Lecture 8 – Genetic analysis/Modifications to Mendelian ratios

I. Gene products may not act independently
   A. pleiotropy –
      eg. fly white gene

   B. many genes may affect single trait

   C. How can many genes affect one trait?

   - consider hypothetical pathway for red pigment production
     - many steps required to make product
     - each step catalyzed by different enzyme (1, 2, 3……)
     - so, often, many genes are required to synthesize a single product

II. Test for allelism
   Q. If many genes can contribute to single product, how do we know if 2 mutations causing same phenotype are in same gene?
   A. We use a simple genetic test, called a complementation test
      1. How does complementation test work?
         - What would happen if 1 copy of gene1 was defective?
           - haploinsufficient –

         - What would happen if both copies of gene1 were defective?

         - What would happen if one copy of gene1 and one copy of gene2 were defective?

   2. Complementation test example:
      a. Studying purple color formation in peas. Suppose you already have mutations in two genes, p and c, and you want to find more.

      b. Results: you find 4 new mutations, How do you know if they’re in new gene or in p, or in c?
         - answer:
c. complementation test to determine whether \( x_1, x_2, x_3 \) and \( x_4 \) are new mutations in \( P, C \) or in a new gene.

- typical complementation test results:

3. molecular basis of complementation test:
   a. if both copies of gene wild type
b. if one copy mutant, and second copy wild type

c. if both copies mutant

What if \( alb^+/alb^-; c^+/c^-? \)

What if \( alb^-/alb^-? \)

4. Another example: You isolate 6 new mutations in adenine biosynthetic pathway in yeast (i.e. mutants can’t synthesize adenine). You perform all possible pairwise crosses and obtain the results shown in the table.

Which mutations are allelic?

How many genes were identified in the screen?

5. How does multiple genes in pathway affect Mendelian ratios?

What color is \( c^+/c^-; p^+/p^-? \)

Cross \( c^+/c^-; p^+/p^- X c^+/c^-; p^+/p^- \)

II. Other factors that can influence Mendelian ratios

A. partial dominance

1. incomplete dominance (= semidominance)

eg. 1: snapdragon flower color

\[
\begin{array}{ccc}
Ii & X & Ii \\
\uparrow & & \downarrow \\
II & & WW \\
Ii & & Ww \\
i & & wW \\
\end{array}
\]

eg. 2: wrinkled pea seeds

\[
\begin{array}{ccc}
Ww & X & Ww \\
\uparrow & & \downarrow \\
WW & & WW \\
wW & & Ww \\
wW & & wW \\
wn & & wn \\
\end{array}
\]
2. codominance
e.g. human blood type

\[ I^A \text{ blood type } A \]
\[ I^B \text{ blood type } B \]
\[ I^A I^B \text{ blood type } AB \]
\[ I^O \text{ blood type } O \]

\[ I^A I^A \times I^O I^O \]
\[ I^A I^B \times I^B I^B \]

- may depend on trait being examined

<table>
<thead>
<tr>
<th></th>
<th>disease</th>
<th>blood</th>
<th>protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb^A/Hb^A</td>
<td>viable</td>
<td>not sicked</td>
<td>Hb^A made</td>
</tr>
<tr>
<td>Hb^A/Hb^B</td>
<td>viable</td>
<td>partly sicked</td>
<td>both Hb^A &amp; Hb^B</td>
</tr>
<tr>
<td>Hb^B/Hb^B</td>
<td>lethal</td>
<td>all sicked</td>
<td>Hb^B made</td>
</tr>
</tbody>
</table>

B. Multiple alleles of a gene
1. Different mutations may affect phenotype differently
2. Alleles often ranked in allelic series of increasing severity

**eg. rabbit coat color**

\[ \text{dom} C^+ \text{ brown} \]
\[ \text{dom} Cch \text{ chinchilla (gray)} \]
\[ \text{dom} ch \text{ Himalayan (white, black extremities)} \]
\[ \text{dom} C^- \text{ null (all white)} \]

How do we know they're allelic?

C. partial expressivity vs. incomplete penetrance
1. expressivity

2. penetrance
D. lethality

1. mouse *yellow* gene – causes lighter coat
   a. Yellow X wild type
   b. Yellow X Yellow
   c. *yellow* homozygotes die before birth

   - Is fur color dominant or recessive?
   - Is lethality dominant or recessive?

2. Manx cat
   a. Manx is tailless

   - Is tailless dominant or recessive?
   - Is lethality dominant or recessive?

3. most lethals are fully recessive