

## **Chapter 16→Dissection of Gene Function (11-18-05)      Problems (1, 7, 18, 19, 21)**

### **Germinal Mutation**

A mutation in gamete-forming tissue.

An individual with the “new” germinal mutation will not show the phenotype but the mutation can be transmitted to progeny.

### **Somatic Mutation**

A mutation in any non-gamete producing tissue.

The individual with the “new” somatic mutation may exhibit a mutant phenotype but the mutation can't be transmitted to progeny.

### **Conditional Mutation**

The allele only expresses the mutant phenotype under certain environmental conditions.

(e.g., ts→temperature sensitive)

The protein product functions at the permissive temperature but is non-functional at the restrictive (non-permissive) temperature.

### **Auxotrophic Mutation**

The individual must be supplied with certain nutrients (amino acids, nucleotides, vitamins).

Commonly used when studying microorganisms. WT is **prototrophic** (nutritionally self-sufficient).

### **Resistance Mutation**

Confers the ability to grow in the presence of an inhibitor. (e.g., antibiotic or virus/phage)

Antibiotic resistance mutations can arise from a mutation in the gene encoding the target of the drug or a mutation in the gene encoding a transporter of the drug.

### **Human Genetics**

Germinal mutations are detected by the sudden appearance of the abnormal phenotype in a pedigree with no previous record of abnormality.

Dominant mutations are relatively easy to detect.

Recessive mutations can go unnoticed for several generations.

X-linked recessive mutations are easier to detect than autosomal.

### **Mutant Hunts**

Experiments designed to isolate mutants that affect a specific biological function.

### **Genetic Selections**

Techniques designed to separate rare mutant individuals from WT.

Need a selectable phenotype.

Only the appropriate mutants survive.

### **Genetic Screens**

Strategies designed to identify desired mutant individuals (mutant phenotype) from a large number of individuals.

(Figure 16-4)

### **Mutagens**

Used to increase mutation rates.

(e.g., chemicals or UV radiation)

### **Forward Genetics**

Analyzing heritable mutant phenotypes at the genetic level before performing molecular analyses of the isolated mutants.

Requires methods to identify the mutant genes (e.g., gene mapping)

### **Reverse Genetics**

This approach starts with a WT molecule (typically a cloned gene or a purified protein).

The WT gene is then mutated to identify the mutant phenotype.

### **Single Cell Haploid Organisms-Bacteria and Fungi (advantages)**

- 1) Grow as single cells in liquid culture or as colonies.
- 2) Easy to examine millions of individuals.
- 3) Isolated single cells generate a clonal population (colony) of genetically identical cells.
- 4) Mutants are easily identified (dominant or recessive).

## **I. Forward Genetic Selections**

### **A. Detection of Reverse Mutations (auxotroph→prototroph)**

- 1) Grow mutant culture in minimal medium + supplement.
- 2) Plate cells on minimal medium without supplement.
- 3) Survivors are prototrophs.

The use of a mutagen in step 1 above will increase the mutation rate.

1. The survivors can be a true reversion (WT genotype).
2. The survivors may be second site suppressors that result in the complete or partial phenotypic reversion to WT.
  - a. The second site suppressor can be in a new gene.  
Often identifies interacting proteins.
  - b. The second site suppressor can be in the same gene.  
Often identifies a critical contact within the protein that is required for function.

### **B. Penicillin Enrichment**

Auxotrophic selection in bacteria.

Penicillin kills actively growing cells by interfering with cell wall synthesis.

- 1) Grow cells in rich medium (with or without a mutagen).
- 2) Transfer to minimal medium.
- 3) Add penicillin (prototrophs die, auxotrophs survive).
- 4) Plate cells on rich medium.

Screen cells on minimal medium + various supplements.

Identifies mutants that now require a specific supplement for growth.

### **C. Resistance Mutations**

Bacteria

- 1) Grow cells in liquid culture (with or without a mutagen).
- 2) Plate cells on selective medium (antibiotic or phage).

**D. Selection of Fungal Auxotrophs**

Filter enrichment.

Prototrophs grow as fuzzy balls, auxotrophs do not grow.

- 1) Grow cells in rich medium (with or without a mutagen).
- 2) Transfer to minimal medium.
- 3) Filter cells and save the filtrate containing the auxotrophs.  
(The prototrophic fuzzy balls are retained on the filter).
- 4) Plate cells on rich medium.

Screen cells on minimal medium + various supplements.

Identifies mutants that now require a specific supplement for growth.

(Figure 16-6)

## **Chapter 16→Dissection of Gene Function (11-21-05)**

### **II. Forward Genetic Screens**

#### **A. Morphogenesis Mutants in Fungi**

- 1) Grow cells in rich medium (with or without a mutagen).
- 2) Plate cells and visually screen for abnormal colonies.

Identifies mutants that have defects in hyphal tip growth and branching  
(Figure 16-8)

#### **B. Yeast Cell Cycle**

Mutant screens of yeast are responsible for much of our understanding about the cell cycle.

*cdc* (cell-division cycle) mutants were first obtained in a screen looking for mutants that blocked the mitotic cell cycle at specific points.

(Figure 16-9)

Leland Hartwell and Paul Nurse (Nobel Prize).

Comparative genomics has shown that these same genes function in a similar manner in humans. Many of these genes are defective in cancers.

### III. Reverse Genetics

#### A. Random Mutagenesis

Combine new mutants with a known mutation of the gene of interest.

##### 1. Diploid organism (germinal)

Mutagenize the WT parent.

$$\begin{array}{ccc} a^+a^+b^+b^+ & X & aabb \\ & \downarrow & \\ a^+a^+b^+b & a^+abb & aab^+b \\ & \text{mutant 1} & \text{mutant 2} \end{array}$$

##### 2. Diploid organism (somatic)

Mutagenize the individual.

Look for sectoring in a heterozygote.

#### B. Gene-specific Mutagenesis

##### 1. Gene Replacement (Inactivation)

See notes for exam 3.

Replace the wild type gene with a gene that has been disrupted by a drug resistance gene.  
(Figure 16-15)

##### 2. Site-directed Mutagenesis

See notes from exam 3.

Introduce point mutations, deletions or insertions in a gene of interest using mutagenic oligonucleotides.

(Figure 16-16)

##### 3. Error-prone PCR

Use conditions in which PCR exhibits reduced fidelity of a coding region.

Then use a genetic selection or screen to identify interesting mutants.

## **Somatic Cell Genetics**

Applying mutagenic and selective techniques to animal and plant cell cultures.

Often only identify dominant mutations because the organism is diploid.

## **Analysis of Recovered Mutations**

Once several mutants are identified in a selection or screen, it is important to identify the mutant genes.

There could be one or several different genes giving rise to a particular phenotype.

(e.g., the inability to grow in the absence of an amino acid)

### **A. Prokaryotes**

1. Use conjugation and transduction mapping techniques to localize the mutant gene.
2. Clone by complementation.

### **B. Eukaryotes**

Use the complementation test.

## **Chapter 17 → Genetic Regulation of Cell Number: Normal and Cancer Cells (11-22-05)**

**(Problems 4, 7, 8, 9)**

### **Cell Cycle Control and Apoptosis**

Mechanisms exist to ensure that cell numbers remain balanced.

Cancer is a genetic disease of somatic cells that is caused by mutations that result in the failure of cell cycle control and/or the failure of apoptosis (programmed cell death).

### **The Cell Cycle**                      **(G<sub>1</sub>-S-G<sub>2</sub>-M)**

**G<sub>1</sub> (Gap 1)** → Time between mitosis and DNA replication.

**S** → DNA synthesis.

**G<sub>2</sub> (Gap 2)** → Time between DNA replication and mitosis.

**M** → Mitosis

**G<sub>0</sub>** → Optional "resting" phase.

    Early embryonic cells (no G<sub>0</sub>)

    Differentiated cells (continuous G<sub>0</sub>)

    Stem cells (fluctuate between G<sub>0</sub> and the cell division cycle)

Rates of cell division are regulated to ensure sufficient cells to replace dying ones, and to prevent production of excess cells.

### **How does the cell “know” when to divide?**

Progression of one stage of the cell cycle to the next depends on protein complexes consisting of a **cyclin** and a **cyclin-dependent protein kinase (CDK)**.

Protein kinases phosphorylate specific proteins.

Cyclins only expressed at specific cell cycle stages.

(Figure 17-2)

Cyclins tether the CDK to a specific target protein so that the target protein can be phosphorylated, thereby changing the activity of the target protein.

(Figure 17-3)

The timing of gene expression of different cyclins results in phosphorylation of different target proteins at different times.

Phosphorylation of the target initiates a chain of events leading to the activation of transcription factors that promote transcription of genes required for the next stage of the cell cycle.

Sequential activation of different CDK-cyclins leads to sequential activation of transcription factors and, in turn, progression of the cell cycle.

Various checkpoints serve as monitors of the status of DNA replication, spindle apparatus formation, etc.

**CDK-cyclin-binding proteins** inhibit the kinase activity of the CDK until the cell is ready to progress into the next stage of the cell cycle.

### **G<sub>1</sub> to S Transition Checkpoint**

(Figures 17-4 and 17-5)

**E2F** is a transcription factor that turns on genes encoding enzymes for DNA synthesis (i.e., replication).

**Rb** (retinoblastoma) protein binds to and inhibits E2F function.

cyclin A-Cdk2 complex phosphorylates Rb (i.e., Rb is the target protein).

Phosphorylated Rb can't bind to E2F.

p21 is the cyclin A-Cdk2 binding protein, which prevents Rb phosphorylation.

p53 activate p21 expression in the presence of DNA damage.

Thus, enzymes for DNA synthesis are not turned on until the DNA damage is repaired.

The key is the negative regulators that inhibit the kinase activity of the CDK-cyclin complexes.

(e.g., p21 in the example above)

## **Apoptosis (Programmed Cell Death)**

Elimination of damaged (potentially harmful) cells through a self-destruct and disposal mechanism.

Activation of the self-destruct mechanism leads to fragmentation of the chromosomes, disruption of organelle structure, and loss of normal cell shape.

Eventually the cells are fragmented and eaten by scavenger cells.

(Figure 17-6)

**Caspases** → The engines of self-destruction.

A group of enzymes that cleave other proteins (proteases).

In normal cells, each **executioner caspase** is present in an inactive state called the **zymogen** form.

The zymogen is converted to an active caspase by proteolytic removal of a portion of the polypeptide.

(Figure 17-7)

The active caspase then cleaves its target proteins.

Target proteins may include:

1. Other zymogens
2. A protein responsible for inactivating a DNA endonuclease.  
Leads to activation of the endonuclease and chromosomal fragmentation.
3. Actin (a component of the cytoskeleton)-leads to abnormal cell shape.
4. others

In addition to its role in cell cycle control, p53 is an activator of apoptosis.

Thus, p53 function is critical in controlling cell number and the elimination of abnormal cells.

## **Chapter 17 → Genetic Regulation of Cell Number: Normal and Cancer Cells (11-28-05)**

### **Intercellular Communication**

Cells communicate with each other via signal transduction pathways.

### **Signal Transduction**

A small molecule (ligand) is released from one cell and interacts with a membrane bound receptor of another cell.

(Figure 17-11)

Ligand bound receptors dimerize.

Dimerized receptors autophosphorylate the cytoplasmic domain.

The phosphate is then transferred to another protein in the signaling pathway.

Often the next step in propagating the signal is to activate a G-protein

(Figure 17-12).

G-proteins cycle between GDP bound (inactive) and GTP bound (active) forms.

The active G-protein eventually leads to phosphorylation of transcription factors, and thereby changes in gene expression.

(Often occurs through phosphorylated intermediates)

(Figure 17-13)

## **CANCER**

Cancerous cells are uncoupled from the regulatory mechanisms that keep cell proliferation in check.

Caused by multiple mutations in a single cell that causes it to:

- 1) Proliferate out of control.
- 2) Decrease the susceptibility to apoptosis.
- 3) Increase the general mutation rate of the cell so that proliferation or apoptotic mutation is more likely to occur.

Some of these mutations are inherited, while others originate in the somatic cell lineage.

### **Dominant Oncogene Mutations**

Mutations resulting in proteins that are activated when they shouldn't be.

Typically these proteins are components of intracellular communication pathways such that the cell always behaves as if it is receiving a signal to proliferate. (e.g., Ras) (Figure 17-16)

Ras (G-protein) mutations result in Ras always being in the GTP bound (active) form. Results in the continuous propagation of the signal that promotes cell proliferation.

### **Recessive Tumor Suppressor Genes**

Mutations in genes whose proteins normally contribute to the inhibition of cell proliferation.

- A. Proteins involved in inhibiting progression of the cell cycle (i.e., inhibitor protein is inactive).
- B. Proteins involved in the repair of DNA damage (e.g., p53).
- C. Proteins that promote apoptosis (e.g., p53).

p53 is a DNA-binding regulatory protein that is activated by DNA damage.

p53 prevents progression of the cell cycle until the DNA is repaired.

(Figure 17-5).

If p53 is non-functional, cell division proceeds in the absence of DNA repair, which leads to the accumulation of additional mutations.

This increases the chance of mutations in other genes involved in controlling the cell cycle and/or apoptosis leading to uncontrolled cell growth and cancer.

**p53 is non-functional in more than 50% of human cancers!!**

## **Xeroderma Pigmentosum**

Autosomal recessive predisposition to skin cancer caused by a mutation in a gene involved in repairing UV damaged DNA.

## **Retinoblastoma (Retinal cancer)**

(Figure 17-20)

### **A. Hereditary Predisposition (Family history)**

- 1) Inherited as RB rb (recessive).
- 2) rb rb is generated by rare mitotic X-overs.

Two eyes are often affected because only one mitotic X-over is required in each retina.

### **B. Sporadic (No previous family history)**

- 1) Inherited as RB RB
- 2) RB rb is generated from a new somatic mutation.
- 3) rb rb is then generated by a rare mitotic X-overs.

Only one eye affected.

Two affected eyes would require two independent mutations (one in each eye).

**Chapter 18→The Genetic Basis of Development (11-30-05)**      **(Problems 15, 16, 23)**

**DEVELOPMENTAL BIOLOGY**

The study of the events that occur during the transfiguration of a single cell (fertilized egg) to an adult organism that is composed of thousands, millions or trillions of cells organized into tissues and organs.

**Cell determination**

Cells adopt specific fates or the capacity to differentiate into specific types of cells (gradual process).

Periodic decisions are made in each cell lineage to more exactly specify the fates of the daughter cells.

In general, the same basic sets of regulatory proteins govern the major developmental events in many, if not all, higher animals.

Many highly differentiated organisms can regenerate new organs and tissues.  
(e.g., starfish arms, damaged human liver, gecko tails).

**PATTERN FORMATION**

Establishing the body plan.

**Role of the Cytoskeleton in Pattern Formation**

In addition to their role in determining cell shape, **Microtubules** and **Microfilaments** serve as molecular highways in the cell.

Proteins, and vesicles are transported throughout the cell by molecular motors.  
(e.g., kinesin and microtubules)      (Figure 18-5)

Proteins are targeted to various geographic regions within a cell because they contain a "molecular address".

Localization of RNA to geographic regions can occur via interaction with a protein that is already localized to its address.

The cytoskeleton plays a critical role in early pattern formation of developing animals.

*C. elegans* → nematode (roundworm)

The adult nematode is composed of only a few thousand cells.

The cell lineage has been traced from fertilized egg to adult.

(Figure 18-6)

P granules become restricted to one side of the egg upon fertilization and give rise to the germ line of the worm (gamete producing cells).

Early cell divisions are asymmetric giving rise to two distinct cells.

The dorsal-ventral (top-bottom) (D/V) and anterior-posterior (head-tail) (A/P) axes of the nematode are established very early during development.

Cell position is also important because neighboring cells communicate to each other via signal transduction.

The potential fate of a cell becomes progressively restricted as cell divisions continue.

## **DROSOPHILA**

### **A. Oogenesis**

Generation of the egg cell.

Stem cell → primary oocyte → 16 cells, one of which becomes the oocyte itself.

The other 15 cells are nurse cells that dump their cytoplasmic contents into the oocyte.

Polar granules (RNA & protein) form at the posterior pole of the oocyte (tethered by the cytoskeleton).

Nuclear division without complete cell division forms a syncytium.

Pole cells form at the posterior end, which form the entire germ line of the fly.

(Figure 18-7)

The other cells in the syncytium give rise to the soma (all other cell types).

## **B. Formation of the Body Plan**

The *Drosophila* larva is highly differentiated along the A/P & D/V axes.

(Figure 18-8)

### **Segmentation Pattern**

~10 hrs after fertilization 14 body segments are formed along the A/P axis.

(3 head, 3 thoracic, 8 abdominal)

Each segment gives rise to body parts of the adult.

### **How are segmentation patterns established?**

The egg contributes localized gene products that establish polarity along the A/P & D/V axes, which ultimately determines cell fates.

Cell fate is determined during development by the selective local activation of a set of master regulatory proteins due to the concentration gradient of localized determinants (RNA & protein) established in the egg (Maternal-effect genes).

## **Chapter 18 → The Genetic Basis of Development (12-2-05)**

### **A/P Concentration Gradients**

Concentration gradients of the maternal-effect proteins are established while the soma nuclei are part of the syncytium (one common cytoplasm).

(Figure 18-9)

#### **BCD (bicoid)** (A maternal-effect gene)

bcd mRNA is localized to the anterior pole of the embryo by association with microtubules.

Following translation, BCD protein diffuses forming a concentration gradient from anterior to posterior.

BCD is a transcription factor that is directed to the nuclei.

Nuclei closest to the anterior pole have the highest BCD concentration

#### **NOS (nanos)** (A maternal-effect gene)

nos mRNA is localized to the posterior tip of the embryo by association with microtubules.

Following translation, NOS protein diffuses forming a concentration gradient from posterior to anterior.

NOS protein is a translational repressor of hb-m mRNA.

#### **HB-M (hunchback)** (A maternal-effect gene)

Hb-m mRNA is uniformly distributed throughout the embryo.

NOS represses translation of hb-m mRNA.

Thus, HB-M is most highly expressed in the anterior pole.

HB-M protein is also a transcription factor and is directed to the nuclei such that the concentration is highest at the anterior pole.

Similar gradients define the D/V axis.

Gradients of protein products establish **polarity** (different geographic positions) along the A/P & D/V axes of the Drosophila embryo.

## **Hierarchy of Gene Expression**

As development continues a hierarchy of gene expression establishes the number of body segments, then subsegments, then segment identity, etc...

## **Segmentation Pattern**

BCD and HB-M are transcriptional regulatory proteins that activate and/or repress a set of genes called **cardinal genes** (also called **gap genes**).

## **Gap Genes** (Figure 18-23a)

### **kr (kruppel)**

Repressed by high [BCD] but activated by low [BCD] and low [HB-M].

### **kni (knirps)**

Activated by low [HB-M] and repressed by BCD.

Thus, kni is expressed more posteriorly than kr.

This differential gene expression is caused by BCD and HB-M concentration gradients that was originally established in the syncytium.

Gap genes encode the next layer of regulatory proteins (transcription factors).

Cellularization of the syncytium at this point traps the transcription factors in the resulting cells at various concentrations depending on their geographic location. (Figure 18-20)

**Gap genes** regulate expression of the **pair-rule genes**. (Figure 18-23b)

Pair-rule genes encode transcription factors that regulate expression of **segment-polarity genes**.

Some of the segment-polarity genes also encode regulatory proteins while others encode different classes of proteins.

BCD and HB-M--->gap--->pair-rule--->segment-polarity.

## **Segment Identity**

Parallel cascades establish segment identity.

## **Homeotic Genes**

Mutations in homeotic genes change the segmental identity into that of another.

(i.e., same number of segments but a duplication of one segment with another segment missing).

All homeotic genes encode transcription factors.

Gap gene proteins activate homeotic genes.

Thus, the number and identity of segments are determined in the early embryo.

(Figure 18-26)

The **antp** mutation (**antennapedia**) results in legs instead of antenna in the head.

(Chapter 18-cover figure)

Legs are the default.

Antp is required for antenna formation.

Another mutation doubles the number of wings (bithorax).

(Figure 18-25a-c)

Wings are the default and the Bithorax complex is required for haltere formation.

(Transparency figures of Drosophila mutants)

## **Applications to Higher Animals**

Homeotic (segment identity) genes exist in humans and mice, etc... (i.e.) homologous genes

Developmental strategies in animals are ancient.

Animals as divergent as Drosophila and humans develop using the same regulatory switches.

**Chapter 19 → Population Genetics (12-5-05) (Problems 1, 2, 3)**

Organisms don't live as isolated individuals; they live in populations.

Population genetics tries to understand the genetic composition of a population and the forces that determine and change that composition.

Genetic variation within and between populations arises from the existence of various alleles at different genetic loci.

Population geneticists want to determine the allele frequency at any given gene locus.

The allele frequency in a population can be changed by mutation, natural selection, migration, nonrandom mating, and genetic drift.

**Allele Frequency**

Frequency Distribution of a Genotype

(e.g., MN blood types) (Table 19-1)

More typically the allele frequencies are used.

Determine the **allele frequency** by counting the homozygotes and half the heterozygotes.

$$A/A = 0.36; A/a = 0.48, a/a = 0.16$$

$$\text{Allele frequency of A} = 0.36 + 0.24 = 0.60$$

$$p + q = 1$$

$$\text{If } p(A) = 0.60, \text{ then } q(a) = 1 - 0.60 = 0.40$$

## **Polymorphism**

The occurrence in a population of several phenotypic forms associated with alleles of a particular gene.

### **A. Morphologic Variation**

Can easily see with the naked eye.

Doesn't tell you anything about what is actually changed.

(Figure 24-1 7<sup>th</sup> edition)

### **B. Protein Polymorphism**

#### **1. Immunologic polymorphism**

ABO Blood groups

(Table 19-2)

#### **2. Amino acid sequence polymorphism**

(e.g., change in number of charged amino acids)

Only detects a few of the total number of changes.

Only examines protein-coding sequences.

(Figures 19-2, 19-3)

### **C. DNA Sequence Polymorphism**

#### **1. RFLP Mapping**

Only detects some of the changes.

Don't know where they are located.

Green sea turtle RFLP study.

#### **2. Complete Sequence**

Detects all of the changes, including regulatory changes.

## Hardy-Weinberg Equilibrium

A/A A/a a/a

$$p^2 + 2pq + q^2 = 1$$

Random mating results in an equilibrium distribution of genotypes after only one generation.

Sexual reproduction does not cause a reduction in genetic variation.

Genetic variation is maintained.

	<u>f (A/A)</u>	<u>f (A/a)</u>	<u>f (a/a)</u>
1	0.3	0.0	0.7
2	0.2	0.2	0.6
3	0.1	0.4	0.5

$$1 \quad p = f(A/A) + 1/2 f(A/a) = 0.3 + 1/2(0) = 0.3 + 0.0 = 0.3$$

$$2 \quad p = 0.2 + 1/2 (0.2) = 0.2 + 0.1 = 0.3$$

$$3 \quad p = 0.1 + 1/2 (0.4) = 0.1 + 0.2 = 0.3$$

In each case:  $q = 1 - p = 0.7$

Despite the different genotypic compositions, they all have the same allele frequency.

After one generation of random mating, each of the 3 populations will have the same genotypic frequency.

<b>A/A</b>	<b>A/a</b>	<b>a/a</b>
<b><math>(0.3)^2 = 0.09</math></b>	<b><math>2(0.3)(0.7) = 0.42</math></b>	<b><math>(0.7)^2 = 0.49</math></b>

They will remain identical through each generation unless something perturbs the equilibrium.

## Heterozygosity

The total frequency of heterozygotes for a given gene.

Heterozygosity can be calculated using the Hardy-Weinberg equilibrium (**2pq**).

Heterozygosity is greatest when several alleles of a gene exist in equal frequency.

(Figure 19-6)

## **Chapter 19→Population Genetics (12-7-05)**

### **Sources of Variation**

Evolution is dependent on renewed variation.

#### **A. Mutation**

Mutation rates are very slow and they take an extremely long time to be fixed into the population.

#### **B. Recombination**

The generation of recombinants via intrachromosomal recombination (X-overs) contributes to variation.

Requires preexisting mutations.

#### **C. Immigration**

Migration of genes into a population from another population.

Requires preexisting mutations.

The ultimate source must be mutation.

### **Non-random Mating**

Hardy-Weinberg assumes random mating but this is not always the case.

#### **A. Inbreeding**

When mating between relatives is more common than what would occur purely by chance.

#### **B. Outbreeding**

When mating between relatives is less common than what would occur purely by chance.

#### **C. Positive Assortative Mating**

A bias towards mating because of a resemblance caused by a particular locus.

#### **D. Negative assortative mating**

Mating with unlike partners.

Inbreeding and positive assortative mating lead to decreased heterozygosity.

Outbreeding and negative assortative mating lead to increased heterozygosity.

## **SELECTION**

Differential rates of survival and reproduction of particular genotypes (Natural Selection).

### **Darwinian Fitness**

Relative probability of survival and rate of reproduction of a phenotype or genotype.

Fitness is a consequence of the interaction of the phenotype with its environment.

The fitness of a particular phenotype (genotype) will differ in different environments.

### **Frequency Independent Selection**

The fitness of the individual does not depend on the composition of the population.

No competition.

(e.g., plants in a desert depend on depth of roots to obtain water)

### **Frequency Dependent Selection**

The fitness of the individual depends on the composition of the population.

Competition!

(e.g., carnivores)

The allele with the highest average fitness increases in the population.

### **Random Genetic Drift**

All populations are finite in size.

If two parents only have a small number of offspring, even in the absence of selective forces, the frequency of a gene will not be exactly reproduced in the next generation (sampling error).

New mutations can be fixed even if they are not favored by natural selection due to random genetic drift.

New favorable mutations can also be lost.

### **Founder effect**

Occurs when a small group breaks off from a larger population to found a new colony.

Probably responsible for the virtual lack of blood type B in Native Americans.

## **Chapter 21→Evolutionary Genetics (No Problems)**

### **Darwin's Theory of Evolution**

1. Populations of a given species includes individuals with varying characteristics (i.e., different phenotypes and genotypes)
2. The population of the next generation will contain a higher frequency of those types that are most successful at surviving and reproducing. (i.e., natural selection)
3. The frequencies of the various types within the species will change over time.

(Figure 21-2)

99.9% of all species that ever existed are extinct.

Yet, the number of species has increased during the past billion years.

Thus, evolution gives rise to new species.

### **Darwin's Finches in the Galapagos Islands**

13 different finch species with variation in form and function.

(Figure 21-4)

Evolution occurs within populations and not between individuals.

(i.e., the gene pool)

## **Chapter 21 → Evolutionary Genetics (12-9-05)**

### **Species**

A group of organisms which are capable of exchanging genes within the group but are genetically unable to exchange genes in nature with other groups.

New species form as a result of geographic isolation.

(e.g., continental drift, different islands)

Populations that are geographically isolated will diverge from one another genetically as a consequence of:

- 1) unique mutations
- 2) natural selection
- 3) genetic drift

Migration interferes with evolution.

In the absence of migration, genetic differences between populations become so great that the formation of hybrids becomes impossible.

These biologically isolated populations are new species.

### **Prezygotic Isolation**

The failure to form zygotes.

### **Postzygotic Isolation**

The failure of fertilized zygotes contribute gametes to future generations.

(e.g., sterility of the hybrids)

horse + donkey = sterile mule (horses and donkeys are different species)

## Origin of New Genes

Evolution consists of more than substitution of one allele for another.

In some cases, continuous transformation leads to new form and function without totally new genes.  
(e.g., development of the mammalian inner ear from reptilian jaw bones)

New genes and proteins are necessary in many instances.

(e.g., photosynthesis, hemoglobin, immune system)

## Where does the DNA for new genes come from?

### A. Polyploidy (Figure 21-9)

Duplication of the entire genome.

The duplicated genes can diverge and take on altered or new function.

Common occurrence in plants.

When  $n$  (haploid number)  $> 12$ , most plants have an even number of chromosomes.

### B. Duplications

Following duplication of a chromosome region,

the duplicated genes can diverge and take on altered or new function.

#### Human Hemoglobin

1) Adult hemoglobin ( $\alpha_2\beta_2$ )  $\rightarrow$   $\alpha$  and  $\beta$  are 50% identical.

$\alpha$  on chromosome 16,  $\beta$  on chromosome 11

2) Fetal hemoglobin ( $\alpha_2\gamma_2$ )  $\rightarrow$   $\gamma$  and  $\beta$  are 75% identical.

$\gamma$  and  $\beta$  are adjacent to one another on chromosome 11. (Figure 21-10)

From embryos to adults, the relative makeup of hemoglobin changes in the order of the genes on chromosomes 11 and 16. (Figure 21-11)

### C. Imported DNA

1) Mitochondria and chloroplasts

Bacterial engulfment  $\rightarrow$  symbiosis  $\rightarrow$  organelle

2) Horizontal transfer

Transposable elements and plasmids can transfer DNA from one species to another.

## **Molecular Evolution**

Mutations can have three consequences.

- 1) Decrease fitness
- 2) Increase fitness
- 3) No effect on fitness (neutral)

## **Molecular Clock**

Evolution of a gene proceeds according to a molecular clock that is dictated by the mutation frequency.

Synonymous substitutions occur at a faster rate than non-synonymous substitutions.

(Figure 21-13)

Different proteins have different molecular clocks.

(Figure 21-14)

## **Common Ancestry in Evolution**

All organisms are descended from a single common ancestor.

(Figure 21-15)