BIMM 110 Molecular Basis of Human Disease, Fall 2012

Syllabus

Location – Ledden Auditorium Time – 3 – 3:50 PM MWF Instructor: Dr. Ella Tour Instructor's office hours: Wed., 1-2:15PM in York Hall 2300 Website for the course: http://classes.biology.ucsd.edu/bimm110.FA12/index.shtmlTed: only for clicker registration, grades, discussion forums, paper pdf's: https://ted.ucsd.edu/webapps/login/

Course Description:

This course presents 1) genetic, biochemical, and molecular biological approaches used to identify the molecular basis of human diseases; 2) current understanding of selected major human diseases at the molecular and cellular levels; 3) successful and possible therapeutic treatments of these diseases. Since this is an upper level undergraduate class, it is expected that students who take BIMM 110 already have a good background in molecular biology, metabolic biochemistry, and genetics.

Course goals

1. Present the current understanding and the available treatments of several representative human diseases

2. Evaluate scientific evidence, identify questions that remain to be answered, and possible ways to answer them

3. Practice oral and written scientific communication – how to clearly explain your reasoning

Reference textbooks:

There is no required course textbook. All lecture slides will be posted on the website and are available for download. The lectures will be podcasted. In addition, helpful websites or pdfs with background material for course subjects will be posted on the website or WebCT. Please check the website frequently for updates on the posted material.

1. Molecular Biology of the Cell, 5th Edition, by Bruce Alberts et al. provides useful background information for many subjects in this course. A searchable online edition of the 4th edition of this textbook can be found at:

http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowTOC&rid=mboc4.TOC &depth=10

2. For some topics on human genetics:

Human Molecular Genetics (3rd Edition), T. Strachan & A.P. Read, 2004. Available at BML.

3. Wikipedia is a searchable reference website with explanations for nearly all of the specialized terminology used in the course.

Discussion Sections (starting on the second week of classes)

Schedule of the sections and TA's office hours is posted on the Website. Attendance is mandatory only for the 3 research papers discussions (weeks 2, 6, and 9). Activities in the non-mandatory discussion sections: TA's will explain the more difficult parts of the material and answer questions; you will solve problems (example exam questions). You can attend any discussion sections.

Required materials:

iClicker - a small handheld radio frequency device that you will use to answer questions posed in

class each day. Only the iClicker brand will work. New or used iClickers can be purchased at the bookstore.iClicker is a response system that will allow you to solve problems in-class and get immediate feedback from the instructor, gauge your understanding of a topic relative to the rest of the class, and provide your feedback to improve my teaching methods. You Clicker participation will contribute to 2% of your final grade. You will be graded based on your participation, regardless whether your answer was right or wrong. To get full credit, you will need to participate (=click) at least once in 75% of the lectures. There is no need to notify the instructor or the TA's if you forgot your clicker or ran out of battery - as long as you've participated in 75% of the lectures, you are fine.

Grading

Grading

Components of the final grade: <u>2 Quizzes -</u> 14% each, 28% final grade <u>FINAL EXAM, comprehensive</u>: 60% of the final grade. 5% - participation in discussion sections, particularly the discussions of 4 research papers 5% - homework and in-class group work 2% clicker participation

Overall course letter grades will be assigned using the following scheme: 100% - assigned as an average of the total grade by top **ten** students 90-100% - A (A-, A, A+)

90-100% - A (A-, A 79-89% - B 65-78% - C 50 - 64% - D 0-50% - F

All exams will be closed book/closed computer. Questions will be derived from lecture material and homework reading of papers.

Students with disabilities

Reasonable accommodations will be provided for qualified students with disabilities. If you have any disability that may impair your ability to complete the course successfully, please contact me during the first week of the course.

Academic Integrity

Absolutely no cheating will be tolerated UCSD Policies enforced on Academic integrity will be enforced <u>For further information:</u> <u>http://blink.ucsd.edu/Blink/External/Topics/Policy/0,1162,19400,00.html</u>

All work must be done by the student to whom it is assigned, without any unauthorized aid of any kind. For the homework assignments, you can discuss the questions with your peers and your TA's, but you must write it on your own, in your own words.

Syllabus

Schedule of classes and reading (will be updated frequently)

Week dates	Subject	Sources, reading
Week 0 Sept. 28	Overview of course procedures and the syllabus Recent evolutionary and ecological history of humans and its dramatic influence on the types of disease that afflict humankind.	Human evolution: <u>http://tolweb.org/tree/</u> <u>http://anthropology.si.edu/humanorigins/faq/En</u> <u>carta/encarta.htm</u> <u>http://www.bradshawfoundation.com/journey/</u> <u>http://en.wikipedia.org/wiki/Domestication</u>
Week 1 Oct. 1	Part 1: Genetic Diseases Achondroplasia as an example of a caused by a mutation in one gene. Normal bone growth: cellular and molecular mechanisms.	No sections this week <u>Supplementary reading:</u> <u>Pedigree analysis</u> : Strachan, Tom. Human Molecular Genetics, 4th Edition. Garland Science, Ch. 3, pp. 61-78 or any textbook on Genetics: types of inheritance, symbols used in pedigree analysis <u>Great resource on how bones grow, how</u> <u>growth is regulated (with animations)</u> <u>http://depts.washington.edu/bonebio/ASBMRe</u>

Oct. 3	Molecular pathways that control bone elongation: RTK signaling, role of FGFR3	<u>d/growth.html</u>
Oct. 5	Use of model organisms to understand the mechanisms of human disease: Mouse model of Achondroplasia: gene knock-out and gene knock- in Tackling primary literature: background information on the first paper we will analyze	Great summary of gene targeting techniques in Molecular Cell Biology. 4th edition by Lodish, et al can be found here: <u>http://www.ncbi.nlm.nih.gov/books/NBK21632</u> /#A198 (focus on Gene Targeting Makes It Possible to Produce Transgenic Mice That Are Missing Specific Genes) Using the guidelines (posted <u>here</u>), read Wang et al. (1999) A mouse model for achondroplasia produced by targeting fibroblast growth factor receptor 3 (posted on Ted)
Week 2		Mandatory sections this week. In sections: Paper discussion #1:Wang et al. (1999) A mouse model for achondroplasia produced by targeting fibroblast growth factor receptor 3
Oct. 8	Summary: studies of gene function in model organisms. Knock-out, knock-in, and conditional knock-out Single-gene diseases,	Supplementary reading: Gene targeting: http://www.ncbi.nlm.nih.gov/books/NBK26818 /#A1654 Cre recombinase:
Oct. 10	contd. Cystic fibrosis.	http://cre.jax.org/introduction.html
Oct. 12	Single-gene diseases: Cystic fibrosis, contd. Identification of disease- causing genes in humans	Supplementary reading: Alberts et al., Molecular Biology of the Cell: <u>http://www.ncbi.nlm.nih.gov/books/NBK26818</u> /#A1654 (Read: Genes Can Be Located by Linkage Analysis) Genetic linkage analysis: Mol bio of the cell Alberts, p. 561-62, Figs 8-58, 8-59

		Problem set #1 is posted <u>here</u>
Week 3 Oct.15 Oct. 17 Oct. 19	Hemophilia Human Karyotype. Meiotic non-disjunction. Chromosomal numerical abnormalities. Down syndrome. X inactivation. Sex chromosomal abnormalities	In sections: discussion of Problem set #1 Supplementary reading on the clotting cascade: Biochemistry. 5th edition. Berg JM, Tymoczko JL, Stryer L. New York: W H Freeman; 2002. Available online: http://www.ncbi.nlm.nih.gov/books/NBK22589 / Section 10.5.5 Required reading: Human chromosomes, Parts 2.3 – 2.6 in http://www.ncbi.nlm.nih.gov/books/bv.fcgi?hig hlight=xxy&rid=hmg.section.196#207 Complete a short homework #3 on Ted before Wed class Data from the following paper will be discussed: Korbel et al., (2009) The genetic architecture of Down syndrome phenotypes revealed by high-resolution analysis of human segmental trisomies. PNAS 106 (29), 12031–12036 pdf Supplementary reading: X inactivation, Part 2.2.3 http://www.ncbi.nlm.nih.gov/books/bv.fcgi?hig hlight=xxy&rid=hmg.section.144#152
Week 4 Oct. 22 Oct. 24	Quiz #1 (based on material from Sept. 28 – Oct.15, paper #1) Critical thinking: evaluation of a scientific investigation Part 2 - Multifactorial diseases – interactions of	

	mechanisms Epidemiological studies: The influence of fruit and vegetables the incidence of cancer.	Guest lecturer: Chris Abdullah
Oct. 26	Breast cancer as an example of investigation of molecular mechanisms of cancer	
Week 5 Oct. 29	Breast cancer as an example of investigation of molecular mechanisms of cancer	Guest lecturer: Chris Abdullah
Oct. 31	Cardiovascular disease	Guest lecturer: Bill McGinnis Guest lecturer: Bill McGinnis
Nov. 2	Cardiovascular disease, contd	
Week 6 Nov. 5	Diabetes	Mandatory sections: discussion of Paper 2
Nov. 7	Diabetes, contd.	
Nov. 9	Quiz #2 Part 3: Infectious Diseases Infectious diseases, past and present. Immune system and other means of resistance to pathogens	Background on innate immunity. http://www.ncbi.nlm.nih.gov/sites/entrez?db=b ooks&cmd=Search&term=innate%20immunity %20AND%20mboc4[book]&doptcmdl=TOCV iew On adaptive immunity http://www.ncbi.nlm.nih.gov/sites/entrez?db=b ooks&cmd=Search&term=antibody%20AND%

		20mboc4[book]&doptcmdl=TOCView
Week 7 Nov.	Veterans day – no class	
Nov.	Bacterial pathogens and antibiotics	Guest speaker: Annabel Guichard
14	Anthrax - research and historical perspective.	
Nov. 16		
Week 8 Nov. 19	Anthrax - research and historical perspective, contd.	
Nov. 21	Using fruit flies and human cells to investigate the mechanisms of anthrax infection	
	Happy Thanksgiving! No class	
Nov. 23		
Week 9 Nov. 26	Viruses and other pathogens	Paper 3 discussion in <u>mandatory sections</u> : Guichard et al., (2010) Anthrax toxins cooperatively inhibit endocytic recycling by the Rab11/Sec15 exocyst.
Nov. 28	Allergies, asthma	
Nov.	Part 4: diseases of the brain Molecular biology of neurodegenerative	

Dec. 14	Final Exam 3-6 PM	Location TBA
Dec. /	Solution Summary	
Dec. 5	An inexplicable disease: class activity	
Week 10 Dec. 3	Molecular biology of neurodegenerative disorders: Alzheimer's and Hungtington's disease.	
30	disorders: Alzheimer's and Hungtington's disease.	