Extensions of Mendelian Genetics

(CHAPTER 4- Brooker Text)

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BIO 184
Dr. Tom Peavy

Lethal Alleles

- Essential genes are those that are absolutely required for survival
  - The absence of their protein product leads to a lethal phenotype
- Nonessential genes are those not absolutely required for survival
- A lethal allele is one that has the potential to cause the death of an organism
  - These alleles are typically the result of mutations in essential genes
  - They are usually inherited in a recessive manner

Some lethal alleles exert their effect later in life

=Late age of onset

e.g. Huntington disease (progressive degeneration of the nervous system, dementia and early death; onset between 30-50 yrs old

- Conditional lethal alleles may kill an organism only when certain environmental conditions prevail
  - Temperature-sensitive (*ts*) lethals
    - A developing *Drosophila* larva may be killed at 30 C
    - But it will survive if grown at 22 C
- Semilethal alleles
  - Kill some individuals in a population, not all of them
  - Environmental factors and other genes may help prevent the detrimental effects of semilethal genes

- In a simple dominant/recessive relationship, the recessive allele does not affect the phenotype of the heterozygote
  - So how can the wild-type phenotype of the heterozygote be explained?
- There are two possible explanations
  - 1. 50% of the normal protein is enough to accomplish the protein's cellular function
  - 2. The heterozygote may actually produce more than 50% of the functional protein
    - The normal gene is "up-regulated" to compensate for the lack of function of the defective allele

Figure 4.1

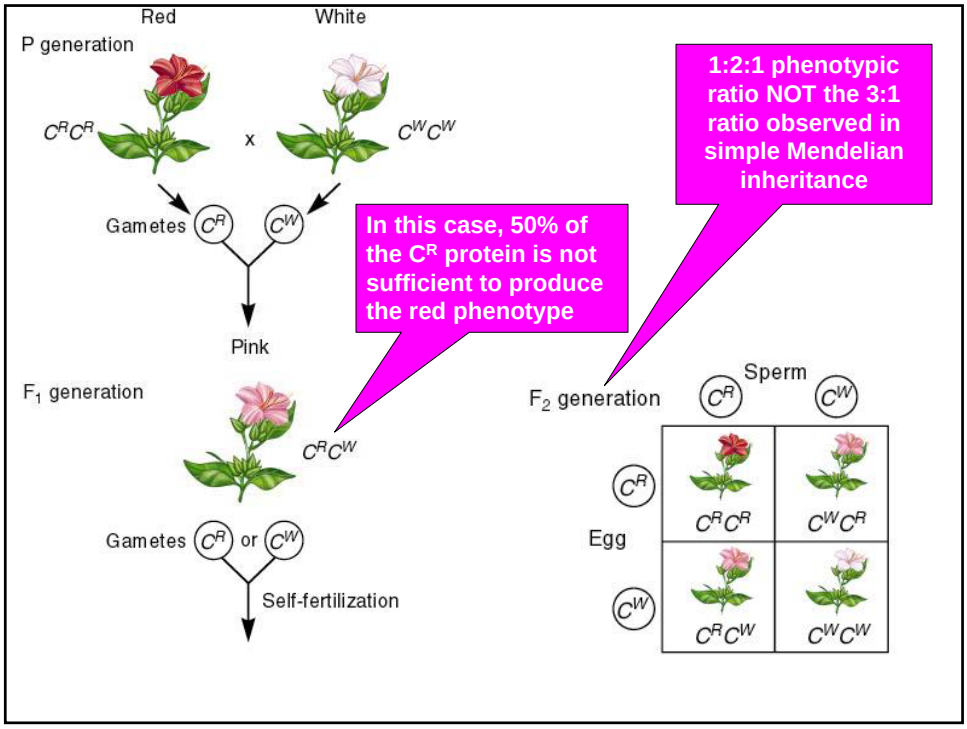
Normal allele: *P* (purple)
Recessive (defective) allele: *p* (white)

Genotype	*PP*	*Pp*	*pp*
Amount of functional protein P	100%	50%	0%
Phenotype	Purple	Purple	White
Simple dominant/ recessive relationship			

Incomplete Dominance

- In incomplete dominance the heterozygote exhibits a phenotype that is intermediate between the corresponding homozygotes

- Example:
  - Flower color in the four o'clock plant
  - Two alleles
    - C^R = wild-type allele for red flower color
    - C^W = allele for white flower color



Example of Lethalilty and Incomplete Dominance

Creeper chicken= shortened legs and creep along
this is a incomplete dominant trait
heterozygotes are Creeper individuals
but homozygote condition is lethal

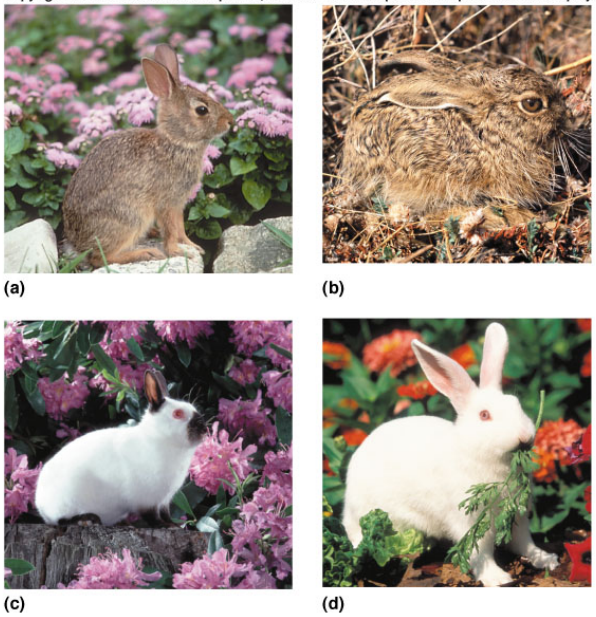
What are the phenotypic ratios of the following crosses?

Creeper x Normal

Creeper x Creeper

Multiple Alleles (3 or more alleles)

- An interesting example is coat color in rabbits
  - Four different alleles
    - *C* (full coat color)
    - c^{ch} (chinchilla pattern of coat color)
      - Partial defect in pigmentation
    - c^{h} (himalayan pattern of coat color)
      - Pigmentation in only certain parts of the body
    - *c* (albino)
      - Lack of pigmentation
  - The dominance hierarchy is as follows:
    - $C > c^{ch} > c^{h} > c$

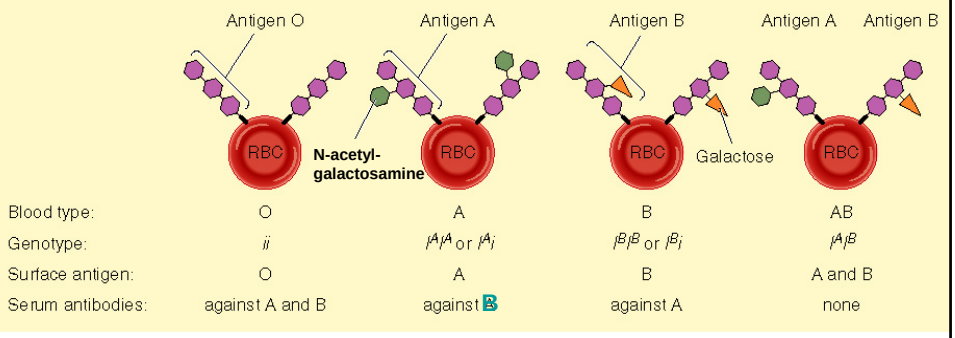


(a) (b) (c) (d)

- The himalayan pattern of coat color is an example of a temperature-sensitive conditional allele
  - The enzyme encoded by this gene is functional only at low temperatures
    - Therefore, dark fur will only occur in cooler areas of the body
    - This is also the case in the Siamese pattern of coat color in cats
    - Refer to Figures 4.4*c* and 4.5

- The ABO blood group provides another example of multiple alleles
- It is determined by the type of antigen present on the surface of red blood cells
  - Antigens are substances that are recognized by antibodies produced by the immune system
- There are three different types of antigens found on red blood (Table 4.3)
  - Antigen A, which is controlled by allele I^A
  - Antigen B, which is controlled by allele I^B
  - Antigen O, which is controlled by allele *i*

- Allele *i* is recessive to both I^A and I^B
- Alleles I^A and I^B are codominant
  - They are both expressed in a heterozygous individual



- For safe blood transfusions to occur, the donor's blood must be an appropriate match with the recipient's blood

- For example, if a type O individual received blood from a type A, type B or type AB blood
  - Antibodies in the recipient blood will react with antigens in the donated blood cells (= agglutination and clogging)

Overdominance

- Overdominance is the phenomenon in which a heterozygote is more vigorous than both of the corresponding homozygotes
  - It is also called heterozygote advantage

- Example = Sickle-cell anemia
  - Autosomal recessive disorder
  - Affected individuals produce abnormal form of hemoglobin
  - Two alleles
    - Hb^A → Encodes the normal hemoglobin, hemoglobin A
    - Hb^S → Encodes the abnormal hemoglobin, hemoglobin S

- Hb^SHb^S individuals have red blood cells that deform into a sickle shape under conditions of low oxygen tension
  - This has two major ramifications
    - 1. Sickling phenomenon greatly shortens the life span of the red blood cells
      - Anemia results
    - 2. Odd-shaped cells clump
      - Partial or complete blocks in capillary circulation
  - Thus, affected individuals tend to have a shorter life span than unaffected ones

- The sickle cell allele has been found at a fairly high frequency in parts of Africa where malaria is found
  - How come?
- Malaria is caused by a protozoan, *Plasmodium*
  - This parasite undergoes its life cycle in two main parts
    - One inside the *Anopheles* mosquito
    - The other inside red blood cells
  - Red blood cells of heterozygotes, are likely to rupture when infected by *Plasmodium sp*.
    - This prevents the propagation of the parasite
- Therefore, Hb^AHb^S individuals are "better" than
  - Hb^SHb^S, because they do not suffer from sickle cell anemia
  - Hb^AHb^A, because they are more resistant to malaria