BIOSCIENCES 741 - GENOMICS
FALL SEMESTER, 2013
BULL RUN HALL, ROOM 247
TUESDAY, 4:30 PM - 7:10 PM

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Summary: Biology reached a turning point in February, 2001, with the publication of the euchromatic portion of the human genome. Progress since then in genetics, medicine, biotechnology, pharmacology, and many other fields has been increasingly dependent on the data, techniques and concepts of genomics. The basic facts of biology rely upon the molecular anatomy of our chromosomes, just as basic facts of physiology rely upon the anatomy of our nerves and muscles. However, the volume and complexity of genomic sequence data pose significant problems of interpretation, which will occupy biologists for generations to come.

Prerequisites: Graduate standing, plus at least one undergraduate course in genetics and one undergraduate course in molecular biology.

Readings: There is one required text books for this class: Gibson and Muse (2009) *A Primer of Genome Science* (3rd edition, Sinauer, Sunderland, MA). The assigned readings from this text are listed below.

Additional readings from the primary research literature will be assigned. Most of these papers are available through the GMU library web site (click on electronic journals), except that a few may be available from other sources (if so, it will be noted in the reading list or the course web site).

Grading: Grades will be based on midterm (30%) and final (30%) examinations, plus participation in class discussions (15%), an abstract of your term paper (5%) and a final draft of your term paper (20%).

Midterm and final exams will be short essay, in-class, closed book exams. The use of cell phones (spoken or texting) during exams is not allowed. The midterm exam will cover the first half of the course, and the final will cover the second half of the course. Midterm and final exams typically consist of about 5 questions, each of which requires an answer about one page in length. These exam questions will focus on the main points in the lectures and assigned readings. In the first half of the course, most of the main points are identified in the Summary and Discussion Questions at the end of each chapter in the Gibson text. Other discussion questions will be posted on the course web site. Students are expected to do the assigned readings before coming to class, and be prepared to participate in class discussions after the lectures.

Each student will select a paper from the reading list, to be used as an initial focus for their term paper, and then choose a related focus (such as a hypothesis, controversy, or specific subfield) for their research and conclusions. The abstract (150-300 words) will summarize and justify this specific focus. The final draft of the written term paper will be an expanded, critical discussion of the current scientific state of the art in the area of genomics. Term papers will be typed, double-spaced, including at least 15+ pages of text (plus additional required title page, and abstract page, and reference pages). Please note that other items, such as illustrations, quotes, or acknowledgements, do not count towards the required 15 pages of text. Your paper should cite at least 30 scientific papers, all of which are included in your bibliography, and properly cited in your text. Please note that newspapers, internet web sites, course text books, etc. do not count as "scientific papers", and listing a paper in your bibliography without citing it does not count as a "citation". Plagiarism (copying text without proper attribution) is an Honor Code violation and will be prosecuted. However, you may paraphrase text from the scientific literature, provided that you immediately cite your source at the end of that sentence. Your abstract should state your own (preferably novel) conclusions regarding the state of that area. These conclusions should be justified in the text. Term papers and abstracts are due in class on the dates stated (see below), in paper printouts, with a 10% per day penalty for late papers.

Week 1 (August 27) Introduction to genomics

Gibson text: chapter 1.

van Nimwegen, E. (2003) Scaling laws in the functional content of genomes. *Trends Genet*. **19**, 479-484.

Week 2 (September 3) Sequencing methods, BAC fingerprinting, physical maps and FISH

Gibson text: pp. 65-94.

Lander, E.S. *et al*. (2001) Initial sequencing and analysis of the human genome. *Nature* **409**, 860-921 (we will focus this week on pp. 860-875)

Week 3 (September 10) cDNA libraries, EST clusters, gene prediction and functional annotation

Gibson text: pp. 95-132.

Nekrutenko, A. (2004) Reconciling the numbers: ESTs versus protein-coding genes. *Mol. Biol. Evol*. **21**, 1278-1282.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* **409**, 860-921. (we will focus this week on pp. 894-903).

Week 4 (September 17) Genetic polymorphisms, population genetics and human genetics

Gibson text: chapter 3.

Bentley, D. B. (2003) DNA sequence variation of *Homo sapiens*. *Cold Spring Harbor Symp. Quant. Biol*. **68**, 55-63. (A PDF copy of this article will be posted on the course web site.)

Weischenfeldt, J. et al. (2013) Phenotypic impact of genomic structural variation: insights from and for human disease. Nat Rev Genet 14, 125-138.

Week 5 (September 24) Gene expression analysis

Gibson text: chapter 4.

Martin, J. A. and Wang, Z. (2011) Next generation transcriptome assembly. Nat Rev Genet 12, 671-682.

Lenhard, B., et al. (2012) Metazoan promoters: emerging characteristics and insights into transcriptional regulation. Nat Rev Genet 13, 233-245.

Furey, T. S. (2012) ChIP-seq and beyond: new and improved methodologies to detect and characterize protein-DNA interactions. Nat Rev Genet 13, 840-852.

Week 6 (October 1) Alternative splicing

Wang, Z. and Burge, C. B. (2008) Splicing regulation: from a parts list of regulatory elements to an integrated splicing code. RNA 14, 802-813.

Kalsotra, A. and Cooper, T. A. (2011) Functional consequences of developmentally regulated alternative splicing. Nat Rev Genet 12, 715-729.

Davuluri, R. V. et al. (2008) The functional consequences of alternative promoter use in mammalian genomes. Trends Genet 167-177.

Week 7 (October 8) Midterm Examination - covers weeks 1-6

Week 8 (October 15) Columbus Day – this week Monday classes meet on Tuesday, and Tuesday classes do not meet!!

Week 9 (October 22) Characterization of the human genome: codon bias, gene density, GC content, recombination, CpG islands (ABSTRACTS of term papers due today)

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 875-879; 885-887; 892-894).

Hinch, A. G. et al. (2011) The landscape of recombination in African Americans. Nature 476, 170-175.

Week 10 (October 29) Characterization of the human genome: noncoding DNA, transposable elements, *Hox* genes, chromosome rearrangements and gene families

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 879-885; 887-889).

Waterston, R.H., K. Lindblad-Toh, E. Birney et al. (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* **420**, 520-562.

Levin, H. L. and Moran, J. V. (2011) Dynamic interactions between transposable elements and their hosts. Nat Rev Genet 12, 615-627.

Week 11 (November 5) Proteomics, functional genomics, and systems biology

Gibson text: chapters 5-6.

Ghosh, S. et al. (2011) Software for systems biology: from tools to integrated platforms. Nat Rev Genet 12, 821-832.

Maarten Altelaar, A. F. et al. (2013) Next-generation proteomics: towards an integrative view of proteome dynamics. Nat Rev Genet 14, 35-48.

Week 12 (November 12) class does not meet (Society for Neuroscience meetings in San Diego)

Week 13 (November 19) Epigenetics – DNA methylation

Jones, P. A. (2012) Functions of DNA methylation: islands, start sites, gene bodies and beyond. Nat Rev Genet 13, 484-492.

Smith, Z. D. and Meissner, A. (2013) DNA methylation: roles in mammalian development. Nat Rev Genet 14, 204-220.

Branco, M. R. et al. (2012) Uncovering the role of 5-hydroxymethyl cytosine in the epigenome. Nat Rev Genet 13, 7-13.

Week 14 (November 26) Epigenetics - histone modifications.

Jin, C. et al. (2009) H3.3/H2A.Z double variant-containing nucleosomes mark 'nucleosome-free regions' of active promoters and other regulatory regions. Nat Genet 41, 941-945.

Ernst, J. et al. (2011) Mapping and analysis of chromatin state dynamics in nine human cell types. Nature 473, 43-49.

Greer, E. L. and Shi, Y. (2012) Histone methylation: a dynamic mark in health, disease and inheritance. Nat Rev Genet 13, 343-357.

Week 15 (December 3) Microbial genomes. Term papers due today! Late penalty is 10% per day!

Wang, X. et al. (2013) Organization and segregation of bacterial chromosomes. Nat Rev Genet 14, 191-203.

Jackson, R. W. et al. (2011) Bacterial pathogen evolution: breaking news. Trends Genet 27, 32-40.

December 10 - Final Exam - 4:30 pm to 7:15 pm. Covers weeks 9-15.