Phenotypic Expression & Multi-Factorial Traits (Learning Objectives)

• Understand and explain the factors affecting the phenotypic expression of Mendelian inheritance and provide examples for each: a) Lethal alleles, b) Incomplete dominance, c) Multiple alleles- codominance, d) Influence of other genes- Epistasis, e) Pleiotropy, f) Genetic heterogeneity, g) Polygenic inheritance, h) Phenocopy

• Explain the multi-factorial or complex interaction between genes and the environment affecting the manifestation of inherited monogenic and polygenic traits.

• Understand “linkage” as an factor that affects Mendelian ratios
Factors Affecting Phenotypic Expression of Mendelian inherited characteristics

• Most genes do not exhibit simple inheritance
• Genotypic ratios persist but phenotypic ratios may be influenced by other factors:
  1. Lethal alleles
  2. Incomplete dominance
  3. Multiple alleles- co-dominance
  4. Influence of other genes- Epistasis
  5. Pleiotropy
  6. Genetic heterogeneity
  7. Polygenic inheritance
  8. Phenocopy
Lethal Alleles

A lethal genotype causes death before the individual can reproduce

A double dose of a dominant allele may be lethal

- Achondroplastic dwarfism
- Mexican hairless dogs

(Dominant trait, homozygous dominant genotype is lethal)
Incomplete Dominance

The heterozygous phenotype is between those of the two homozygous ones.

Genotypic ratio same as phenotypic ratio.
Incomplete dominance affects severity of disease
Example: Familial hypercholesterolemia (FH)

Genotypes:

- **HH**: Homozygous for ability to make LDL receptors
- **Hh**: Heterozygous
- **hh**: Homozygous for inability to make LDL receptors

Phenotypes:

- Normal
- Mild disease
- Severe disease
Familial hypercholesterolemia (FH)

Figure 5.2

Multiple Alleles

• An individual carries two alleles for each autosomal gene
• A gene can have multiple alleles in the population caused by different mutations
• Different allele combinations can produce variations in the phenotype
  - PKU gene has hundreds of alleles resulting in four basic phenotypes www.ygyh.org
  - CF gene has over 1500 alleles
Co-dominance

The heterozygous phenotype results from the expression of both alleles.

The human ABO blood system: an example of multiple alleles & co-dominance.
Multiple alleles of the ABO blood system
- Three alleles, $I^A$, $I^B$, and $I$.  
  Both the $I^A$ and $I^B$ alleles are dominant to the $i$ 
  allele 
  The $I^A$ and $I^B$ alleles are co-dominant to each 
  other.

- Because each individual carries two alleles, there are six possible genotypes and four 
  possible blood types.
Epistasis

The phenomenon where one gene affects the expression of a second gene

Example: **Bombay phenotype**
- The $H$ gene is epistatic to the $I$ gene
- $H$ protein places a molecule at the cell surface to which the A or B antigens are attached
- $hh$ genotype = no $H$ protein
- Without $H$ protein the A or B antigens can not be attached to the surface of the RBC
- All $hh$ genotypes have the phenotype of type O, although the ABO blood group can be anything (A, B, AB, or O)
Pleiotropy

- One gene controls several functions or has more than one effect (Heme synthesis defect)

Porphyria variegata
- Symptoms including reddish teeth and photosensitivity, may have inspired the vampire and werewolf legends

Sickle cell Disease
http://www.ygyh.org/
Genetic Heterogeneity

Different genes can produce identical phenotypes

- Hearing loss – 132 autosomal recessive forms
- Osteogenesis imperfecta – At least two different genes involved
- Alzheimer disease – At least four different genes involved

Genes may encode enzymes that catalyze the same biochemical pathway, or different proteins that are part of the pathway
Polygenic Traits

- Individual genes follow Mendel’s laws, but their expression is hard to predict.
- Effect of genes is additive or synergistic.
  - However, input of genes is not necessarily identical.
- The frequency of distribution of phenotypes forms a bell-shaped curve!

Examples: Height and skin color.
Height

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a.

b.

Figure 7.3

Polygenic inheritance

Quantitative characters show additive effect of multiple genes, e.g. skin color and height in humans.
Phenocopy

A trait that appears inherited but is caused by the environment, symptoms resemble an inherited trait or occur within families

Examples:
- Exposure to teratogens
  Thalidomide causes limb defects similar to inherited phocomelia

- Infection
  AIDS virus can be passed from mother to child, looking like it is inherited
Environmental Effects

Phenotype of Hydrangea flower color

- Blue flowers in highly acid soil
- Pink flowers in neutral or slightly acid soil
Genes, Environment and Traits

Few, if any, genes act alone

Environmental factors and other genes may modify expression

Traits can be described as

- **Mendelian** = Caused by a single gene
- **Polygenic** = Caused by multiple genes

Both can be **multifactorial** or complex due to an interaction between genes and the environment
Genes, Environment and Traits

Figure 7.1

Penetrance

Frequency

Rare, single-gene disorder
Krabbe disease
1/100,000 births

Not-as-rare, single-gene disorder
Cystic fibrosis
1/3,000 births

Common SNPs, each contribute small amount of risk
Hypertension
Heart disease
Osteoporosis
Diabetes

Environmental influences
Modifier genes
Disease genotype
Linkage

Genes that are close on the same chromosome are said to be **linked**

Linked genes do not assort independently in meiosis - usually inherited together when the chromosome is packaged into a gamete

- do not produce typical Mendelian ratios
Figure 5.15

Linkage versus Non-linkage

Linked Genes

A A
B B
a a

B b

Crossing over

Meiosis

A a
B b

Parental allele configuration

Recombinant allele configuration (may approach 50%)

Nonlinked Genes

A A
B B
a a

b b

Independent assortment

Meiosis

A B
a b

Parental allele configuration

Recombinant allele configuration
Crossing Over Disrupts Linkage

Figure 5.12

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