Classical Genetics Principles

BIT 220

Chapters 4-7, part of 9
End of chapter 3

• P. 63-end - Mendel and Human Genetics
• Pedigree analysis - diagrams that show the relationships - Figure 3.13/3.15
• Pedigree conventions- squares for male, circles for female; different colors with individual who express the trait
Chapter 4 - Extensions of Mendelism

- **Figure 4.1** - Incomplete or Partially dominant (note in this figure new designation) - can also be called semidominant

- different amounts of gene product produced
Multiple Alleles

- antigen reacts with serum blood factors
- Table 4.1 (p. 75)- ABO blood typing system
- Alleles (alternate forms of the same gene) listed as $I^A$, $I^B$, or $ii$
- can have A, B, AB, and O
- A and B said to be codominant - both expressed.
Allelic Series

• **Figure 4.4** - coat colors in animals
• many alleles involved- by making heterozygotes, dominance relationships can be determined
• See **Figure 4.3** for color descriptions
• Wild-type allele completely dominant over all other alleles
• $c^+ > c^{ch} > c^h > c$ : shows effect on coat color
Testing Mutations for Allelism

- Mutant allele - created when existing allele changes to a new genetic state
- always different genetic composition; may be different phenotype
- Can test mutation if recessive - Figure 4.5 - much like the complementation test - applies more to higher organisms (complementation in bacteria)
Allelism

• Another example Figure 4.6 - *Drosophila*

• *cinnabar & scarlet* (eye color)

• cross homozygous mutant strains with each other

• shows allelism many more than one eye color gene involved
Types of Mutations

• Visible- change appearance of organism usually recessive
• Sterile - limit reproduction - recessive or dominant, affect males and females
• Lethal - kill organism - interfere with a vital function; Dominant disappears after one generation; recessives show up normal frequency - Figure 4.7 - dominant visible and recessive lethal
Why Dominant or Recessive?

- Recessive: loss-of-function - affect only homozygotes
- Dominant - affect both heterozygotes and homozygotes - dominant-negative or gain-of-function
- Explained in Figure 4.9
From Genotype to Phenotype

- Environmental effects - diet and PKU - babies tested early so low phenylalanine diet = normal development

- Pattern baldness - testosterone levels equate with more hair loss (why worse in men than women)
Penetrance and Expressivity

- Incomplete penetrance - mutation does not show appropriate phenotype even though genetic mutation is present
- Example is Figure 4.11
- Expressivity - variable phenotype among individual with same genotype - Figure 14.12 - Dominant Lobe mutation in Drosophila
Gene Interactions

• Traits can be influenced by more than one gene

• Punnett square Figures 4.14 and Figure 4.13 - comb shapes in chickens - crosses between rose and pea produce another type, called walnut - 2 independently assorting genes, each with 2 alleles
Epistasis

• Two or more genes influence a trait
• An allele of one has overriding effect on phenotype - it is epistatic to other genes involved in the trait (Greek work to “stand above”)
• Conceals the presence of another mutation in the same gene

• Example Figure 14.15 - *Lathyrus odoratus* (sweet pea)
Pleiotropy

• Gene affects many phenotypes
• Greek “to take many turns”
• PKU - mutation also interferes with melanin synthesis (color pigment)
• PKU sufferers have light hair
• Blood and urine of PKU sufferers additional compounds absent in non-PKU individuals
Chapter 5 - Inheritance of Complex Traits

• Not covering much of this chapter
• Know pages 90-92
• Quantitative traits - accumulation of many genes that influence a trait - example is Figure 5.1 - 3 genes with independent assortment and incomplete dominance accounts for kernel color variation
• Table 5.4, page 105
Effects of Inbreeding

• Pages 105 - 107
• Consanguineous (Latin for “same blood”) mating - mating between relatives
• Pedigree Figure 5.9, page 106 - all homozygous albino individuals from consanguineous matings
• Amish, Mormon, French Canadians, Royalty
Chapter 6 Chromosomal Basis of Mendelism

• Chromosomes - light and dark regions when stained - euchromatin (light), heterochromatin (dark)

• Number - Table 6.1, varies among species

• Number:
  – haploid - n (usually 1/2 the full complement)
  – diploid - 2n
  – tetraploid - 4n, etc.
Sex Chromosomes

- X - females - XX
- Y - male - XY
- Sex chromosomes and autosomes
Chromosomes

- Arrays of genes - Figure 6.5
- Morgan and colleagues - *Drosophila*
- Locus (loci) - where a gene is located on a chromosome
- produced map like one in figure for genetic loci
- Chromosome theory (heredity) proved by non-disjunction - Figure 6.6
Mendel’s Laws

• Segregation - Figure 6.7 - based on separation of chromosomes during anaphase (first meiotic division)

• Independent Assortment - Figure 6.8 - random alignment of different pairs of chromosomes at metaphase (genes on same chromosome linked, so don’t assort independently)
Sex-Linkage in Humans

- Male needs only one recessive gene to express phenotype; female needs 2
- Hemophilia, color blindness, examples of sex-linkage
- Figure 6.9 - shows pedigree of Czar Nicholas II - only males have the disease; females are carriers
- Figure 6.10 shows color blindness
Fragile X syndrome

- Causes mental retardation - appears to follow an X-linked inheritance
- Abnormality at tip of X chromosome - looks like tip is ready to detach (chromosome doesn’t really brake)
- 1/2000 incidence; expansion of repeats
- Incomplete penetrance - Figure 6.11
- No treatment currently (diagnostic test)
Sex Determination in Humans

- Absence of Y chromosome = female
- XO and XXX are females
- XXY are males
- product of SRY (sex-determining region Y) gene - testis determining factor (TDF) - found on short arm of Y chromosome

- Figure 6.12
Sex Determination in *Drosophila*

- Y chromosome no role in sex determination
- Sex determined by ratio of X chromosomes to autosomes
- Flies have XX or XY; 3 pairs of autosomes (3 pairs considered 1 set) A considered one haploid set – Table 6.2, page 128
- When X’s to A’s is ≥ 1, fly is female
- X to A is ≤ 0.5, fly is male
- between 0.5 and 1 is both sexes
Dosage Compensation of X-Linked Genes

- In *Drosophila*, increase of activity of X-chromosome genes in males (hyperactivation)
- In placental mammals, X-linked genes are inactivated on one of the X chromosomes (inactivation); Reactivated during oogenesis (Figure 6.18)
- Inactivated X does not look or behave like a normal X – Barr body (Murray Barr)
Chapter 7 Variation in Chromosome Number & Structure

- Cytological staining – stains to reveal chromosome banding
- Cytogenesis – analysis of stained chromosomes
- Compound with insertional power – intercalating agent (Ethidium bromide in DNA, Quinacrine, chromosomes)
Banding patterns

- Stained chromosomes light and dark bands
- Q banding - Quinacrine
- G banding – Giemsa
- R banding – R banding – opposite of G
- C banding – stains region around centromere
Human Karyotype

- See Figure 7.4 and 7.5
- XY and 22 autosomes
- Can see gross abnormalities this way –
  - Down syndrome (extra chromosome 21)
  - Fragile X syndrome
  - *Cri-du-chat* – deletion in short arm of Chromosome 5 (cry of the cat) – **Figure 7.16**
  - Can look at rearrangements
Ploidy

- Greek word “fold”
- Changes in number of chromosome in cells
- Euploid – complete, normal set of chromosomes (humans diploid)
- Polyploid – organisms that are not diploid normally (triploids (3n), tetraploid (4n), etc. – more common in plants than animals
Aneuploidy

• A numerical change in part of the genome – change in dosage of a single chromosome
• E.g., Down syndrome, Trisomy 21 (3 copies of chromosome 21) – this called a trisomy
• Other examples:
  – 47, XXY (Klinefelter’s)
  – 47, X (Turner’s) – this one a monosomy
Other chromosome abnormalities

- Deletion - *Cri-du-chat* – short arm chromo 5
- Duplication – extra chromosome segment
- Inversions – Figure 7.19 – chromosome segments are flipped around
- Translocations – segment detached and reattaches to another chromosome (Figure 7.21)
- Reciprocal translocations – Figure 7.22
Chapter 9 – pages 188-196
Linkage analysis in Humans

- Knowledge of genes and their chromosomal location
- Knowledge of relationships from one gene to another
- Genes on X chromosome easiest to find - see inheritance pattern more clearly
- Sidelight – linkage between hemophilia and color blindness (page 189)