# MCB 240 Advanced Genetic Analysis, Spring 2018

The course material will explore fundamental concepts in genetics through the sophisticated "eyes" of geneticists working with model organisms. The goals are to attain an appreciation for remarkable biological insights achieved through genetics and to discuss the virtues and limitations of genetics as a tool to study complex biological problems.

## 1/16. Lecture: Mutations, Mutagenesis and Mutants (Genetics begins with mutations) *(Koshland)*

Why are we interested in mutations?
Mutations impact on gene function
Mutations structural and functional nomenclature
Mutation information value
Getting mutations - mutagenesis, screens and selections

*Leland H Hartwell, R.K.M.J.C.M.C. (1973). Genetic Control of the Cell Division Cycle in Yeast: V. Genetic Analysis of cdc Mutants. Genetics *74*, 267. Note: ignore all text and figures related to execution point.

Schnorrer, F., Schönbauer, C., Langer, C. C. H., Dietzl, G., Novatchkova, M., Schernhuber, K., et al. (2010). Systematic genetic analysis of muscle morphogenesis and function in Drosophila. *Nature*, *464*(7286), 287–291. http://doi.org/10.1038/nature08799

Winston, F., and Koshland, D. (2016). Back to the Future: Mutant Hunts Are Still the Way To Go. Genetics *203*, 1007–1010.

## 1/18. Lecture: Synthetic Alleles (Un-natural biology to study nature) *(Koshland)*

Recombinant DNA changes allele landscape

Examples of synthetic alleles
    Underlying features that make synthetic alleles useful
    Combining activities
    Inventing new activities
Caveats for synthetic alleles

**Hoess, R.H., and Abremski, K. (1985). Mechanism of strand cleavage and exchange in the Cre-lox site-specific recombination system. J. Mol. Biol. 181, 351–362.

*Winzeler, E.A., Shoemaker, D.D., Astromoff, A., Liang, H., Anderson, K., Andre, B., Bangham, R., Benito, R., Boeke, J.D., Bussey, H., et al. (1999). Functional characterization of the S. cerevisiae genome by gene deletion and parallel analysis. Science *285*, 901–906.

Nishimura, K., Fukagawa, T., Takisawa, H., Kakimoto, T., & Kanemaki, M. (2009). An auxin-based degron system for the rapid depletion of proteins in nonplant cells. *Nature Methods*, *6*(12), 917–

922. http://doi.org/10.1038/nmeth.1401

### 1/22. Discussion: CRISPR *(Koshland and Meyer)*

Chen, S., Sanjana, N.E., Zheng, K., Shalem, O., Lee, K., Shi, X., Scott, D.A., Song, J., Pan, J.Q., Weissleder, R., Lee, H., Zhang, F., Sharp, P. (2015), Genome-wide CRISPR Screen in a Mouse Model of Tumor Growth and Metastasis, Cell, Volume 160, Issue 6, 12 March 2015, Pages 1246-1260

### 1/23. Lecture: Linkage *(Koshland)*

Methods for establishing linkage: crosses, recombinant DNA, reversion, multiple alleles
  Strengths and weaknesses
  Assuming linkage
  Missing linkage

Burnett, C., Valentini, S., Cabreiro, F., Goss, M., Somogyvári, M., Piper, M.D., Hoddinott, M., Sutphin, G.L., Leko, V., McElwee, J.J., et al. (2011). Absence of effects of Sir2 overexpression on lifespan in C. elegans and Drosophila. Nature *477*, 482–485.

Rogina, B., and Helfand, S.L. (2004). Sir2 mediates longevity in the fly through a pathway related to calorie restriction. Proc. Natl. Acad. Sci. U.S.A. *101*, 15998–16003.

Edwards, M.D., Symbor-Nagrabska, A., Dollard, L., Gifford, D.K., and Fink, G.R. (2014). Interactions between chromosomal and nonchromosomal elements reveal missing heritability. Proc. Natl. Acad. Sci. U.S.A. *111*, 7719–7722.

### 1/25. Lecture: Suppressors (the power of genetic interactions) *(Koshland)*

Review of Revertant, intragenic, extragenic,
Suppressor screen
    Setting the paramters; Starting mutation and strength of suppressor
    Identifying suppressor mutation
Examples of suppressors
    “Specific” Suppressors for Protein-protein interaction or Regulation
    Non-Specific Suppressors; activities common to multiple processes

*Norris, A., Bianchet, M.A., and Boeke, J.D. (2008). Compensatory Interactions between Sir3p and the Nucleosomal LRS Surface Imply Their Direct Interaction. PLoS Genet 4, e1000301.

Wang, J., Reddy, B.D., and Jia, S. (2015). Rapid epigenetic adaptation to uncontrolled heterochromatin spreading. Elife *4*, e06179.

### 1/29. Discussion: Suppressors *(Koshland and Meyer)*

**Crick, F.H., Barnett, L., Brenner, S., and Watts-Tobin, R.J. (1961). General nature of the genetic code for proteins. Nature 192, 1227–1232.

### 1/30. Lecture: Tools to establish a model organism (nematode developmental genetics) *(Meyer)*

Diploid genetics in a sexually reproducing multi-cellular organism,
Genome editing,

Brenner S. The genetics of *Caenorhabditis elegans. Genetics.* 1974 May;77(1):71-94. PMID: 04366476

Herman RK, Yochem J. Genetic enhancers. *WormBook*. 2005 Sep 16:1-11. Review. PMID: 18023119

Hodgkin J. Genetic suppression. *WormBook*. 2005 Dec 27:1-13. Review. PMID: 18023120

### 2/1. Lecture: Cell Death: Building a Genetic Pathway *(Meyer)*

Analysis of developmental decisions: specification and implementation of developmental choices through genetic pathways to determine cell survival or to specify organ development

Suppressor genetics: intragenic and extragenic, *cis-trans* tests

Hengartner, M.O., Ellis, R.E., Horvitz, H.R. (1992). *Caenorhabditis elegans* gene *ced-9* protects cells from programmed cell death. *Nature* 356, 494-499.

Horvitz, H.R. (2002). Worms, Life, and Death (Nobel lecture). ChemBioChem 2003, 4, 697-711.

### 2/5. Discussion. Genetics of Cell Death and basic nematode genetics *(Meyer)*

Conradt B, Horvitz HR. The TRA-1A sex determination protein of *C. elegans* regulates sexually dimorphic cell deaths by repressing the *egl-1* cell death activator gene. *Cell.* 1999 Aug 6;98(3):317-27. PMID: 10458607

### 2/6. Lecture: Cell Signaling *(Meyer)*

Genetic dissection of cell-cell communication for tissue specificity
Tools to assess gene function within or outside a cell to specify cell fate and organ development

Seydoux G, Greenwald I. Cell autonomy of *lin-12* function in a cell fate decision in *C. elegans. Cell.* 1989 Jun 30;57(7):1237-45. PMID: 2736627

Sternberg PW. Vulval development. *WormBook.* 2005 Jun 25:1-28. Review. PMID: 18050418

## 2/8. Lecture: Synthetic Phenotypes (Genetic interactions run amuck) *(Koshland)*

Phenotype from combination of alleles different in quality from either allele alone
Molecular explanation of synthetic phenotypes
Functional overlap of homologous proteins
Functional overlap of non-homologus proteins/pathways
    Synergistic change in activity
Using synthetic phenotypes by candidate and genomic approaches
Do synthetic phenotypes lie?

Smida, M., la Cruz, de, F.F., Kerzendorfer, C., Uras, I.Z., Mair, B., Mazouzi, A., Suchankova, T., Konopka, T., Katz, A.M., Paz, K., et al. (2016). MEK inhibitors block growth of lung tumours with mutations in ataxia–telangiectasia mutated. Nat Commun *7*, 13701.

Schuldiner, M., Collins, S.R., Thompson, N.J., Denic, V., Bhamidipati, A., Punna, T., Ihmels, J., Andrews, B., Boone, C., Greenblatt, J.F., et al. (2005). Exploration of the function and organization of the yeast early secretory pathway through an epistatic miniarray profile. Cell *123*, 507–519.

*Breslow, D.K., Collins, S.R., Bodenmiller, B., Aebersold, R., Simons, K., Shevchenko, A., Ejsing, C.S., and Weissman, J.S. (2010). Orm family proteins mediate sphingolipid homeostasis. Nature 463, 1048–1053.

## 2/12. Discussion: *(Koshland)*

Edgar, R.S., and Wood, W.B. (1966). Morphogenesis of bacteriophage T4 in extracts of mutant-infected cells. Proc. Natl. Acad. Sci. U.S.a. *55*, 498–505.

Ventura, A., Kirsch, D.G., McLaughlin, M.E., Tuveson, D.A., Grimm, J., Lintault, L., Newman, J., Reczek, E.E., Weissleder, R., and Jacks, T. (2007). Restoration of p53 function leads to tumour regression in vivo. Nature *445*, 661–665.

## 2/13. Lecture: Non-conventional Inheritance (Somebody has always got to buck rules) *(Koshland)*

Review non-Mendelian inheritance
Mitochondria
Prions

*Wickner, R.B. (1994). [URE3] as an altered URE2 protein: evidence for a prion analog in Saccharomyces cerevisiae. *Science* 264, 566–569.

Nelson, J.L. (2012). The otherness of self: microchimerism in health and disease. Trends in Immunology *33*, 421–427.

### **2/15. Lecture: Genetic screens in vertebrates** *(Miller)*

Mouse mutagenesis and Oak Ridge specific locus test
Phenotype-based forward genetic screens in mice
Saturation mutagenesis in zebrafish

Davis, A.P., and Justice, M.J. (1998). An Oak Ridge legacy: the specific locus test and its role in mouse mutagenesis. Genetics *148*, 7–12.

Haffter, P., Granato, M., Brand, M., Mullins, M.C., Hammerschmidt, M., Kane, D.A., Odenthal, J., van Eeden, F.J., Jiang, Y.J., Heisenberg, C.P., et al. (1996). The identification of genes with unique and essential functions in the development of the zebrafish, Danio rerio. Development. *123*, 1–36.

Kasarskis, A., Manova, K., and Anderson, K.V. (1998). A phenotype-based screen for embryonic lethal mutations in the mouse. Proc. Natl. Acad. Sci. U. S. A. *95*, 7485–7490.

### **2/19. No Discussion: holiday**

### **2/20. Lecture: Building a genetic pathway II** *(Miller)*

Agouti and MC1R: epistasis in vertebrate pigmentation genetics
Epistatic relationships are context-specific

Duhl, D.M., Vrieling, H., Miller, K.A., Wolff, G.L., and Barsh, G.S. (1994). Neomorphic agouti mutations in obese yellow mice. Nat. Genet. *8*, 59–65.

Phillips, P.C. (2008). Epistasis--the essential role of gene interactions in the structure and evolution of genetic systems. Nat. Rev. Genet. *9*, 855–867.

Våge, D.I., Lu, D., Klungland, H., Lien, S., Adalsteinsson, S., and Cone, R.D. (1997). A non-epistatic interaction of agouti and extension in the fox, Vulpes vulpes. Nat. Genet. *15*, 311–315.

### **2/22. Lecture: Genetics of regulatory alleles: the cis-trans test** *(Miller)*

Determining what gene a regulatory allele is affecting
Lmbr1 vs. Shh: the cis-trans test

Clark, R.M., Marker, P.C., Roessler, E., Dutra, A., Schimenti, J.C., Muenke, M., and Kingsley, D.M. (2001). Reciprocal mouse and human limb phenotypes caused by gain- and loss-of-function mutations affecting Lmbr1. Genetics *159*, 715–726.

Lettice, L.A., Horikoshi, T., Heaney, S.J.H., van Baren, M.J., van der Linde, H.C., Breedveld, G.J., Joosse, M., Akarsu, N., Oostra, B.A., Endo, N., et al. (2002). Disruption of a long-range cis-acting regulator for Shh causes preaxial polydactyly. Proc. Natl. Acad. Sci. U. S. A. *99*, 7548–7553.

### 2/26. Discussion: Genetics of regulatory alleles: the serpentized mouse *(Miller)*

Kvon, E.Z., Kamneva, O.K., Melo, U.S., Barozzi, I., Osterwalder, M., Mannion, B.J., Tissières, V., Pickle, C.S., Plajzer-Frick, I., Lee, E.A., et al. (2016). Progressive Loss of Function in a Limb Enhancer during Snake Evolution. Cell *167*, 633–642.e11.

### 2/27. Lecture: Quantitative *Genetics*: Hindlimb variation *(Miller)*

Quantitative vs. Mendelian variation
Genetic analyses of evolved phenotypic differences: QTL mapping vs. association mapping

Shapiro MD, Marks ME, Peichel CL, Blackman BK, Nereng KS, Jónsson B, Schluter D, Kingsley DM. Genetic and developmental basis of evolutionary pelvic reduction in threespine sticklebacks. *Nature.* 2004 Apr 15;428(6984):717–723. PMID: 15085123

Chan YF, Marks ME, Jones FC, Villarreal G, Shapiro MD, Brady SD, Southwick AM, Absher DM, Grimwood J, Schmutz J, Myers RM, Petrov D, Jónsson B, Schluter D, Bell MA, Kingsley DM. Adaptive evolution of pelvic reduction in sticklebacks by recurrent deletion of a Pitx1 enhancer. *Science.* 2010 Jan 15;327(5963):302–305. PMCID: PMC3109066

Domyan ET, Kronenberg Z, Infante CR, Vickrey AI, Stringham SA, Bruders R, Guernsey MW, Park S, Payne J, Beckstead RB, Kardon G, Menke DB, Yandell M, Shapiro MD. Molecular shifts in limb identity underlie development of feathered feet in two domestic avian species*. eLife.* 2016 Mar 15;5:e12115. PMCID: PMC4805547

### 3/1. Lecture: Quantitative Genetics: Dogs *(Miller)*

Mapping complex traits with QTL mapping and association studies in dogs

Sutter NB, Bustamante CD, Chase K, Gray MM, Zhao K, Zhu L, Padhukasahasram B, Karlins E, Davis S, Jones PG, Quignon P, Johnson GS, Parker HG, Fretwell N, Mosher DS, Lawler DF, Satyaraj E, Nordborg M, Lark KG, Wayne RK, Ostrander EA. A single IGF1 allele is a major determinant of small size in dogs. *Science.* 2007 Apr 6;316(5821):112–115. PMCID: PMC2789551

Cadieu E, Neff MW, Quignon P, Walsh K, Chase K, Parker HG, Vonholdt BM, Rhue A, Boyko A, Byers A, Wong A, Mosher DS, Elkahloun AG, Spady TC, André C, Lark KG, Cargill M, Bustamante CD, Wayne RK, Ostrander EA. Coat variation in the domestic dog is governed by variants in three genes. *Science.* 2009 Oct 2;326 (5949):150–153. PMCID: PMC2897713

### 3/5. Discussion. Quantitative genetics of evolved song variation in flies *(Miller)*

Ding Y, Berrocal A, Morita T, Longden KD, Stern DL. Natural courtship song variation caused by an intronic retroelement in an ion channel gene. *Nature.* 2016 Aug 18;536(7616):329–332. PMID: 27509856

### 3/6. Lecture: Epistasis for quantitative variation *(Miller)*

Testing for genetic interactions for quantitative trait loci
The role of epistasis in quantitative variation
The genetics of artificial selection on chicken growth and higher order epistasis

Huang, W., Richards, S., Carbone, M.A., Zhu, D., Anholt, R.R.H., Ayroles, J.F., Duncan, L., Jordan, K.W., Lawrence, F., Magwire, M.M., et al. (2012). Epistasis dominates the genetic architecture of Drosophila quantitative traits. Proc. Natl. Acad. Sci. U. S. A. *109*, 15553–15559.

Carlborg, O., Jacobsson, L., Ahgren, P., Siegel, P., and Andersson, L. (2006). Epistasis and the release of genetic variation during long-term selection. Nat. Genet. *38*, 418–420.

Pettersson, M., Besnier, F., Siegel, P.B., and Carlborg, O. (2011). Replication and explorations of high-order epistasis using a large advanced intercross line pedigree. PLoS Genet. *7*, e1002180.

### 3/8. Lecture: Evolutionary Genetics*:* Supergenes, mimicry, and industrial melanism *(Miller)*

Supergenes: history to Heliconius
Industrial melanism genetics: cortex in butterflies/moths

Nadeau, N.J., Pardo-Diaz, C., Whibley, A., Supple, M.A., Saenko, S.V., Wallbank, R.W.R., Wu, G.C., Maroja, L., Ferguson, L., Hanly, J.J., et al. (2016). The gene cortex controls mimicry and crypsis in butterflies and moths. Nature *534*, 106–110.

Van't Hof, A.E., Campagne, P., Rigden, D.J., Yung, C.J., Lingley, J., Quail, M.A., Hall, N., Darby, A.C., and Saccheri, I.J. (2016). The industrial melanism mutation in British peppered moths is a transposable element. Nature *534*, 102–105.

### 3/9. DUE BY 10 AM: SYNTHETIC ALLELE PROPOSALS.

**3/12. Synthetic allele presentations**
**3/13. Synthetic allele presentations**
**3/15. Synthetic allele presentations**

**3/19. Discussion cancelled.**

**3/20. Lecture: Cell Signaling and Convergence of Signaling Pathways to Specify Cell Fate** *(Meyer)*

Functional overlap of diverse genetic pathways
Synthetic phenotypes

Cui M, Chen J, Myers TR, Hwang BJ, Sternberg PW, Greenwald I, Han M. SynMuv genes redundantly inhibit lin-3/EGF expression to prevent inappropriate vulval induction in C. elegans. *Dev Cell.* 2006 May;10(5):667-72. PMID: 16678779

Myers TR, Greenwald I. lin-35 Rb acts in the major hypodermis to oppose ras-mediated vulval induction in C. elegans. *Dev Cell.* 2005 Jan;8(1):117-23. PMID:15621535

**3/22. Lecture: Ligands and Genetic Redundancy** *(Meyer)*

Discovery and analysis of single or multiple ligands for one or more receptors
Functional overlap of homologous proteins
Genetics of redundancy

Chen N, Greenwald I. The lateral signal for LIN-12/Notch in *C. elegans* vulval development comprises redundant secreted and transmembrane DSL proteins. *Dev Cell.* 2004 Feb;6(2):183-92. PMID: 14960273

**3/26-3/30 Spring break**

**4/2. Discussion Gene Drive Cas9** *(Meyer)*

Esvelt, KM, Smidler, AL, Catterucchi, F, Church, GM. Concerning RNA-guided gene drives for the alteration of wild populations. eLife 2014;3:e03401. DOI: 10.7554/eLife.03401

Gantz VM, Jasinskiene N, Tatarenkova O, Fazekas A, Macias VM, Bier E, James AA. Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito *Anopheles stephensi.* PNAS E6736-E6743. www.pnas.org/cgi/doi/10.1073/pnas.1521077112

### 4/3. Lecture: Genetic Control of Aging *(Meyer)*

Multi-faceted genetic control of lifespan involving cell-cell communication

Arantes-Oliveira N, Berman JR, Kenyon C. Healthy animals with extreme longevity. *Science.* 2003 Oct 24;302(5645):611. No abstract available. PMID: 14576426

Bohnert, KA, Kenyon C. Nature 2017 Nov30;551(7682):629-633. doi: 10.1038/nature2460. Epub 2017 Nov 22. PMID: 29168500.

Greer EL, Maures TJ, Hauswirth AG, Green EM, Leeman DS, Maro GS, Han S, Banko MR, Gozani O, Brunet A. Members of the H3K4 trimethylation complex regulate lifespan in a germline-dependent manner in C. elegans. *Nature.* 2010 Jul 15;466(7304):383-7. doi: 10.1038/nature09195. Epub 2010 Jun 16. PMID: 20555324

Kenyon CJ. The genetics of ageing. *Nature.* 2010 Mar 25;464(7288):504-12. doi: 10.1038/nature08980. Review. Erratum in: Nature. 2010 Sep 30;467(7315):622. PMID: 20336132

### 4/5. Lecture: Temporal Control of Development and Function of RNAi Pathways *(Meyer)*

Use of microRNA pathways to control developmental timing
Genetic analysis of RNAi pathway genes, transport of active RNAi species, function of RNAi in the animal

Reinhart BJ, Slack FJ, Basson M, Pasquinelli AE, Bettinger JC, Rougvie AE, Horvitz HR, Ruvkun G. The 21-nucleotide *let-7* RNA regulates developmental timing in Caenorhabditis elegans. *Nature.* 2000 Feb 24;403(6772):901-6. PMID: 10706289

Buckley BA, Burkhart KB, Gu SG, Spracklin G, Kershner A, Fritz H, Kimble J, Fire A, Kennedy S. A nuclear Argonaute promotes multigenerational epigenetic inheritance and germline immortality. *Nature.* 2012 Sep 20;489(7416):447-51. doi: 10.1038/nature11352. Epub 2012 Jul 18. PMID: 22810588

### 4/9. Discussion Epigenetics of Aging and Germline Expression *(Meyer)*

Greer EL, Maures TJ, Ucar D, Hauswirth AG, Mancini E, Lim JP, Benayoun BA, Shi Y, Brunet A. Transgenerational epigenetic inheritance of longevity in Caenorhabditis elegans. *Nature.* 2011 Oct 19;479(7373):365-71. doi: 10.1038/nature10572. PMID: 22012258

Gaydos, L., Wang, W., Strome, S. H3K27me and PRC2 transmit a memory of repression across generations and during development. *Science*, 2014 Sept 19; 345(6203):1515-1518. doi: 10.1126/science.1255023

### 4/10. Lecture: Evolution *(Meyer)*

Co-option of old genes for new functions during nematode evolution
Rapid genome shrinkage from change in reproduction mode

Bento G, Ogawa A, Sommer RJ. Co-option of the hormone-signalling module dafachronic acid-DAF-12 in nematode evolution. *Nature,*2010 Jul 22;466(7305):494-7. doi: 10.1038/nature09164. Epub 2010 Jun 30. PMID: 20592728

Yin, D. et al., Rapid genome shrinkage in a self-fertile nematode reveals sperm competition proteins. *Science* 2018 Jan 4

### 4/12. Lecture: Genome Instability and Genome Evolution (Shattering the genome) *(Koshland)*

Yeast whole genome duplication
Aneuploidy
Polyploidy
Synthetic genomes

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

Crasta, K., Ganem, N.J., Dagher, R., Lantermann, A.B., Ivanova, E.V., Pan, Y., Nezi, L., Protopopov, A., Chowdhury, D., and Pellman, D. (2012). DNA breaks and chromosome pulverization from errors in mitosis. *Nature* 1–8.

Sheltzer, J.M., Blank, H.M., Pfau, S.J., Tange, Y., George, B.M., Humpton, T.J., Brito, I.L., Hiraoka, Y., Niwa, O., and Amon, A. (2011). Aneuploidy drives genomic instability in yeast. *333*, 1026–1030.

**4/13. DUE BY 10 AM: PROPOSAL DRAFT**

### 4/16. Discussion. *(Miller)*

Evolutionary genomics, introgression, macroevolution vs. microevolution

Lamichhaney S, Berglund J, Almén MS, Maqbool K, Grabherr M, Martinez-Barrio A, Promerová M, Rubin C-J, Wang C, Zamani N, Grant BR, Grant PR, Webster MT, Andersson L. Evolution of Darwin's finches and their beaks revealed by genome sequencing. Nature. 2015 Feb 19;518(7539):371–375. PMID: 25686609

### 4/17. Lecture: Evolution: Applications and insights in microorganisms *(Koshland)*

Switching master regulators of complex regulatory
Evolution of pathways and processes
Using species differences to elucidate processes

Lee, M.G., and Nurse, P. (1987). Complementation used to clone a human homologue of the fission yeast cell cycle control gene cdc2. Nature *327*, 31–35.

Rutherford, S.L., and Lindquist, S. (1998). Hsp90 as a capacitor for morphological evolution. Nature *396*, 336–342.

Medina, E.M., Turner, J.J., Gordân, R., Skotheim, J.M., and Buchler, N.E. (2016). Punctuated evolution and transitional hybrid network in an ancestral cell cycle of fungi. Elife *5*, e09492.

**4/19. Lecture: Population Genetics** *(Miller)*

Recent evidence of pervasive genetic introgression within and between species

Colosimo PF, Hosemann KE, Balabhadra S, Villarreal G, Dickson M, Grimwood J, Schmutz J, Myers RM, Schluter D, Kingsley DM. Widespread parallel evolution in sticklebacks by repeated fixation of Ectodysplasin alleles. *Science.* 2005 Mar 25;307(5717):1928–1933. PMID: 15790847
Heliconius Genome Consortium. Butterfly genome reveals promiscuous exchange of mimicry adaptations among species. *Nature.* 2012 Jul 5;487(7405):94–98. PMCID: PMC3398145

**4/23. PROPOSAL PRESENTATIONS**
**4/24. PROPOSAL PRESENTATIONS**
**4/26. PROPOSAL PRESENTATIONS**

**4/30-5/4. RRR week, no class**

**5/7. DUE BY 10 AM: PROPOSAL FINAL DRAFT**

**Description of Challenge Assignment**
Synthetic alleles like epitope tags, GFP fusions, Cre-Locs recombination, or enhancer traps are powerful genetic tools to elucidate many aspects of biology. Your charge is to invent a new synthetic allele. To get your patent for this invention, you must provide a one page (max of two) description of your invention. Provide an intro that includes the biological/molecular problem that your invention addresses, a description of the synthetic allele including its construction and its relevant functional assay/phenotype, and finally one example of the use of this synthetic allele.

An abbreviated example: Pretending you were doing this challenge twenty years ago. You might introduce the problem that many processes require protein localization to specific tissues or subcellular locations….. Understanding the contribution to protein localization to any process has been greatly compromised by the lack of tools to visualize localization….. While antibodies have been used successfully, their application has been limited by the antigencity of the protein of interest. I propose to overcome this by fusing a known well established epitope from the oncogene myc to any proteins of interest …. I will demonstrate proof of principle by fusing myc to protein X ….