BIOSCIENCES 741 - GENOMICS
FALL SEMESTER, 2011
BULL RUN HALL, ROOM 253
TUESDAY, 4:30 PM - 7:15 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 one verbal presentation to the class of a paper from the primary research literature (10%), participation in class discussions (10%), and a term paper that expands on your verbal presentation (20%).

Midterm and final exams will be short essay, in-class, closed book exams. 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 and presentations (this counts for 10% of your grade, see above).

Each student will give a verbal presentation of one paper, which they select from the reading list. The presentation includes the background and significance of this paper (about 20-30 min) and leading the subsequent class discussion (about 10 min). Your written term paper will be an expanded, critical discussion of the current scientific state of the art in the area of genomics related to your presentation. Term papers will be typed, double-spaced, including at least 10 pages of text (not counting the title page, abstract page, acknowledgements page, figures, illustrations, references, quotes, etc), and citing at least 20 scientific papers. 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. Term papers **must** include a separate title page, abstract page, and references page. Your abstract should state your own (preferably novel) conclusions regarding the state of that area. Your conclusions should be justified in the text.

<u>Week 1 (August 30) Introduction to genomics</u>

Gibson text: chapter 1.

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

Week 2 (September 6) 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 13) 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 20) Single nucleotide 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.)

Week 5 (September 27) Gene expression analysis

Gibson text: chapter 4.

Birney, E. *et al*. (2007) Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project. *Nature* **447**, 799-816.

Ozsolak, F., and Milos, P.M. (2011). RNA sequencing: advances, challenges and opportunities. Nat Rev Genet *12*, 87-98.

Week 6 (October 4) Alternative splicing and RNA structural studies

Yeo, G. *et al*. (2004) Variation in sequence and organization of splicing regulatory elements in vertebrate genes. *Proc. Natl. Acad. Sci. USA* **101**, 15700-15705.

Nilsen, T.W., and Graveley, B.R. (2010). Expansion of the eukaryotic proteome by alternative splicing. Nature *463*, 457-463.

Wan, Y., Kertesz, M., Spitale, R.C., Segal, E., and Chang, H.Y. (2011). Understanding the transcriptome through RNA structure. Nat Rev Genet *12*, 641-655.

Week 7 (October 11) Columbus Day break – Tuesday classes do not meet

Week 8 (October 18) Midterm Examination - covers weeks 1-6

Week 9 (October 25) Epigenetics

Bonasio, R., Tu, S., and Reinberg, D. (2010). Molecular signals of epigenetic states. Science (New York, NY *330*, 612-616.

Lister, R., Pelizzola, M., Dowen, R.H., Hawkins, R.D., Hon, G., Tonti-Filippini, J., Nery, J.R., Lee, L., Ye, Z., Ngo, Q.M., *et al*. (2009). Human DNA methylomes at base resolution show widespread epigenomic differences. Nature *462*, 315-322.

Northrup, D.L., and Zhao, K. (2011). Application of ChIP-Seq and related techniques to the study of immune function. Immunity *34*, 830-842.

Week 10 (November 1) Proteomics, functional genomics, and systems biology

Gibson text: chapters 5-6.

Kondrashov, N., Pusic, A., Stumpf, C.R., Shimizu, K., Hsieh, A.C., Xue, S., Ishijima, J., Shiroishi, T., and Barna, M. (2011). Ribosome-mediated specificity in Hox mRNA translation and vertebrate tissue patterning. Cell *145*, 383-397.

Week 11 (November 8) Microbial genomes

Dujon, B. *et al*. (2004) Genome evolution in yeasts. *Nature* **430**, 35-44.

King, N. *et al*. (2008) The genome of the choanoflagellate *Monosiga brevicollis* and the origin of metazoans. *Nature* **451**, 783-788.

Week 12 (November 15) class does not meet (Society for Neuroscience)

Week 13 (November 22) Characterization of the human genome: codon bias, gene density, GC content, recombination, CpG islands

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).

Gordon, G. *et al*. (2007) Comparative analysis of chicken chromosome 28 provides new clues to the evolutionary fragility of gene-rich vertebrate regions. *Genome Res*. **17**, 1603-1613.

Week 14 (November 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.

Week 15 (December 6) Comparative genomics. Term papers due today! Late penalty is 10% per day!

Mikkelsen, T. S. *et al*. (2005) Initial sequence of the chimpanzee genome and comparison with the human genome. *Nature* **437**, 69-87.

Reich, D., Green, R.E., Kircher, M., Krause, J., Patterson, N., Durand, E.Y., Viola, B., Briggs, A.W., Stenzel, U., Johnson, P.L., *et al*. (2010). Genetic history of an archaic hominin group from Denisova Cave in Siberia. Nature *468*, 1053-1060.

Green, R. E., J. Krause, A. W. Briggs, T. Maricic, U. Stenzel *et al*. (2010) A draft sequence of the Neandertal genome. *Science* **328,** 710-722.

December 13 - Final Exam - 4:30 pm to 7:15 pm. Covers weeks 9-15.