

BIOLOGY 579: MOLECULAR EVOLUTION AND CONSERVATION GENETICS

KARL J. FRYXELL SPRING, 2018

Readings. There is one required text for this course, “Molecular and Genome Evolution” by Dan Graur (2016). Additional assigned reading will include primary research articles in scientific journals. These are available through the GMU library through the E-journals web link (or will be posted on Blackboard). Many of these articles are also available on paper in the Fenwick and/or Mercer Libraries.

Dates, Times, and Contact Information. This course meets Wednesdays at 1:30 - 4:15 pm, in Bull Run Hall, room 247. My office hours this semester will be Fridays, from 1-3 pm in Discovery Hall, room 305. Phone: 703-993-1069. E-mail: kfryxell@gmu.edu. Course materials such as lecture notes will be posted on Blackboard.

Introduction. The field of molecular evolution originated in the 1960s when Emile Zuckerkandl and Linus Pauling showed that biological evolution occurs through continuing small changes in gene sequences, punctuated by episodes of gene duplication. Fundamental discoveries have followed in every subsequent decade – such as the discovery that all genes belong to gene families, statistical methods of analyzing protein functions, methods of understanding the evolution of gene regulation, the neutral theory, whole-genome analysis of natural selection, genetic pathways, and human ancestry. The field of molecular evolution has become the conceptual foundation of genomics and drug discovery, and the basis of our methods of gene discovery and biotechnology.

These results provide the basis for any bioinformatic analysis of gene structure and function, and thus are having a major impact on biotechnology and the biomedical sciences, particularly in analyzing genetic pathways. Molecular evolution also has applications in conservation genetics, including molecular definitions of the effective population size of a species, molecular definitions of species boundaries, and particularly the concept of a minimal sustainable population size (which is the basis of the Endangered Species Act). It has recently become possible to study the molecular evolution of human ancestors, which is providing new answers to the question of who we are and where we came from.

Grading summary: 30% midterm exam, 30% final exam, 30% term paper, 10% participation. Exams are in-class, closed-book, short answer (one sentence) and short essay (one paragraph) questions, based primarily on the study questions that are posted each week on Blackboard. Makeup examinations are not given in this course. Excused absences from exams require the prior permission of the instructor (not just firing off an e-mail or voice mail at the last minute). Cell phone use of any kind (including texting) is not allowed during written examinations.

The term paper topic should be based on one of the assigned papers as a starting point. The selection of the topic is by mutual agreement between the student and instructor. Term papers are expected to include at least 12 pages of text, double-spaced (in addition to the required title page, abstract page, bibliography and any optional figures), and at least 25 references. The bibliography must contain complete citations of primary scientific research papers. For example, newspaper or popular articles, Wikipedia entries or blogs are never acceptable references. Listing of online databases in a bibliography is not usually appropriate, although it may be allowed in circumstances where there is no other source and that is clearly explained. Term papers should advocate a specific point of view, hypothesis and/or conclusion, and present evidence for and against your conclusions. The term paper is due, on paper, in class, during the last day of class (see below). Late papers will receive a penalty of 10% per day.

The participation grade is a small incentive based on both attendance and active participation in class discussions. In order to be fair to everyone, the first absence will be dropped for all students, but subsequent absences will count in proportion to your participation.

January 24 – introduction (lecture 1)

Text, chapter 1.

January 31 - Basic rates and patterns of DNA sequence change (lecture 2)

text, pp. 107-125; pp. 130-138.

Petrov, D. A., and D. L. Hartl (1999) Patterns of nucleotide substitution in *Drosophila* and mammalian genomes. *Proc. Natl. Acad. Sci. USA* **96**, 1475-1479.

Bustamante CD, Fledel-Alon A, Williamson S, Nielsen R, Hubisz MT, Glanowski S *et al* (2005) Natural selection on protein-coding genes in the human genome. *Nature* **437**, 1153-1157.

February 7 - Natural selection, the neutral theory, and the nearly neutral theory (lecture 3)

text, pp. 35-62; 72-77; pp. 163-164.

Gojobori, T., E. N. Moriyama and M. Kimura (1990) Molecular clock of viral evolution, and the neutral theory. *Proc. Natl. Acad. Sci. USA* **87**, 10015-10018.

McDonald, J. and M. Kreitman (1991) Adaptive protein evolution at the *Adh* locus in *Drosophila*. *Nature* **351**, 652-654.

Ohta, T. (1993) Amino acid substitution at the *Adh* locus of *Drosophila* is facilitated by small population size. *Proc. Natl. Acad. Sci. USA* **90**, 4548-4551.

February 14 - Genetic diversity – population bottlenecks vs. positive selection (lecture 4)

text, pp. 66-71; pp. 128-130.

Glenn, T. C., W. Stephan, and M. J. Braun (1999) Effects of a population bottleneck on whooping crane mitochondrial DNA variation. *Conservation Biol.* **13**, 1097-1107.

Tishkoff, S. A. *et al.* (2007) Convergent adaptation of human lactase persistence in Africa and Europe. *Nat. Genet.* **39**, 31-40.

February 21 - Phylogenetic trees, speciation, gene coalescence, and the molecular clock (lecture 5)

text, pp. 149-162; pp. 165-197; pp. 205-220.

Palumbi, S. R., F. Cipriano and M. P. Hare (2001) Predicting nuclear gene coalescence from mitochondrial data: the three-times rule. *Evolution* **55**, 859-868.

Wu, C.-I. and Ting, C.-T. (2004) Genes and speciation. *Nat. Rev. Genet.* **5**, 114-122.

February 28 - Gene duplication, pseudogenes, and the evolution of gene families (lecture 6)

text, chapter 7.

Nei M, Niimura Y, and Nozawa M (2008) The evolution of animal chemosensory receptor gene repertoires: roles of chance and necessity. *Nat. Rev. Genet.* **9**, 951-963.

Podlaha O, Zhang J (2010) Pseudogenes and their evolution. In: *Encyclopedia of Life Sciences (ELS)*, John Wiley & Sons, Chichester. DOI: 10.1002/9780470015902.a0005118.pub2

March 7 - Midterm Exam (covers lectures 1-6)

March 14 – Spring Break

March 21 – class does not meet (VYTP Research Coalition meeting)

March 28 – Protein evolution, multidomain proteins, and alternative splicing (lecture 7)

Text, pp. 232-235; chapter 8; pp. 427-428.

Kawashima, T. *et al.* (2009) Domain shuffling and the evolution of vertebrates. *Genome Res.* **19**, 1393-1403.

Keren H, Lev-Maor G, Ast G (2010) Alternative splicing and evolution: diversification, exon definition and function. *Nat. Rev. Genet.* **11**, 345-355.

April 4 – The evolution of gene regulation and development (lecture 8)

Text, chapter 12.

Necsulea, A. and H. Kaessmann (2014) Evolutionary dynamics of coding and noncoding transcriptomes. *Nat. Rev. Genet.* **15**, 734-748.

Mazo-Vargas, A. et al. (2017) Macroevolutionary shifts of *WntA* function potentiate butterfly wing-pattern diversity. *Proc. Natl. Acad. Sci. USA* **114**, 10701-10706.

April 11 – The evolution of prokaryotic genomes (lecture 9)

Text, pp. 432-438; chapter 10.

Boyd, E. F. et al. (2009) Genomic islands are dynamic, ancient integrative elements in bacterial evolution. *Trends Microbiol.* **17(2)**, 47-53.

Shapiro, B. J. (2016) How clonal are bacteria over time? *Curr. Opin. Microbiol.* **31**, 116-123.

April 18 – The evolution of eukaryotic genomes and chromosomes (lecture 10)

Text, pp. 522-573.

Veyrunes, F. et al. (2008) Bird-like sex chromosomes of platypus imply recent origin of mammal sex chromosomes. *Genome Res.* **18**, 965-973.

Nuttle, X. et al. (2016) Emergence of a *Homo sapiens*-specific gene family and chromosome 16p11.2 CNV susceptibility. *Nature* **536**, 205-209.

April 25 – Early humans and our Neanderthal legacy (lecture 11)

Tishkoff, S. A. et al. (1996) Global patterns of linkage disequilibrium at the CD4 locus and modern human origins. *Science* **271**, 1380-1387.

Prüfer, K. et al. (2014) The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* **505**, 43-49.

McCoy, R. C. et al. (2017) Impacts of Neanderthal-introgressed sequences on the landscape of human gene expression. *Cell* **168**, 916-927.

May 2 – Genetic consequences of the Neolithic revolution (lecture 12) (term papers due in class)

Karmin M et al. (2015) A recent bottleneck of Y chromosome diversity coincides with a global change in culture. *Genome Res.* **25**, 459-466.

Haak, W. et al. (2015) Massive migration from the steppe was a source for Indo-European languages in Europe. *Nature* **522**, 207-211.

Allentoft, M. E. et al. (2015) Population genomics of Bronze Age Eurasia. *Nature* **522**, 167-172.

May 9 – Final Exam (lectures 7-12)