BIOL 356 – Biomedical Informatics – Spring 2016

Instructor: Dr. Eric S. Ho (hoe@lafayette.edu)
Office: Kunkel 13
Class hours: MWF 11:00-11:50 am
Office hours: Tuesday 2-4 pm

Course Description:
Two patients received the same treatment, why was one cured but not the other? To answer this puzzle, scientists are trying to search for the answer from the "source code of life", i.e. the human genome. From a biological perspective, the human body is the product of the genome. No two individuals have identical genomes even for monozygotic twins due to random mutations. By taking genome personal, doctors hope that better treatments can be formulated by decoding the information embedded in patients' genomes. This is not a pipedream anymore; the revolution has already started. In 2015, the Whitehouse with the support from the Congress has launched the Precision Medicine Initiative. Biomedical informatics plays the role of integrating distributed information across disciplines from genomes, clinical prognosis, and treatments into a unified view of medicine, the medicine that hones in to specific needs of individuals. Students will learn human variations and major biomedical informatics approaches in translating the fount of genomic information into promising, actionable treatments through lectures, journal discussions, and oral presentations.

Learning Outcomes:
At the completion of this course, you should be able to:
- Recognize the benefits of biomedical informatics and the challenges faced by Precision medicine
- Identify disease related genomic variations
- Demonstrate the use of major genotype-to-phenotype methods
- Explain the genomic basis of rare and complex diseases
- Interpret information from major genomic variations data sources
- Read critically results, methods, and conclusion from primary biomedical informatics literature

Prerequisites:
Prerequisite: BIOL 101-102, preferably BIOL 255 or 336, or permission of instructor.

Grading Policy:
- Assignments 20%
- Computer exercises 10%
- One midterm exam 20%
- One 45-minute oral presentation followed by a 45-minute Q&A session 30%
- Participation in your classmates' oral presentations 20%

Course Materials:

There is no required textbook for this course. But the following three books provide excellent and comprehensive background information in genomics, human genetics, gene mapping, recombinant DNA, and DNA sequencing. Some lecture materials are based on selected topics from these books. I highly recommend you to reference these books if you encounter unfamiliar concepts or topics in reading assigned research articles.

eBook from Skillman Library:

Bioinformatics and Functional Genomics. Jonathan Pevsner. 3rd Edition. Wiley 2015

Books reserved in Skillman Library:

A Primer of Genome Science, Greg Gibson and Spencer V. Muse, Third edition, 2009. QH447 .G534 2009

Exploring personal genomics, Dudley, Joel T, Oxford University Press, 2013. QH447 .D83 2013

Federal Credit Hour Policy:
The student work in this course is in full compliance with the federal definition of a four [two or one as appropriate for half and quarter unit courses] credit hour course. Please see the Registrar's Office web site (http://registrar.lafayette.edu/additional-resources/cep-course-proposal/) for the full policy and practice statement.

Academic Honesty:
You are expected to abide by the college policy on Intellectual Honesty (see Student Handbook p.7).

Useful Links:

1. Lecture notes, reading materials, reading assignments and announcements are disseminated through Moodle http://moodle.lafayette.edu
2. Genetics Home Reference: Your guide to understanding genetics conditions. Chapter 4-6. http://ghr.nlm.nih.gov/handbook.pdf
3. NCBI outreach and education: http://www.ncbi.nlm.nih.gov/About/outreach/courses.html
4. A science primer: http://www.ncbi.nlm.nih.gov/About/primer/index.html
5. The Human Genome Project: http://www.genome.gov/10001772
6. GenomeTV: http://www.youtube.com/user/GenomeTV
7. TEDMED http://www.tedmed.com
8. Biomedical literatures database (PubMed): http://www.ncbi.nlm.nih.gov/pubmed/

Tentative Schedule:

Date	Major Topics	Reading Materials
Jan 25	Introduction	A1: TED video
27	Human disease	*Pevsner ch21*
29	Human disease	*A2: Genomic Variations*
Feb 1	OMIM database	
3	Human genome architecture	*A3: OMIM NAR 2015*
5	Human genome architecture	Pevsner ch20
8	Mendelian disease mapping	
10	Genome physical map	
12	Positional Cloning	*A4: Primer Design*
15	Hierarchical genome sequencing	
17	Whole genome shotgun sequencing	*Initial sequencing and analysis of the human genome.* Nature Feb 15th, 2001
19	Whole genome shotgun sequencing	
22	SNP & Haplotypes	
24	SNP Array	
26	Genetic Association Tests	*Hints of hidden heritability*
29	Complex disease mapping	
Mar 2	Genome wide association study (GWAS)	The search for association 2010
4		Summarize two articles for preview presentation
7*	How to read a research article	Assignment of midterm exam article
9	GWAS	
11	Class cancelled	Due to the outbreak of norovirus
14	Preview of presentation article cum How to present a research article	
16	aCGH & Next Generation Sequencing	Assignment of presentation article
18	NGS	Midterm exam has been postponed to April 1st.
Mar 21-25	Spring Break ☺	
28	Pharmacogenomics	
30	Pharmacogenomics	*Charting the course of genomic medicine Nature vol.740 10 Feb 2011*

	Student presentations
Apr 1*	** Midterm Exam ** 11-12:30 pm
Apr 4	Group 1: Alan Tu and Jose Baez *Paternally induced transgenerational environmental reprogramming of metabolic gene expression in mammals*
6	Q&A 1
8	Group 2: Meryl Hahne and Kristin Cabrera *Absolute quantification of somatic DNA alterations in human cancer*
11	Q&A 2
13	Group 3: Jessica Rupp *Mechanisms of Pharmacogenomic effects of genetic variation within the Cardiac adrenergic Network in heart failure*
15	Q&A 3
18	Group 4: Sean Menarguez and Henry Boozan *Effect of direct-to-consumer genomewide profiling to assess disease risk*
20	Q&A 4
22	Group 5: Jacquelyn Cobb and Catherine Newsom-Stewart *Exome sequencing identifies the cause of a Mendelian disorder*
25	Q&A 5
27	Group 6: Michael Smitelli and Haleigh Waite *An integrated map of genetic variation from 1,092 human genomes*
29	Q&A 6
May 2	Group 7: Jon Gruden and Conrad Stoerker *A genome scan for loci shared by autism spectrum disorder and language impairment*
4	Q&A 7
6	Precision Medicine – The Road Ahead

Articles for Presentation:

Genetic Disorders & Epigenetics

1. Xiong et al. RNA splicing. The human splicing code reveals new insights into the genetic determinants of disease. Science. 2015 Jan 9;347(6218):1254806.
2. NG SB et al. Exome sequencing identifies the cause of a mendelian disorder. Nature Genetics Jan 2010 Vol 42. No. 1, 30-36.
3. Carone BR et al. Paternally induced transgenerational environmental reprogramming of metabolic gene expression in mammals. Cell. 2010 Dec 23;143(7):1084-96.

Genomic variations

4. Mapping and sequencing of structural variation from eight human genomes. Nature 453, 56-64 (1 May 2008)
5. An integrated map of genetic variation from 1,092 human genomes. Nature Nov 2012
6. Global variation in copy number in the human genome. Nature Nov 2007

Biology of Cancer

7. Discovery and saturation analysis of cancer genes across 21 tumor types. Nature 2014.
8. Fu Y, Sun Y, Li Y, Li J, Rao X, Chen C, Xu A. Differential genome-wide profiling of tandem 3' UTRs among human breast cancer and normal cells by high-throughput sequencing. Genome Res. 2011 May;21(5):741-7.

Genome wide association studies

9. The Wellcome Trust Case Control Consortium, "Genome-wide association study of CNV in 16,00 cases of eight common diseases and 3,000 shared controls". Nature. 2010 Apr 1;464(7289):713-20.
10. Jarick et al. Novel common copy number variation for early onset extreme obesity on chromosome 11q11 identified by a genome-wide analysis. Hum Mol Genet. 2011 Feb 15;20(4):840-52.
11. Bartlett CW et al. A genome scan for loci shared by autism spectrum disorder and language impairment. Am J Psychiatry. 2014 Jan;171(1):72-81.
12. Bloss CS, Schork NJ, Topol EJ. Effect of direct-to-consumer genomewide profiling to assess disease risk. N Engl J Med. 2011 Feb 10;364(6):524-34.

Genetic profiling technologies

13. Carter SL, Cibulskis K, Helman E, McKenna A, Shen H, Zack T, Laird PW, Onofrio RC, Winckler W, Weir BA, Beroukhim R, Pellman D, Levine DA, Lander ES, Meyerson M, Getz G. Absolute quantification of somatic DNA alterations in human cancer. Nature Biotech. 2012 May;30(5):413-21. doi: 10.1038/nbt.2203.
14. Wang Y et al. Clonal evolution in breast cancer revealed by single nucleus genome sequencing. Nature. 2014 Aug 14;512(7513):155-60.
15. Frampton GM et al. Development and validation of a clinical cancer genomic profiling test based on massively parallel DNA sequencing. Nature Biotech. 2013 Nov; 30(11) 1023-33.

Pharmcogenomics

16. Kimmel SE, et al. A pharmacogenetic versus a clinical algorithm for warfarin dosing. N Engl J Med. 2013 Dec 12;369(24):2283-93. doi: 10.1056/NEJMoa1310669. Epub 2013 Nov 19.
17. Dorn GW et al. Mechanisms of Pharmacogenomic effects of genetic variation within the Cardiac adrenergic Network in heart failure. Mol Pharmacol. 2009 Sep;76(3):466-80.