BIOLGU4001_001_2023_1 - ADVANCED GENETIC ANALYSIS

Edit Settings

COURSE MATERIALS AND RESOURCES

Reading:

Most of the assigned readings (listed below) is of original research papers and reviews. In addition some classes have associated material in handouts that should be read before class. These materials can be accessed by going to Files & Resources or by clicking the links below. In addition, sections from R. Scott Hawley and Michelle Y. Walker (2003) *Advanced Genetic Analysis. Finding Meaning in the Genome*, Blackwell (indicated below as "HW:") may be helpful. These sections provide additional background and an alternative perspective as do the additional readings that are listed for each class period. This reading is not required. Hawley and Walker is available at the Columbia Book Store. An electronic version can be purchased directly from Wiley (http://www.wiley.com/WileyCDA/WileyTitle/productCd-1444313088.htmlLinks to an external site.). However, because I prefer that you do not spend any money on the course, I have arranged with the Columbia Libraries to have the book available as an eBook. You can find the link to access the book under "Library Reserves" in the list to the left.

Study Guides: Virtually all lectures have an associated study guide, which contains background material and questions that must be answered **before class** as the material will be the basis of the class discussion. I suggest that each student read the required material and try to work out the problems over a day or so. Then students should work together in groups of 3 or 4 and determine the answers to all of the questions. Students will be asked **randomly** for answers during class. The main idea is to do as much of the learning of the material before class, so that the class time can be used for discussion.

Useful Sources

Elementary Texts

None of the material is entirely covered by any introductory textbook, but the first two books listed below are probably the most useful general texts; the other works are classic texts.

1. A.J.F. Griffiths, S. Wessler, S. Carroll, and J. Doebley (2010) *Introduction to Genetic Analysis*, 10th edition, Freeman.
2. L.H. Hartwell, L. Hood, M.L. Goldberg, A.E. Reynolds, and L.M. Silver

(2011) *Genetics: From Genes to Genomes*, 4rd edition, McGraw Hill
3. A.H. Sturtevant and G.W. Beadle (1962) *An Introduction to Genetics*, Dover Press
4. F.J. Ayala and J.A. Kiger, Jr. (1984) *Modern Genetics*, 2nd ed., Benjamin/Cummings
5. M.W. Strickberger (1985) *Genetics*, 3rd edition, Macmillan Publishing Company

Journals

The official journal of the Genetics Society of America is *Genetics*. Each issue usually contains one "Perspectives" article (these are usually historical notes). The best introduction to the various topics in genetics is found in various review journals including *Nature Reviews Genetics*, *Annual Review of Genetics*, *Trends in Genetics*, and *Current Opinion in Genetics and Development* (and Minireviews and News-and-Views articles in *Cell*, etc.). *Nature Review Genetics* has commissioned several general series over the years that you may find useful (www.nature.com/nrg/series/Links to an external site.) e.g., The Art and Design of Genetic Screens (Extra Reading for the second lecture) is from one of these series.

Web sites

Mendel Web: www.mendelweb.orgLinks to an external site.
WormBook: www.genetics.org/content/wormbookLinks to an external site. (since 2016) www.wormbook.org Links to an external site.(before 2016; but also has *C. elegans* history papers)
Virtual Library - Genetics: www.ornl.gov/TechResources/Human_Genome/genetics.htmlLinks to an external site.
ESP Foundations of Classical Genetics: http://www.esp.org/foundations/genetics/classical/Links to an external site.
The Henry Stewart Talks (advanced seminars on various topics) www.hstalks.comLinks to an external site.

Model Organism Databases

Alliance of Genome Resources (brings together data from multiple organisms) www.alliancegenome.orgLinks to an external site.
The *Saccharomyces* Genome Database www.yeastgenome.orgLinks to an external site.
Wormbase www.wormbase.orgLinks to an external site.
Flybase www.flybase.orgLinks to an external site.
The *Arabidopsis* Information Resource (TAIR) www.Arabidopsis.orgLinks to an external site.
Mouse Genome Informatics www.informatics.jax.orgLinks to an external site.
Online Mendelian Inheritance in Man (OMIM) www.ncbi.nlm.nih.gov/omimLinks to an external site.

GRADES

Participation and Attendance

Group quizzes (6 possible, drop 1)

Assignments

SUPPLEMENTAL PROBLEMS

These four problems sets are good practice for the quizzes. They include problems from past exams.

Problem Set #1

Actions

Problem Set #2

Actions

Problem Set #3

Actions

Problem Set #4

Actions

COURSE SCHEDULE

1. January 23: Genetic Terms.

CLASS SLIDES Download CLASS SLIDES PDF

Actions

(NOTE: Recordings of the lectures are found using the Tab "Course Video Recordings (Panopto)" on the left; recordings and transcripts can be found using the Tab "Zoom Class Sessions" on left and then the Tab "Cloud Recordings.")

Preclass Letter

Actions

This class provides a review of the terms from introductory genetics that students should have learned before. This first session also provides the background needed to read the Brenner (1974) paper that is discussed in the next two lectures (see the other handouts).

HW: pp. 15-30

Study Guide

Actions

Handouts: Reading Papers and Giving Presentations

Actions

, Genetic Rules

Actions

Extra Reading:

J.M. Diamond (1987) Abducted orphans identified by grandpaternity testing. *Nature* **327**: 552-553.

Actions

2. January 30: Transmission Genetics.

Link to Presentation Sign-up Document Links to an external site.

Joke Assignments

Actions

CLASS SLIDES Download CLASS SLIDES PDF

Actions

We will spend two sessions on Brenner (1974). The first covers through three-factor crosses. Topics include choice of model organisms, non-true breeding mutants (phenocopy, dominant, and incomplete penetrance) and how to distinguish them, linkage, 2-factor distances, 3-factor distances, and multifactor crosses (e.g., using polymorphisms). The little paper I wrote on 3-factor crosses is meant to convey the ideas, one more time. Much of this material has been outlined in the Study Guide, which has a series of problems to help navigate through the material.

S. Brenner (1974) The genetics of *Caenorhabditis elegans*. *Genetics* **77**: 71-94.

Actions

M. Chalfie (1997) Is the traditional way of teaching three-factor mapping sufficient? *Trends Genetics* **13**: 94-95.

Actions

HW: Chapter 2 except 2.4.4

Actions

Study Guide,

Actions

3-Factor Crosses

Actions

, *C. elegans* Nomenclature

Actions

Extra Reading:

A.K. Corsi, B. Wightman, and M. Chalfie (2015) A transparent window into biology: A primer on *Caenorhabditis elegans*. *Genetics* **200**: 387-407.

Actions

G. Mendel (1865) Experiments in plant hybridization. Verhandlungen des naturforschenden Vereines in Brünn, Bd. IV für das Jahr 1865, Abhandlungen, 3-47.

Actions

E.M. Jorgensen and S.E. Mango (2002) The art and design of genetic screens: *Caenorhabditis elegans*. *Nat. Rev. Genet.* **3**: 356-369.

Actions

B.D. Williams. B. Schrank, C. Huynh, R. Shownkeen, and R.H. Waterston (1992) A genetic mapping system in *Caenorhabditis elegans* based on polymorphic sequence-tagged sites. *Genetics* **131**: 609-624.

Actions

HW: Section 7.5

3. February 6: Review of Brenner paper

CLASS SLIDES Download CLASS SLIDES **PDF**

Actions

This session will cover the rest of the Brenner paper. Topics include mutageneses (M and S sets of Brenner, mutageneses for non-complementing, dominant, X-linked, maternal effect, and multiple generation mutations), saturation of mutageneses (determining saturation intuitively, calculating the number of genes that can be mutated to produce a particular phenotype using the Poisson, assumptions in these estimates), mutants found by Brenner, calculating X-linked lethals, calculating mutation rates and the total number of genes, the C-value paradox and its resolution.

HW: Section 2.4.4

Actions

Study Guide

Actions

Predicting Gene Numbers

Actions

Extra Reading:

J.F. Crow (1988) A diamond Anniversary: The first chromosome map. *Genetics* **118**: 1-3.

Actions

W.G. Quinn and J.L. Gould (1979) Nerves and genes. *Nature* **278**: 19-23.

Actions

4. February 13: Genotype vs. Phenotype: Concepts

Quiz on Sessions 1-3

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Actions

(Areas Covered on CRISPR/Cas, Fluorescent Proteins, and Genomes

Actions

)

Topics include the problem of genotype vs. phenotype, pleiotropy, loss and gain of gene function instead of recessive and dominant, “standard” or “ordinary” genes and their properties (frequency, number of dominant, ts, and nonsense alleles), implications of Drosophila deletions about gene loss, complete loss-of-function (a.k.a. amorph, null), partial loss-of-function (hypomorph, e.g., ts alleles and ts periods), haploinsufficiency, and gain-of-function mutations (hypermorph, misexpression in space, misexpression in time (*lin-14d*), neomorphic, and toxic product (a.k.a. antimorph).

I. Herskowitz (1987) Functional inactivation of genes by dominant negative mutations. *Nature* **329**: 219-222.

Actions

HW: Chapter 1

Study Guide

Actions

Extra Reading:

H.J. Muller (1932) Further studies on the nature and causes of gene mutations. *Proc. Sixth Internat. Cong. Genetics* **1**: 213-255 (relevant part is pp. 231-255).

Actions

D.T. Suzuki (1970) Temperature-sensitive mutations in *Drosophila melanogaster*. *Science* **170**: 695-706.

Actions

M. Chalfie and M. Au (1989) Genetic control of differentiation of the *C. elegans* touch receptor neurons. *Science* **243**: 1027-1033.

Actions

5. February 20: Genotype vs. Phenotype: Readings

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Actions

This session continues the discussion of genotypes and phenotypes by considering pleiotropy, an example of a gene that questions many of the assumption of the "standard gene," and an example of a study how mutation of a gene leads to a human disease.

Study Guide

Actions

J. Hodgkin (1998) Seven types of pleiotropy. *Int. J. Dev. Biol.* **42**: 501-505.

Actions

A. Bejsovec and P. Anderson (1990) Function of the myosin ATP and actin binding sites are required for C. elegans thick filament assembly. *Cell* **60**: 133-140.

Actions

P.J. Rosenfeld, G.S. Cowley, T.L. McGee, M.A. Sandberg, E.L. Berson, and T.P. Dryja (1992) A *null* mutation in the rhodopsin gene causes rod photoreceptor dysfunction and autosomal recessive retinitis pigmentosa. *Nature Genetics* **1**: 209-213.

Actions

6. February 27: Reducing and Eliminating Gene Expression

Quiz on Sessions 4 and 5

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Actions

After a consideration of how the null phenotype can be determined genetically, we will discuss several method that have been found to lower or eliminate gene activity, concentrating on RNA inference, microRNAs, and CRISPR/Cas 9.

Study Guide

Actions

, Genetically Identifying Null Alleles

Actions

A. Fire, S. Xu, M.K. Montgomery, S.A. Kostas, S.E. Driver, and C.C. Mello (1998) Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* **391**: 806 - 811.

Actions

R.C. Lee, R.L. Feinbaum, and V. Ambros (1993) The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. *Cell* **75**: 843-854.

Actions

Extra Reading:

O. Thompson, M. Edgley, P. Strasbourger, S. Flibotte, B. Ewing, R. Adair, V. Au, I. Chaudry, L. Fernando, H. Hutter, A. Kieffer, J. Lau, N. Lee, A. Miller, G. Raymant, B. Shen, J. Shendure, J. Taylor, E. Turner, L. Hillier, D.G. Moerman, and R.H. Waterston (2013) The Million Mutation Project: A new approach to genetics in *Caenorhabditis elegans*. *Genome Res.*, **23**: 1749-1762.

Actions

7. March 6: CRISPR and Its Applications

CLASS SLIDES Download CLASS SLIDES PDF

Actions

A detailed examination of the many uses of CRISPR/Cas9. After covering the basics, we will expand on newer applications of CRISPR, including those that do not directly relate to making genetic changes. We will focus on one of CRISPR's biggest leaps, gene drives. We will conclude class with a discussion of the ethical considerations of the deployment of gene drives in the wild and the use of gene editing in medicine.

The Nobel Foundation has produced an excellent introduction to CRISPR-Cas9: Advanced information.

Actions

NobelPrize.org. Nobel Media AB 2021. Thu. 18 Feb 2021. <https://www.nobelprize.org/prizes/chemistry/2020/advanced-information/>

Study Guide

Actions

Student Papers:

Timothy Chang: Klann et al., (2017) Cas9 epigenome editing to reveal functional regulatory elements *Nat Biotechnol* **35:** 561–568.

Actions

Victor de la Peña: Anzalone, A.V., Randolph, P.B., Davis, J.R. *et al.* (2019) Search-and-replace genome editing without double-strand breaks or donor DNA. *Nature* **576:** 149–157 .

Actions

Shuangyi Xu: Haideri T, Howells A, Jiang Y, Yang J, Bao X, Lian XL. (2022) Robust genome editing via modRNA-based Cas9 or base editor in human pluripotent stem cells. *Cell Rep Methods*. **2:** 100290.

Actions

Extra Reading:

D.J. Dickinson and B. Goldstein (2016) CRISPR-based methods for *Caenorhabditis elegans* genome engineering. *Genetics* **202**: 885-901. (Note: read pages 886-888).

Actions

K. Kyrou, A.M. Hammond, R. Galizi, N. Kranjc, A. Burt, A.K. Beaghton, T. Nolan, and A. Crisanti (2018) A CRISPR-Cas9 gene drive targeting *doublesex* causes complete population suppression in caged *Anopheles gambiae* mosquitoes. *Nature Biotech*. advanced online publication.

Actions

L. Cong, F.A. Ran, D. Cox, S. Lin, R. Barretto, N. Habib, P.D. Hsu, X. Wu, W. Jiang , L.A. Marraffini, F. Zhang (2013) Multiplex genome engineering using CRISPR/Cas systems.
Science **339**: 819-823.Download L. Cong, F.A. Ran, D. Cox, S. Lin, R. Barretto, N. Habib, P.D. Hsu, X. Wu, W. Jiang , L.A. Marraffini, F. Zhang (2013) Multiplex genome engineering using CRISPR/Cas systems. Science 339: 819-823.

D. Bhaya, M. Davison, R. Barrangou (2011) CRISPR-Cas systems in bacteria and archaea: versatile small RNAs for adaptive defense and regulation. *Annu. Rev. Genet.* **45**: 273-297.

Actions

A. Regalado (2016) The extinction invention. *MIT Technology Review*Links to an external site.
HHMI (2018) CRISPR-Cas9 mechanisms and applicationsLinks to an external site.

8. March 20: Gene Expression Methods

CLASS SLIDES Download CLASS SLIDES PDF

Actions

Topics include labeling methods such as antibodies, in situ hybridization, lacZ, GFP, etc. and using these methods as phenotypes

E. Bier *et al.* (1989) Searching for Pattern and Mutation in the *Drosophila* genome with a *P-lacZ* vector. *Genes & Develop.* **3**: 1273-1287.

Actions

HW: Section 5.2

Study Guide

Actions

Student Papers (CRISPR):

William Hyatt: Halperin et al. (2018)

Actions

CRISPR-guided DNA polymerases enable diversification of all nucleotides in a tunable window. *Nature* **560**: 248-252.

Actions

Karinna Pe: Thege, F. I., Rupani, D. N., Barathi, B. B., Manning, S. L., Maitra, A., Rhim, A. D., & Wörmann, S. M. (2022). A Programmable *In Vivo* CRISPR Activation Model Elucidates the Oncogenic and Immunosuppressive Functions of MYC in Lung Adenocarcinoma. *Cancer Research* **82***:* 2761-2776.

Actions

Xiaoyun Li: Shipman, S.L., Nivala, J., Church, G.M. (2016) Molecular recordings by directed CRISPR spacer acquisition. Science. 353: aaf1175.

Actions

Katriona Guthrie-Honea: Sheth, R.U., Yim, S.S., Wu, F.L., and Wang, H.H. (2017) Multiplex recording of cellular events over time on CRISPR biological tape. *Science* **358**: 1457-1461.

Actions

Student Papers (GFP):

Isabella Succi H.K. Shearin, C.D. Quinn, R.D. Mackin,. I.S. macdonald, and R.S. Stowers (2018) t-GRASP, a targeted GRASP for assessing neuronal connectivity. *J. Neurosci. Meth.* **306**: 94-102.

Actions

Monica Cramer Z. Wang, B.M. Batholomai, J.J. Loros, and J.C. Dunlap (2023) Optimized fluorescent proteins for 4-color and photoconvertible live-cell imaging in Neurospora crassa. *Fungal Genet. Biol.* **164**: 103763

Actions

Preston Sheng: Y. Zhang *et al.* (2023) Fast and sensitive GCaMP calcium indicators for imaging neural populations. *Nature*doi: 10.1038/s41586-023-05828-9.

Actions

Devin King-Roberts: Subach, F.V.; Subach, O.M.; Gundorov, I.S.; Morozova, K.S., Piatkevich, K.D., Cuervo, A.M., and Verkhusha, V.V. (2009) Monomeric fluorescent timers that change color from blue to red report on cellular trafficking. *Nat. Chem. Biol.* **5**: 118–126.

Actions

Extra Reading:

M. Chalfie, Y. Tu, G. Euskirchen, W.W. Ward, and D.C. Prasher (1994) Green fluorescent protein as a marker for gene expression.*Science***263**: 802-805.

Actions

A. Raj, P. van den Bogaard, S. Rifkin, A. van Oudenaarden, and S. Tyagi (2008) Imaging individual mRNA molecules using multiple singly labeled probes. *Nature Methods***5**: 877-879.

Actions

A.H. Brand and N. Perrimon (1993) Targeted gene expression as a means of altering cell fates and generating dominant phenotypes. *Development* **118**: 401-415.

Actions

9. March 27: Mosaic Analysis

Quiz on Sessions 6 and 7 (and CRISPR papers in Session 8)

CLASS SLIDES Download CLASS SLIDES **PDF**

Actions

Topics include mosaic analysis in flies and worms, single and double spot mosaics, relationship of size and number of clones with time of irradiation, cell autonomy and non-autonomy (and using extragenic arrays in *C. elegans*), gynandromorphs, and fate mapping. The Lawrence and Green paper is a terrific paper that uses mosaic analysis to derive an important developmental principle; it also gives a counter example of the relationship between irradiation time and clone number.

P.A. Lawrence and S.M. Green (1979) Cell lineage in the developing retina of *Drosophila*. *Develop. Biol.***71**: 142-152.

Actions

Study Guide

Actions

Student Papers (GFP):

Max Rice: H. Koga *et al.* (2011) A photoconvertible fluorescent reporter to track chaperone-mediated autophagy. *Nat Commun* **2**: 386.

Actions

Arjun Sai Krishnan: E. Bollati et al. (2022) Green fluorescent protein-like pigments optimize the internal light environment in symbiotic reef-building corals *eLife* **11**: e73521

Actions

Kwass Wass: Z. Chen et al. (2013) Ubiquitination-Induced fluorescence complementation (UiFC) for detection of K48 ubiquitin chains *in vitro* and in live cells. *PLOS One* **8**: e73482.

Actions

Carlos Mendonca: S. Cabantous et al. (2013) A new protein-protein interaction sensor based on tripartite split-GFP association. *Sci. Reports* **3**: 2854.

Actions

Extra Reading:

K.G. Golic (1991) Site-specific recombination between homologous chromosomes in *Drosophila*. *Science* **252**: 958-961.

Actions

Y. Hotta and S. Benzer (1972) Mapping behavior in *Drosophila* mosaics. *Nature* **240**: 527-535.

Actions

J. Yochem and R.K. Herman (2003) Investigating *C. elegans* development through mosaic analysis. *Develop.***130**: 4761-4768.

Actions

T. Lee and L. Luo (2001) Mosaic analysis with a repressible cell marker (MARCM) for Drosophila neural development. Trends Neurosci. 24: 251-254.

Actions

10. April 3: Redundancy

CLASS SLIDES Download CLASS SLIDES PDF

Actions

Topics include synthetic phenotypes (and recessive redundancy), comparing the range of mutations and revertants of *mec-4* with those of *deg-1*, intergenic and intragenic

redundancy, and types of redundancy (Thomas review). The Park and Horvitz paper describes how to obtain mutations in other redundant genes.

J.H. Thomas (1993) Thinking about genetic redundancy. *Trends in Genetics* **9**: 395-398.

Actions

HW: Box 3.6

Study Guide

Actions

Extra Reading:

I.S. Greenwald and H.R. Horvitz (1980) *unc-93(e1500)*: a behavioral mutant of *Caenorhabditis elegans* that defines a gene with a wild-type null phenotype. *Genetics* **96**: 147-164.

Actions

M. Chalfie and E. Wolinsky (1990) The identification and suppression of inherited neurodegeneration in *Caenorhabditis elegans*. *Nature* **345**: 410-416.

Actions

J. García-Añoveros, C. Ma, and M. Chalfie (1995) An extracellular domain regulates degenerin channel activity. *Curr. Biol.* **5**: 441-448.

Actions

E.C. Park and H.R. Horvitz (1986) Mutations with dominant effects on the behavior and morphology of the nematode *Caenorhabditis elegans*. *Genetics***113**: 821-852.
Download E.C. Park and H.R. Horvitz (1986) Mutations with dominant effects on the behavior and morphology of the nematode Caenorhabditis elegans. Genetics113: 821-852. F.L. Muller, S. Colla, E. Aquilanti, V.E., Manzo, G. Genovese, J. Lee, D. Eisenson, R. Narurkar, P. Deng, L. Nezi, M.A. Lee, B. Hu, J. Hu, E. Sahin, D. Ong, E. Fletcher-

Sananikone, D. Ho, L. Kwong, C. Brennan, Y.A. Wang, L. Chin, R.A. DePinho (2012) Passenger deletions generate therapeutic vulnerabilities in cancer. *Nature* **488**: 337-342.

Actions

11. April 10: Suppressors/Enhancers

Quiz on Sessions 8 and 9

CLASS SLIDES Download CLASS SLIDES PDF

Actions

Topics include reversion (true and pseudo, i.e., compensating) and the frequencies they are expected to arise, informational suppressors (definition and range, nonsense suppressors, *smg*s, gene and allele specificity, tRNA nonsense suppressors as examples (neomorphic mutations, dominant or recessive action and what this says about the suppressed gene), physiological suppressors (example of an allele-non-specific suppressor and an allele-specific suppressor, protein interaction, and enhancers. The Simon et al. paper uses a sensitized background to identify enhancers that might otherwise not be found in standard genetic screens.

M.A. Simon, D.D. Bowtell, G.S. Dodson, T.R. Laverty, and G.M. Rubin (1991) *Ras1* and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the *sevenless* protein tyrosine kinase. *Cell* 67: 701-716.

Actions

HW: Section 3.5 and Chapter 4

Study Guide

Actions

Extra Reading:

B. M. Cali and P. Anderson (1998) mRNA surveillance mitigates genetic dominance in *Caenorhabditis elegans*. *Mol. Gen. Genet.* **260**: 176-184.

Actions

J. Hodgkin, Genetic suppression (December 27, 2005), *WormBook*, ed. The *C. elegans* Research Community, WormBook, doi/10.1895/wormbook.1.59.1, www.wormbook.org.

Actions

R.H. Waterston (1981) A second informational suppressor, *sup-7 X*, in *Caenorhabditis elegans*. *Genetics* **97**: 307-325.

Actions

N. Wills, RF Gesteland, J. Karn. L. Barnett, S. Bolten, and R.H. Waterston (1983) The genes *sup-7 X* and *sup-5 III* of C. elegans suppress amber nonsense mutations via altered transfer RNA. *Cell* **33**: 575-83.

Actions

N.R. Morris, M.H. Lai, and C.E. Oakley (1979) Identification of a gene for α-tubulin in Aspergillus nidulans. *Cell* **16**: 437-442.

Actions

S.M. Parkhurst and V.G. Corces (1985) *forked*, gypsys, and suppressors in Drosophila. *Cell* **41**: 429-437.

Actions

12. April 17: Epistasis - Genetic Interactions

SIGN-UP FOR 24-7Links to an external site.

CLASS SLIDES Download CLASS SLIDES PDF

Actions

Topics include definition of epistasis, examples using *dpy* and *lon* mutations, identification of sex determination genes in *C. elegans* and using epistasis to develop a

genetic pathway, assumptions and caveats, and drawing conclusions from the pathway. The Lehner review provides molecular examples of different types of epistasis. The genetic compensation paper by El-Brolosy et al. describes an additional means that genes can interact.

B. Lehner (2011) Molecular mechanisms of epistasis within and between genes. *Trends Genet.* **27**: 323-331.

Actions

M.A. El-Brolosy et al. (2019) Genetic compensation triggered by

Actions

mutant mRNA degradation. *Nature* **568**: 193-197.

Actions

HW: Section 5.1

Study Guide

Actions

Extra Reading:

L. Avery and S. Wasserman (1992) Ordering gene function: the interpretation of epistasis in regulatory hierarchies. *Trends Genetics* **8**: 312-316.

Actions

13. April 24: Genomes

Quiz on Sessions 10 - 12

CLASS SLIDES Download CLASS SLIDES PDF

Actions

24-7

Actions

Topics include development of the nematode genome project, cosmid footprinting (as opposed to chromosomal walking or jumping), tying the physical and genetic maps together, social consequences, predicting gene models, using cDNA sequences to refine the map. The Kellis and Pierce papers are terrific examples of the strength of genome sequencing to address biological problems.

M. Kellis, B.W. Birren, and E.S. Lander (2004) Proof and evolutionary analysis of ancient genome duplication in the yeast *Saccharomyces cerevisiae*.*Nature***428**: 617-624.

Actions

S.B. Pierce, T. Walsh, K.M. Chisholm, M.K. Lee, A.M. Thornton, A. Fiumara, J.M. Opitz, E. Levy-Lahad, R.E. Klevit, and M.C. King. (2010) Mutations in the DBP-deficiency protein HSD17B4 cause ovarian dysgenesis, hearing loss, and ataxia of Perrault syndrome. *Amer. J. Human Genetics* **87**: 282–288.

Actions

Study Guide

Actions

Extra Reading:

A. Coulson, J. Sulston, S. Brenner, and J. Karn (1986) Toward a physical map of the genome of the nematode *Caenorhabditis elegans*. *Proc. Nati. Acad. Sci. USA* **83**: 7821-7825.

Actions

J.S. Packer, Q. Zhu, C. Huynh, P. Sivaramakrishnan, E. Preston, H. Dueck, D. Stefanik, K. Tan, C. Trapnell, J. Kim, R.H. Waterston, and J.I. Murray (2019) A lineage-resolved molecular atlas of *C. elegans* embryogenesis at single-cell resolution. *Science*. 365doi: 10.1126/science.aax1971. Epub 2019 Sep 5.

Actions

J. Sulston and G. Ferry (2002) *The Common Thread*, Bantam Press, London, pp. 1-310.

14. May 1: Genomic Methods

CLASS SLIDES

Discussion of using genomic techniques; 24-7's

Student Papers

Naima Okami : Boyle, E. A., Li, Y. I., and Pritchard, J. K. (2017) An expanded view of complex traits: From polygenic to omnigenic. *Cell* **169**: 1177–1186.

Actions
(**Timothy Chang, Will Hyatt, Carlos Mendonca**)

Vicens Vila-Coury: M. Liang et al. (2023) Taxon-specific, phased siRNAs underlie a speciation locus in monkeyflowers. *Science* **379**: 576–582

Actions
(**Devin King-Roberts and Xiaoyun Li**)

Allen Dinh: Y.B. Simons et al. (2022) Simple scaling laws control the genetic architectures of human complex traits. *bioRxiv*

Actions
(**Karinna Pe and Kwass Wass**)

Vicky Hu: E. Lieberman-Aiden et al. (2009) Comprehensive Mapping of Long-Range Interactions Reveals Folding Principles of the Human Genome. *Science* **326**: 289–293.

Actions
(**Shuangyi Xu and Katriona Guthrie-Honea**)

Mead Lockwood: D. G. Gibson et al. (2008) Complete chemical synthesis, assembly, and cloning of a Mycoplasma genitalium genome. *Science* **319**: 1215–1220.

Actions

(**Victor de la Peña and Carlos Mendonca**)

Lina Ruiz : D. Adam et al. (2020) Nanopore sequencing enables comprehensive transposable element epigenomic profiling. *Molec. Cell* **80**: 915–928

Actions
. (**Preston Sheng, Arjun Sai Krishnan**)

Julie Dobkin: A.C. Payne et al. (2021) In situ genome sequencing resolves DNA sequence and structure in intact biological samples. *Science* **371**: eaay3446.

Actions
(**Isabella Succi and Max Rice**)

Jose Pomarino Nima: Dixit et al. (2016) Perturb-seq: dissecting molecular circuits with scalable single-cell rna profiling of pooled genetic screens. *Cell* **167**: 1853-1866.

Actions
(**Monica Cramer and Vicens Vila-Coury**)