MCB240 Advanced Genetic Analysis (Koshland and Meyer)

Topics from Spring, 2013

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. Half the course will be devoted to developmental genetics.

Boot Camp –

Definition of allele, phenotype, genotype, complementation, recombination
Important Parameters of model genetic organisms
- Haploid vs Diploid genetics
- Growth
- Genome size, chromosome structure, Genetic tools

Mutations, Mutagenesis and Mutants (Genetics begins with mutations)

- 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
- Demonstrating causality linking phenotype to genotype

Recombination (You had better understand recombination because you all will use it)

- Overview; Homologous and non-homologous
- Homologous recombination: Reciprocal exchange, gene conversion
- Review DSB Model for recombination
  - DSB as targeting and gap repair
- Implications of recombination chemistry ssDNA, exo, gap, DNA synthesis
- Non Homologous Recombination
  - NHEJ and Transposition
- Competition of recombination pathways implications for recombinant
  - Engineering

Synthetic Alleles (Un-natural biology to study nature)

- Controlling timing/amount of gene expression:
  - Site specific recombination
  - Inducible promoters
  - Degrons
- Gene tagging for biochemistry and cytology

Artficial genomes

Suppressors (the power of genetic interactions)

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 proce

Synthetic Phenotypes (Genetic interactions run amuck)

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?

Pathway Analysis (Simple logic but easy to get your circuits crossed)

Functional Dependency – using conditional off mutations
Functional dependency by epistasis
Kinetic

Genome Instability and Genome Evolution (Shattering the genome)

Evolution: Applications and insights in microorganisms

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

Cytoplasmic Inheritance (Somebody has always got to buck rules)

Review non-mendelian inheritance
Mitochondria
Prions

DEVELOPMENTAL GENETICS

Analysis of developmental decisions: specification and implementation of choices

Build a genetic pathway that specifies, for example, cell death or organ development

Dissect mechanisms by which cells signal to each other to constrain the fate of a single cell or to make group decisions

Convergence of different signaling pathways to specify cell fate
Redundant signaling molecules and receptors

Determine cellular focus of gene action

Dissect whether a gene acts within the tissue it specifies or outside that tissue

Control of developmental timing and life span

Use of micro RNA pathways to control development

Analysis of complex traits, including behavioral traits

Advanced genetic and genomic manipulation

Analysis of the evolution of developmental processes

Conversion of non-model organisms into model organisms