Modification of Mendelian Ratios (chapter 4)

- Non-Mendelian genetic ratios
  - these ratios occur when alleles of one gene do not exhibit simple dominance and recessiveness
  - Mendels laws still govern the distribution of the alleles in the gametes
  - not all genes are simply dominate and recessive

- Different alleles of the same gene alter phenotypes in different ways
  - **wild-type allele**- so called "normal" version of the gene - very often is the dominant over alleles but not always
  - **loss-of-function** (or in extreme case **null**) allele is an allele causes a reduced function of the gene product
  - **gain of function alleles**- usually result from overexpression of a gene
  - **neutral mutations**- have changes that do NOT translate into any visible phenotypic difference
- Incomplete (Partial) Dominance
  - where a cross between parents with contrasting traits results in an offspring with and intermediate phenotype
    - ex) lower color in snapdragon
      - one functional gene does not give the full red color
      - note on genetic notation: different alleles can also be denoted by the letter with superscripts
      - R^1R^1 (red) x R^2R^2 (white) → R^1R^2 (pink) → R^1R^2 (pink) x R^1R^2 (pink) → R^1R^1 (red), R^1R^2 (pink), R^1R^2 (pink), R^2R^2 (white)
- QUESTION: what is the genotypic ratio of offspring if I cross a pea plant with red flowers to one with pink flowers? (use same notation as text) ANSWER: 1:1 $2R^1R^1$ and $2R^2R^2$
- QUESTION: what is the phenotypic ratio in the above cross ANSWER: 1:1 2red 2pink
- Co-Dominance
  - where two alleles of a single locus produce two full functional but distinct products
    - Ex) MN blood type
      - genotype: L^ML^M, L^ML^N, L^NL^N
      - phenotype: M,MN,N
  - At the molecular level these are two distinct glycoproteins (proteins with sugar side-groups)- there are different sugar side groups in each allele with both work well
  - there are NO side effects- unless one gets a blood transfusion ex LNLN individual receives LMLM blood and mounts an immune reaction against it
- Molecular basis of MN blood type
  - Image shows the primary structure of glycophorin A a glycoproteins that spans the plasma membrane of human red blood cells.
  - each RBC has 500,000 copies of the molecule
  - MN blood groups (>40 alleles)

- The M allele encodes Ser at position 1 (Ser-1) and Gly at position 5 (Gly-5) t
- The N allele encodes Leu-1 and Glu-5
- So they are slightly different proteins and the change in the amino acids makes them a look like a threat to the immune system

- QUESTION: A married couple that each have $L^M L^N$ have children. How many different blood types can their children have? ANSWER: 3 $L^M L^M$ $L^N L^N$ $L^M L^N$
- QUESTION: Can all their children donate blood to their parents: ANSWER: Yes because the parents are heterozygous so their immune system in used to the glycoprotein
- QUESTION: Can the parents donate blood to all the children? ANSWER: No only the heterozygous children
- Multiple Alleles
  - Where there are more than two alleles of a single locus produce two fully functional but distinct products
  - ex) ABO blood type
    - Genotype: $I^A I^A$, $I^A I^O$, $I^B I^B$, $I^B I^O$, $I^A I^B$, $I^O I^O$
    - antigen: A, A, B, B, A and B, none
    - phenotype: A, A, B, B, AB, O
  - at the molecular level these are sugars attached to lipids on the end blood cell membrane surface
  - an O phenotype can also occur in the rare instance where the precursor to the sugar is not made
- Molecular basis of ABO blood type
  - the A antigen and the B antigen are derived from a common precursor known as the H antigen (or H substance)
  - The H antigen is a glycosphingolipid (sphingolipid with carbohydrates linked with ceramide moiety)
  - The I gene encodes a glycosyltransferase- that is an enzyme that modifies the carbohydrate content of the RBC antigens
  - The gene is located on the long arm of the ninth chromosome
  - The IA allele gives type A, IB gives type B, and i (nonfunctional enzyme) gives I
- QUESTION: A married couple that are $I^A I^O$ and $I^B I^O$ have kids. How many of their offspring could be universal donors? ANSWER: you have kids that are $I^A I^B$, $I^B I^O$, $I^A I^O$, $I^O I^O$ only one child would be a universal donor ($I^O I^O$) and $I^A I^B$ can get blood from anyone
- QUEISON: what is the genotypic and phenotypic ratios? ANSWER: 1:1:1:1 because every child has a different combination
- Lethal Alleles
  - where a mutation results in a recessive lethal - one wild-type copy is enough but to copies of the mutant allele result in a premature death
    - ex) the agouti gene in mice
      - the agouti gene regulates hair color in mice the (wild-type mice are NOT black) normal A allele gives the agouti color
      - The A^Y allele called yellow is missing a regulatory part of a gene so the gene is always turned on leading to disruption of yellow pigment along the pari shaft (a gain of function mutation)

        - A^YA^Y homozygotes die early in development (before birth)
        - A^YA x A^YA instead of 1:2:1 gives a 2:1 ration the A^YA^Y are never born
        - AA (agouti) x AA (agouti) → AA (agouti) → all survive
        - AA^Y (yellow) x AA^Y (yellow) → AA (agouti) , AA^Y (yellow), A^YA (yellow) , A^YA^Y (lethal) → ⅔ yellow, ⅓ agouti
        - AA (agouti) x AA^Y (yellow) → AA (agouti) , AA^YA (yellow) → ½ agouti, ½ yellow
- QUESTION: Why do A^YA^Y mouse fetuses die before birth? ANSWER: The deletion that causes the yell mutation extends into the next (Merc) gene which is essential for embryonic development
- QUESTION: The rgh1-N1285 mutation of corn is embryo lethal. What is the genotypic ratio of viable offspring in a Rgh1rgh1 x Rgh1rgh1 cross? ANSWER: ¼ have lethal gene so 1:2 for the living
- Gene Interaction (Epistasis)
    - Epistasis is the greek work for "stoppage" and describes where the expression of one gene (or gene pair) can mask or modify the expression of another gene (or gene pair)
    - the presence of zz stops expression of YY
        - ex) X could encode a transcription factor necessary for expression of the Y gene
            - the Y gene is hypostatic to X
                - ex) Bombay Phenotype (hh) can affect AB blood type
                    - the presence of hh causes an A or B individual to show an O phenotype
                    - I^AI^B Hh x I^AI^B Hh gives a 3:6:3:4 modified ration
- Epistasis of locus over blood antigen locus
    - I^AI^B Hh x I^AI^B Hh
    - Consideration of blood types: I^AI^B x I^AI^B → I^AI^A , I^AI^B , I^BI^A , I^BI^B
    - consideration of H substance: Hh x Hh → HH, Hh, hH, hh
    - of all offspring
        - ¼ type A → ¾ for H substance and ¼ do not form H substance → 3/16 type A and 1/16 type O
        - 2/4 type AB → ¾ form H substance and ¼ do not form H substance → 6/16 type AB and 2/16 type O
        - ¼ type B → ¾ form H substance and ¼ do not form H substance → 3/16 type B and 1/16 type O
- QUESTION: You cross a striped corn mutant from mexico with another striped mutant from Peru. All the offspring are green. Are these mutation in the same gene? ANSWER: No
- X-Linkage
    - The Y-chromosome although acting as an homologous of the X-chromosome during meiosis contains only a few genes none of which are contained on the X-chromosome