COURSE: Cell Structure and Function MCDB 5210, Spring 2020

Location: Gold A350
Time: Tue: 4-5:15PM; Friday1:00-2:15PM
Course Organizer: Ken Krauter
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Classes will be taught by faculty in blocks of 3-5 lectures per topic. The class meets Tues 4-5:15PM and Friday 1-2:15 in room A350. First class is January 14. There will be a total of 28 classes. Like all graduate classes you take, you need to achieve a grade of B or better in order for the course to count toward your Ph.D.
Grading will be based on classroom attendance and participation (10%) as well as the average of your scores on the two take-home exams (90%) given over weekends at the ends of Mar. 16 and May 4.
Exams will be designed as problem solving exercises graded by the instructors. Classes are expected to be highly interactive, alternating "seminar/lecture style" and paper discussion similar to last semester. The instructor may call on anyone to lead the discussion of the data.
Please also note that all reading materials can be gotten by clicking the appropriate links OR may be found on the "Module" assigned to the instructor.
Below are the topics to be covered:

Schedule of Classes:

Robin Dowell 1/14 – 1/28

01/14/20	Basic Genomics Class Slides Readings Gerstein et. al. What is a gene, post ENCODE?
01/17/20	Genomics - How many genes and what is a gene? Discussion: What fraction of the human genome is functional? Readings Defining functional DNA elements in the human genome. by Kellis et. al. Getting "function" right by Brunet and Doolittle An upper limit on the functional fraction of the human genome by Graur
01/21/20	Basic Statistics Class Slides Jan 21 Readings Importance of being uncertain Replication Significance, P values and t-tests
01/24/20	Making sense of distributions and graphs from journal articles You must identify a paper that contains a graph (bar graph, line plot, or similar). Prepare a single slide on the figure/graph (email to Dr. Dowell before start of class). Be prepared to discuss what is presented in the figure (the data, error bars, the conclusion) and evaluate the QUALITY of the figure. *Readings* Visualizing samples with boxplots
01/28/20	Using statistics to compare samples Class slides - Jan 28 Readings Designing comparative experiments Comparing samples – part I part II

Min Han – 1/31 – 2/11

01/31/20	Nature of Genetic mutations, Pleiotropism and genetic redundancy in developmental genetics Readings (see Readings for 02/04/20
02/04/20	Genetic interaction, interpretation of genetic interactions, modify screens *Readings* Rubin, GM and Lewis EB. "A brief history of Drosophila's contributions to genome research." Science. 2000 Mar 24;287(5461):2216-8. Horvitz, H. R., and Sulston, J. E. (1990). "Joy of the worm", Genetics 126, 287-92. Paigen, K. (2003). "One Hundred y ears of mouse genetics: an intellectual history." Genetics (PDF) Paigen, K. (2003). "One Hundred y ears of mouse genetics: an intellectual history." Genetics (PDF) Herskowitz, I. "Functional inactivation of genes by dominant negative mutations." (1987) Nature. 17-23;329(6136):219-22. Review Guarente, L. (1993). "Synthetic enhancement in gene interaction: a genetic tool come of age." Trends Genet. 9, 362-366.
02/07/20	Paper presentation/discussion *Readings* Rooke, J., Pan, D., Xu, T. and Rubin GM. (1996). KUZ, a conserved metalloprotease-disintegrin protein with two roles in Drosophila neurogenesis. Science 273:1227-31DOI: 10.1126/science.273.5279.1227 Weaver, BP, Zabinsky, R. Weaver, YM, Lee, ES, Xue, D. and Han, M. (2014) CED-3 caspase acts with miRNAs to regulate non-apoptotic gene expression dynamics for robust development in C. elegans. eLife 04265. DOI:10.7554/eLife.04265.
02/11/20	Paper presentation/discussion *Readings* Simon, M. A. Bowtell, D. D., Dodson, G. S., Laverty, T. R. and Rubin, G. M. (1991). "Ras 1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase." Cell 67, 701-716. DOI: 10.1016/0092-8674(91)90065-7 Sieburth, D., Sun, Q. and Han, M. (1998). "SUR-8, a conserved Ras-binding protein with leucine-rich repeats, positively regulate Ras-mediated signaling in C. elegans." Cell. 94, 119-130. DOI 10.1016/s0092-8674(00)81227-1

Kevin Jones 02/14 - 02/18

02/14/20	Early mammalian development, transgenics and knockouts, neural development Background Readings https://www.ncbi.nlm.nih.gov/books/NBK26818/ (Links to an external site.) Making transgenics and knockouts… https://www.ncbi.nlm.nih.gov/books/NBK26939/ (Links to an external site.) https://www.ncbi.nlm.nih.gov/books/NBK21632/ (Links to an external site.) https://www.ncbi.nlm.nih.gov/books/NBK10094/ (Links to an external site.) Neural development… https://www.ncbi.nlm.nih.gov/books/NBK26814/
2/18/20	Application of knockout technology in sophisticated ways and "the value of persistence" Readings Chen & Maniatis Review First paper - retinal knockouts – Lefebvre et. al Development (2008)- Figs. 1, 4, 5 Second paper - Axon avoidance - Lefebvre et. al Nature 2012)- Figs. 1-4

Jennifer Knight 02/21 - 02/25

02/21/20	Active Learning/Scientific Teaching Approaches and Evidence of efficacy. Readings *Scientific Teaching - book exerpts* *Increased Structure and Active Learning Reduce the Achievement Gap in Introductory Biology*
02/25/20	Metacognition and learning Reading *Metacognition in Upper-Division Biology Students: Awareness Does Not Always Lead to Control*

Mike Klymkowsky 02/28 - 03/10

02/28/20 03/03/20	Readings Watt. 2016: Engineered Microenvironments to Direct Epidermal: Stem Cell Behavior at Single-Cell Resolution (Links to an external site.) • Ladoux et al 2016: Front–Rear Polarization by Mechanical Cues: From Single Cells to Tissues (Links to an external site.) • Lebreton et al., 2018: Molecular to organismal chirality ... conserved myosin 1DLinks to an external site. • Klymkowsky 2019: Filament and phenotypes
03/06/20 03/10/20	Readings Klymkowsky 2019 Conceptual simplicity and mechanistic complexity (Links to an external site.) Li & Elowitz 2019: Communication codes in developmental signaling pathwaysLinks to an external site. Goentoro & Kirscher 2009: Evidence that fold-change not absolute level of β-catenin dictates Wnt Links to an external site.signaling Akieda et al 2019: Cell competition corrects noisy Wnt morphogen gradients to achieve robust patterning in the zebrafish embryoLinks to an external site.

EXAM WILL BE GIVEN OVER THE WEEKEND OF Mar 13 covering Dowell, Han, Klmkowsky, Jones

Lee Niswander 03/13 -03/20

03/13/20	Limb Development as a model of embryonic patterning, signal integration, 3-D tissue organization (Lecture) Read before March 13 lecture Anderson and Hill (2014). Long range regulation of the sonic hedgehog gene.
03/17/20	Evo-devo and molecular mechanisms driving changes in limb morphology (Class Discussion) Read and be prepared to discuss Cell.2016.09.028. Progressive Loss of Function in a Limb Enhancer during Snake Evolution.
03/20/20	Neural crest biology. Part of the class will include lecture and part will be paper discussion. Please read the following sections in the Okuno paper linked below: Introduction: read pages 1 and 2 Results – read the titles of each section, but then only read these sections below Read section: Clinical features of enrolled CHARGE patients and generation of patient-derived iPSCs Read section: Defective scattering of CHARGE iPSC-NCCs and Figure 4 Read section: Migratory disabilities in CHARGE iPSC-NCCs and Figure 5 Read Discussion and Figure 8 Okuno, H. et al. CHARGE syndrome modeling using patient-iPSCs reveals defective migration of neural crest cells harboring CHD7 mutations. Elife 6, 1438 (2017).

Ken Krauter 03/31/20

03/31/20	**Attempt to explain "Modern" gene mapping in the post-genome era** **Readings – optional but read if you're interested** Brieger et al., (2019). Genes for Good: Engaging the Public in Genetics Research via Social Media. American Journal of Human Genetics 105:65–77. **(paper speaks about modern usage of social media to study population genetics – written by Goncalo Abecasis who is a leader in the field and has David Brazel, a student from my lab in IQ Bio and MCDB).** Liu et al. (2019). Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. Nat Genet 51:237-244. **(paper using HUGE numbers to achieve GWAS significance to study addiction that have failed previously)** Bergstrom et al. (2020) Insights into human genetic variation and population history from 929 diverse genomes. Science 367, 1339-*1352.* *(paper describes a comprehensive look at ALL HUMAN GENETIC DIVERSIT'Y using deep sequencing of 1000 human genomes from across the planet)* *Class Slides Core_Genetics_2020.pdf*

Ding Xue 04/04 – 04/16

04/04/20	*Genetic basis of programmed cell death* *In this lecture, I will discuss how genetic screens and subsequent genetic and functional analyses led to the identification of crucial genes involved in central cell-killing pathway.* PowerPoint5
04/07/20	*Paper presentation/discussion* *The paper discussions will include the followings: (1) the background of the research, (2) the important questions addressed by the paper, (3) all figures and tables and the rationales behind these experiments, (4) discussion of key experiments, (5) conclusions from the results, and (6) additional or future experiments that can be pursued. Each paper should be read and discussed by all students. I will randomly pick a student for one of the figure/table discussions/presentations or students can volunteer to lead the one of these discussions/presentations.* Reading Ellis, H. M., and Horvitz, H. R. (1986). Genetic control of programmed cell death in the nematode C. elegans. Cell 44, 817-829
04/10/20	Biochemical basis of apoptosis. *In this lecture, I will discuss how setup of a robust in vitro cell free system and biochemical fractionation and purification can lead to the identification of crucial proteins involved in apoptosis and the potential underlying mechanisms. I will also discuss these two complementary approaches and the pros and cons of each approach.* PowerPoint6
04/14/20	Paper presentation/discussion Reading Luo, X., Budihardjo, I., Zou, H., Slaughter, C., and Wang, X. (1998). Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. Cell 94, 481-490.

Greg Odorizzi – 04/17 – 04/28

Here is the Zoom Link

04/17/20	Endocytosis and lysosomes (Odorizzi lecture) *Slides*
04/21/20	Research article presentation (students) A Flat BAR Protein Promotes Actin Polymerization at the Base of Clathrin-Coated Pits
04/24/20	Autophagy (Odorizzi lecture) *Slides*
04/28/20	Research article presentation (students) ATG8-Binding UIM Proteins Define a New Class of Autophagy Adaptors and Receptors

FINAL EXAM WILL BE GIVEN OVER THE THREE-DAY PERIOD OF Apr 30 - May 3 (Thurs. 5PM -Sun. 11AM)

Covers Odorizzi, Niswander, Xue, Krauter