

Schedule, Spring 05
Bio 4342, Research Explorations in Genomics

Note: M 1:30-5:00; W 1:30-5:00; F 1:30-2:30

- 1/19 W Course structure, research problem (S Elgin, 30 min).
 Lecture: general sequencing (chemistry) intro; the pipeline (E. Mardis, 1 hour).
 20 min break
 Lab: intro to laptop computers, OS, intro to Unix, hand out Unix command sheet and HW1 (C Shaffer, 2 hours).
- 1/21 F Lecture: different approaches, current WU/GSC sequencing strategies: BAC vs. WGS vs. map-assisted (E. Mardis).
- 1/24 M Tour of the Genome Sequencing Center (Virtual Tour, Biocel Robot, etc.)
 Computer help session.
- 1/26 W Lab: Prep samples (96 well plates, hand prep, one fosmid per student); demo Biomek robot; loading the ABI3730 sequencer (D. O'Brien).
 Lecture (interspersed): source of *D. virilis* fosmids (L. Slawson)
- 1/28 F Lab: Using Consed Graphically; hand out Consed tutorial (C. Strong and C. Shaffer)
HW1 due
- 1/31 M Lecture: Intro to Phred, Phrap, Consed and Assessment of sequence quality (B. Fulton)
 Lab: Consed tutorial (C. Strong and C. Shaffer)
- 2/2 W Lecture: prefinishing; alternative chemistries (R. Maupin, A. Reilly)
 Lab: Hand out HW2 group exercise with common weak points (C. Strong, C. Shaffer)
- 2/4 F Lecture/lab: Continue Consed exercise (HW2)
WI subgroup: discussion on scientific writing, peer review
- 2/7 M Lecture: Comparative Genomics (Johnston)
 Lab: **HW2 due.** Introduce mid-term class report requirements (including Finishing Checklist), obtain file for own fosmid, run Phred, Phrap, Consed. Add GSC reads, phrap and compare results.
- 2/9 W Lab: Prefinishing own fosmid with help from GSC finishers available, must order reads today.
- 2/11 F Lecture: Genomes: presence and distribution of repetitious elements (S. Elgin).
 Hand out HW3 (Cot curves, Elgin).
WI subgroup: 1000 word intro paper due
- 2/14 M Lecture: Chromosome Y lessons, finishing problems (R. Wilson)
 Lab: Finishing (C. Strong, C. Shaffer) – student calls vs. Autofinish calls
- 2/16 W Lab: Finishing own fosmid; receive new data, assemble; must order any additional reads today, GSC finishers available for help
- 2/18 F Lecture: Chromatin Structure (S. Elgin) **HW3 due**

WI subgroup: peer review of intro paper

- 2/21 M Lecture: Heterochromatin / silencing (S. Elgin)
Lab: Finishing own fosmid. Discussion of HW3
- 2/23 W Lab: Receive additional data, assemble, compare to GSC autofinish and finish.
Final day for help from GSC finishers
- 2/25 F Lab: Help with problem areas of fosmids as needed
- 2/28 M Lecture: Quality control (K. Pepin)
Lab: Preparation of reports; L. Slawson presents prototype
- 3/2 W Lecture: Drosophila dot chromosome; goals in analyzing *D. virilis* (S Elgin)
Lecture/Demo: More UNIX and Genomics/BLAST (C. Shaffer, 2 hours)
Preparation of reports as time permits
- 3/4 F **Class reports** (10 min) “Finishing my fosmid; problems identified and solved; comparing my analysis to the computer and the GSC.”
- March 7-11 Spring Break
- 3/14 M Lecture: Gene finding: detecting and interpreting genetic homology (begin HW1)
(J Buhler)
- 3/16 W Lab: continue HW1 (J Buhler)
Lecture: Visualizing BLAST output and using EST’s.
- 3/18 F Begin HW2 (J Buhler); **HW1 due**
WI subgroup: peer review of finishing papers.
- 3/21 M Lab: continue HW2 (J Buhler)
- 3/23 W Lecture: gene finding by Twinscan, use of UCSC browser (train with chimp
Contig95) (M Brent)
Lab: continue with Twinscan lab as group **HW2 due**
- 3/25 F Lab: challenge: annotate fragments of the chimp genome (HW3 data sets)
- 3/28 M Lab: introduce Drosophila browser (M Brent), Flybase (C Shaffer).
Lab: help session for preparation of reports
- 3/30 W **HW3 class reports** (10 min) “Genes and pseudogenes in mammals.”
Lab: begin work with own fosmid to identify genes.
- 4/1 F Lecture: Running a sequencing center: information management, quality
control, cost control (L. Fulton)
- 4/4 M Lab: continuation of work on own fosmid, particularly genes
- 4/6 W Lecture: design and use of Repeat Masker; other ways to find repeats (J Buhler).
- 4/8 F Lab: De novo and pairwise searches for repeats (J Buhler)
WI subgroup: peer review of gene/pseudogene papers.
- 4/11 M Lab: Continue analysis and annotation of own fosmid
- 4/13 W Lecture: introduction to multiple sequence alignments; use of Clustal (C Shaffer)

- 4/15 F Lab: comparison of *D. melanogaster*, *D. pseudoobscura*, *D. virilis* for genes from own fosmid.
- 4/18 M Lecture: the ENCODE project (analysis for all features) (S Elgin)
Lab: Continue annotation of own fosmid
- 4/20 W Lecture: SNPs (E Mardis)
Lab: preparation of final reports.
- 4/22 F Lecture: heart disease (A Templeton)
- 4/25 M Lecture: the \$1000 genome: new sequencing technologies (E Mardis)
- 4/27 W Lecture: Human evolution: out of Africa again and again (A Templeton)
Lab: preparation of final report
WI subgroup: exchange drafts
- 4/29 F Lab: preparation of final report
WI subgroup: peer review of drafts

5/5 – 5/11, TBA. Final reports: your fosmid, with a map of genes, middle repetitive elements, and alignment to *melanogaster* and *pseudoobscura*. As time permits, investigation of the nature of the repetitive elements; search for endpoints of genes; search for regulatory elements.

Reading

Papers will be handed out and are available on the web. Reading these papers prior to the following class period will provide greater understanding of the lecture material and will help you to develop an understanding of the foundations of the experimental approaches we are using, as well as providing the antecedents for the scientific problem we are studying.

- 1/19 W Sterky F, Lundeberg J. "Sequence analysis of genes and genomes," (2000) J Biotechnology 76: 1-31.
GSC protocols (skim through)
- 1/21 F Marra MA, Kucaba TA, Dietrich NL, Green ED, Brownstein B, Wilson RK, McDonald KM, Hillier LW, McPherson JD, Waterston RH. (1997) "High-Throughput Fingerprint Analysis of Large-Insert Clones," Genome Res. 7: 1072-1084.
- 1/24 M GSC single step DNA prep protocol
- 1/26 W Hardison RC. (2003) "Primer: Comparative Genomics," PloS Biology 1: 156-160.
- 1/28 F Gordon D, Abajian C, Green P. (1998) "Consed: A Graphical Tool for Sequence Finishing," Genome Res. 8: 195-202.
- 1/31 M Gordon D, Desmarais C, Green P. (2001) "Automated Finishing with Autofinish," Genome Res. 11: 614-625.

- 2/2 W Wendl MC, Dear S, Hodgson D, Hillier L. (1998) "Automated Sequence Preprocessing in a Large-Scale Sequencing Environment," *Genome Res.* 8: 975-984.
- 2/4 F Cliften P, Sudarsanam P, Desikan A, Fulton L, Fulton B, Majors J, Waterston R, Cohen BA, Johnston M. (2003) "Finding functional features in *Saccharomyces* genomes by phylogenetic footprinting," *Science* 301: 71-76.
- Drmitzakis ET, Reymond A, Scamuffa N, Ucla C, Kirkness E, Rossier C, Antonarakis SE. (2003) "Evolutionary discrimination of Mammalian conserved Non-Genic sequences (CNGs)," *Science* 302:1033-1035
- 2/9 W Cot curve packet with HW3. From "Biochemistry: A Problems Approach," 2nd ed., by WB Wood, JH Wilson, RM Benbow, LE Hood; Benjamin/Cummings, CA. 1981.
- 2/11 F Skaletsky H, Kuroda-Kawaguchi T, Minx PJ, Cordum HS, Hillier L, Brown LG, Repping S, Pyntikova T, Ali J, Bieri T, Chinwalla A, Delehaunty A, Delehaunty K, Du H, Fewell G, Fulton L, Fulton R, Graves T, Hou SF, Latrielle P, Leonard S, Mardis E, Maupin R, McPherson J, Miner T, Nash W, Nguyen C, Ozersky P, Pepin K, Rock S, Rohlfing T, Scott K, Schultz B, Strong C, Tin-Wollam A, Yang SP, Waterston RH, Wilson RK, Rozen S, Page DC. (2003) "The male-specific region of the human Y chromosome is a mosaic of discrete sequence classes," *Nature* 423: 825-837.
- 2/16 W Felsenfeld G, Groudine M (2003) "Controlling the double helix," *Nature* 421: 448-453.
- 2/23 W Elgin SCR, Grewal, SIS. (2003) "Primer: Heterochromatin: silence is golden," *Curr. Biol.* 13: R895-R898.
- Grewal SIS, Elgin, SCR. (2002) "Heterochromatin: new possibilities for the inheritance of structure," *Curr. Opin. Genetics & Develop.* 12: 178-187.
- 2/25 F Sun, F.-L., Haynes, K., Simpson, C.L., Lee, S.D., Collins, L., Wuller, J., Eissenberg, J.C., and Elgin, S.C.R. (2004) "Cis-acting determinants of heterochromatic formation on *Drosophila melanogaster* chromosome four," *Mol. Cell. Biol.*, 24, 8210-8220.
- 4/22 F Templeton AR (1999) "Uses of evolutionary theory in the human genome project," *Ann. Rev. Ecol. Syst* 30: 23-49.
- 4/27 W Templeton AR (2002) "Out of Africa again and again," *Nature* 416: 45-51.

The following papers may be helpful during the second half of the course:

Cooper GM, Sidow A. (2003) "Genomic regulatory regions: insights from comparative sequence analysis," *Curr. Opin. Genet. Develop.* 13: 604-610.

Thomas JW...Green ED (2003) "Comparative analyses of multi-species sequences from targeted genomic regions," *Nature* 424: 788-793.

Celniker SE, ...Gibbs RA, Rubin GM. (2002) "Finishing a whole-genome shotgun: release 3 of the *Drosophila melanogaster* euchromatic genome sequence. *Genome Biol.* 3(12):RESEARCH0079. Epub 2002 Dec 23. PMID: 12537568 [PubMed - indexed for MEDLINE]

Kaminker JS, Bergman CM, Kronmiller B, Carlson J, Svirskas R, Patel S, Frise E, Wheeler DA, Lewis SE, Rubin GM, Ashburner M, Celniker SE. (2002) "The transposable elements of the *Drosophila melanogaster* euchromatin: a genomics perspective," *Genome Biol.* 2002;3(12):RESEARCH0084. Epub 2002 Dec 23. PMID: 12537573 [PubMed - indexed for MEDLINE]

Hoskins RA, Smith CD, Carlson JW, Carvalho AB, Halpern A, Kaminker JS, Kennedy C, Mungall CJ, Sullivan BA, Sutton GG, Yasuhara JC, Wakimoto BT, Myers EW, Celniker SE, Rubin GM, Karpn GH, (2002) "Heterochromatic sequences in a *Drosophila* whole-genome shotgun assembly," *Genome Biol.* 2002;3(12):RESEARCH0085. Epub 2002 Dec 31. PMID: 12537574

Bergman CM, Pfeiffer BD, Rincon-Limas DE, Hoskins RA, Gnirke A, Mungall CJ, Wang AM, Kronmiller B, Pacleb J, Park S, Stapleton M, Wan K, George RA, de Jong PJ, Botas J, Rubin GM, Celniker SE. (2002) "Assessing the impact of comparative genomic sequence data on the functional annotation of the *Drosophila* genome. *Genome Biol.* 2002;3(12):RESEARCH0086. Epub 2002 Dec 30. PMID: 12537575

Ohler U, Liao GC, Niemann H, Rubin GM. (2002) "Computational analysis of core promoters in the *Drosophila* genome," *Genome Biol.* 2002;3(12):RESEARCH0087. Epub 2002 Dec 20. PMID: 12537576

Evgen'ev MB, Zelentsova H, Poluectova H, Lyozin GT, Veleikodvorskaja V, Pyatkov KI, Zhivotovsky LA, Kidwell MG (2000) "Mobile elements and chromosomal evolution in the virilis group of *Drosophila*," *Proc Natl Acad Sci U S A.* 97: 11337-42. PMID: 11016976

Zelentsova H, Poluectova H, Mnjoian L, Lyozin G, Veleikodvorskaja V, Zhivotovsky L, Kidwell MG, Evgen'ev MB. (1999) "Distribution and evolution of mobile elements in the virilis species group of *Drosophila*," *Chromosoma* 108:443-56. PMID: 10654083