<td>9:00-10:30am</td>
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<td><a href="mailto:rifkid01@nyumc.org">rifkid01@nyumc.org</a></td>
<td>TGFb/BMP signalosome</td>
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<td>Fri</td>
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<td>TUTORIALS</td>
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<td>10:30-12:00am</td>
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<td>MSB659</td>
<td>Dan Rifkin. <a href="mailto:rifkid01@nyumc.org">rifkid01@nyumc.org</a></td>
<td>Extracellular Matrix</td>
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Lecture Readings
Alberts et. al., Molecular Biology of the Cell, 6th edition
Chapter 19, pp 1057-1080

Matrix-dependent perturbation of TGFβ signaling and disease.
Doyle JJ1, Gerber EE, Dietz HC.

Tutorials
Angiotensin II-dependent TGF-β signaling contributes to Loeys-Dietz syndrome vascular pathogenesis.

Abnormal muscle mechanosignaling triggers cardiomyopathy in mice with Marfan syndrome.
Cook JR, Carta L, Bénard L, Chemaly ER, Chiu E, Rao SK, Hampton TG, Yurchenco P; GenTAC Registry Consortium, Costa KD, Hajjar RJ, Ramirez F.
Week 4: Cell-Cell Adhesion and Wnt signaling, Polarity and Par proteins

Goal: This section will emphasize the role of cell-cell interactions and behaviors in building tissues. The first lecture will contrast fibroblastic and epithelial social behavior, review the history of experimentation and thought in cell adhesion form reconstituting sponges to interfering with slime mold aggregation and the contribution of these model organism studies to the elucidation of the major molecular adhesive mechanisms. We will discuss the physical molecular and structural basis of cell adhesion with emphasis on dynamic transitory (immunological synapse) and the relative roles of adherens junctions in initiating epithelial cell adhesion and desmosomes in reinforcing and stabilizing epithelial associations. The role of the cytoskeleton in regulating cadherin based adhesion in stem cell niche and its loss, switching and deregulation in EMT and cancers will be covered and its modulation in morphogenesis such as during convergent extension. The role of beta-catenin as a modulatable link in cell adhesion and a central signal-transducer-transcriptional factor in Wnt signaling will be reemphasized as will the role of p120 catenin and kaiso as example of dual feedback regulators of adhesion and transcription. In the second lecture students will be introduced to the concepts of different types of polarity (apical-basal, planar polarity, polarity of cell division and front-rear polarity during cell migration and the role of these processes in tissue development and cancer. The role of the PAR proteins will be emphasized.

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<td>SK-3</td>
<td>Dr. Pam Cowin <a href="mailto:Cowinp01@nyumc.org">Cowinp01@nyumc.org</a></td>
<td>Cell-Cell Adhesion</td>
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<td>Thurs</td>
<td>Feb 4</td>
<td>SK-3</td>
<td>Dr. Jeremy Nance <a href="mailto:jeremy.nance@med.nyu.edu">jeremy.nance@med.nyu.edu</a></td>
<td>Asymmetry and Polarity</td>
<td>9:00-10:30</td>
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<td>Markus Schober. <a href="mailto:Markus.Schober@nyumc.org">Markus.Schober@nyumc.org</a></td>
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<td>Pam Cowin <a href="mailto:Cowinp01@nyumc.org">Cowinp01@nyumc.org</a></td>
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<td>Mario Delmar. <a href="mailto:Mario.Delmar@nyumc.org">Mario.Delmar@nyumc.org</a></td>
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Readings


Tutorials


Science. 2003 Oct 3;302(5642):103-6.Talin binding to integrin beta tails: a final common step in integrin activation. Tadokoro S1, Shattil SJ, Eto K, Tai V, Liddington RC, de Pereda JM, Ginsberg MH, Calderwood DA
**Week 5: Cell Division, Protein Degradation And Cell Death**

The first lecture focuses on the roles of cyclins, cdks, phosphatases, protein degradation via F-box proteins and ubiquitination as mechanisms controlling the unidirectional cycle of cell division. The second lecture covers apoptosis, necrosis and programmed cell death and the role of the mitochondria and caspase signaling in these processes.

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<td>SK-3</td>
<td><strong>Dr. Michele Pagano</strong></td>
<td>Cell Cycle &amp; Protein degradation</td>
<td>9:00-10:30am</td>
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<td><a href="mailto:michele.pagano@nyumc.org">michele.pagano@nyumc.org</a></td>
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<td>Thurs</td>
<td>Feb. 11</td>
<td>SK-3</td>
<td><strong>Dr. Don Ryoo</strong></td>
<td>Cell Death mechanisms</td>
<td>9:00-10:30am</td>
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<td><a href="mailto:HyungDon.Ryoo@nyumc.org">HyungDon.Ryoo@nyumc.org</a></td>
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<td>x37257 MSB493</td>
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<td>Fri</td>
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<td><strong>TUTORIALS</strong></td>
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<td>MSB 424</td>
<td>Shafi Kuchay</td>
<td>9:00-10:30 am MSB</td>
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<td>424</td>
<td>Shafi Kuchay</td>
<td>10:30-12:00 am</td>
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<td>MSB659</td>
<td>Don Ryoo. <a href="mailto:HyungDon.Ryoo@nyumc.org">HyungDon.Ryoo@nyumc.org</a></td>
<td>9:00 - 10:30am</td>
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<td>MSB659</td>
<td>Don Ryoo. <a href="mailto:HyungDon.Ryoo@nyumc.org">HyungDon.Ryoo@nyumc.org</a></td>
<td>10:30-12:00am</td>
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**Readings**

Alberts et. al., Molecular Biology of the Cell, 6th edition
Chapter 17, pp 963-1020

Mechanisms and function of substrate recruitment by F-box proteins.

Alberts et. al., Molecular Biology of the Cell, 6th edition Chapter 18, pp 1021-1032


**Tutorials**


Week 6: Microtubule Dynamics Motors and Signaling from the Primary Cilium

Tues  Feb. 16  SK-3  **Dr. Nick Cowan**  Microtubule Dynamics  9:00-10:30am
Nicholas.Cowan@nyumc.org  x38166 MSB315

Thurs  Feb. 18  SK-3  Hh signaling from the primary cilium  TBD

Fri  Feb. 19  TUTORIALS
MSB659  Pam Cowin  9:00-10:30am
MSB 659  Pam Cowin  10:30-12:00am
MSB424  Nick Cowan. Nicholas.Cowan@nyumc.org  9:00-10:30am
MSB424  Nick Cowan. Nicholas.Cowan@nyumc.org  10:30-12:00am

Lecture Readings
Alberts et. al., Molecular Biology of the Cell, 6th edition Chapter 16, pp 925-943

Akhmanova A1, Steinmetz MO.

Tutorials
Cell. 2012 Apr 13;149(2):371-82. EBs recognize a nucleotide-dependent structural cap at growing microtubule ends. Maurer SP1, Fourniol FJ, Bohner G, Moores CA, Surrey T.

PMID: 19701205. Primary cilia can both mediate and suppress Hedgehog pathway-dependent tumorigenesis.
Wong SY, Seol AD, So PL, Ermilov AN, Bichakjian CK, Epstein EH Jr, Dlugosz AA, Reiter JF.
### Week 7: Concepts In Subcellular Membrane Trafficking

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<tr>
<td>Tues</td>
<td>Feb. 23</td>
<td>SK-3</td>
<td><strong>Dr. Don Ryoo</strong> <a href="mailto:HyungDon.Ryoo@nyumc.org">HyungDon.Ryoo@nyumc.org</a> x37257 MSB493</td>
<td>ER, protein translocation folding, processing &amp; trafficking to Golgi</td>
<td>9:00-10:30am</td>
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<tr>
<td>Thurs</td>
<td>Feb. 25</td>
<td>SK-3</td>
<td>Dr. Niels Ringstad <a href="mailto:niels.ringstad@med.nyu.edu">niels.ringstad@med.nyu.edu</a> x33753 SK5-14</td>
<td>Endocytosis, Phagocytosis</td>
<td>9:00-10:30am</td>
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<tr>
<td>Fri</td>
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<td>9:00-10:30am</td>
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<td></td>
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<td>424</td>
<td>Dr. Niels Ringstad <a href="mailto:niels.ringstad@med.nyu.edu">niels.ringstad@med.nyu.edu</a></td>
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<td>10:30-12:00 am MSB</td>
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<td>MSB 424</td>
<td>Dr. Niels Ringstad <a href="mailto:niels.ringstad@med.nyu.edu">niels.ringstad@med.nyu.edu</a></td>
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<td>9:00-10:30 am</td>
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**Readings**

  Koenig PA1, Ploegh HL2.

  Doherty GJ1, McMahon HT.

  Mellman I1, Yarden Y.

**Tutorials**

  Stein A1, Ruggiano A2, Carvalho P2, Rapoport TA3.

- A mutation that impairs the ability of lipoprotein receptors to localise in coated pits on the cell surface of human fibroblasts.
  Anderson RG, Goldstein JL, Brown MS.


  Brown MS, Goldstein JL.