Lecture 4: Gene interactions

1. Multiple alleles
2. Codominance and incomplete dominance
3. Lethal alleles
4. Epistasis
5. Complementation
6. Penetrance and expressivity
7. Chi-square ($\chi^2$) analysis

$Y/-$: elimination of chlorophyll (no green color)
$y/y$: keeps chlorophyll (green color)
$R/-$: red, and $r/r$: yellow carotenoids
$c1$ and $c2$: lighter shadows of red or yellow
$R/-$: $y/y$: brown (red plus green)
Multiple alleles of the same gene

Wild-type gene \( (A) \)

Multiple allelic forms (mutants) of the wild-type gene \( (A) \)

- \( A_1 \)
- \( A_2 \)
- \( A_3 \)
- \( A_4 \)

Mutation site
## Codominance

### ABO Blood Groups in Humans, Determined by the Alleles $I^A$, $I^B$, and $i$

<table>
<thead>
<tr>
<th>Phenotype (Blood Group)</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>$i/i$</td>
</tr>
<tr>
<td>A</td>
<td>$I^A/I^A$ or $I^A/i$</td>
</tr>
<tr>
<td>B</td>
<td>$I^B/I^B$ or $I^B/i$</td>
</tr>
<tr>
<td>AB</td>
<td>$I^A/I^B$</td>
</tr>
</tbody>
</table>

- **A antigen**
- **B antigen**

Red blood cell

- Blood type A
- Blood type B
- Blood type AB
- Universal recipient
- Universal donor
P: \( I^A/I^A \) (blood group A) \( \times \) \( I^B/I^B \) (blood group B)

\[ F_1: \quad I^A / I^B \] (blood group AB \( \Rightarrow \) codominance)

\[ F_2: \quad \frac{1}{4} I^A/I^A \quad \frac{1}{2} I^A/I^B \quad \frac{1}{4} I^B/I^B \]

\[ 1 : 2 : 1 \]

The phenotype and the genotype ratios are the same (1:2:1) because heterozygotes show a distinct **codominant** phenotype.

Codominance – **both alleles** contribute to phenotype in a heterozygote.
Incomplete dominance

R / R
r / r
R / r

“4 o’clock” plant: flowers get open in the afternoon and close by morning
Incomplete dominance

P: \( R/R \) (red) x \( r/r \) (white)

\( F_1: \quad R / r \) (pink)

\( F_2: \quad \frac{1}{4} R/R \quad \frac{1}{2} R / r \quad \frac{1}{4} r/r \)

1 : 2 : 1

The phenotype and the genotype ratios are the same (1:2:1) and again heterozygotes show a distinct phenotype. But this time this is due to **incomplete dominance** – the dominant allele does not fully contribute to phenotype in a heterozygote (it is ‘weakened’ or ‘diluted’).
Lethal alleles

Parental yellow mice, NEVER true-breeding
Lethal alleles

Pleiotropy (multiple effects) of $A^\gamma$

This allele defines two different characters:

- yellow color ($A^\gamma$ is dominant to $A$ because $A^\gamma/A$ are yellow)
- lack of viability ($A^\gamma$ is recessive to $A$ because $A^\gamma/A$ are not dead)
Epistasis, recessive

Ability to make the pigment: 
C, full ability (full color) 
c, albino (no color)

Distribution of the pigment: 
$A^Y$ – no or inefficient distribution along the hair, yellow mice 
A – uneven, normal appearance mice (agouti) 
a – all over the hair, black mice

Recessive epistasis: 
two recessive alleles of the epistatic gene ($c/c$), when present, affect (prevent) expression of alleles of the hypostatic gene ($A$ or $a$)
Epistasis, dominant

Color of vegetables in squash
$Y$: yellow; $y$: green
$W$: no color (white); $w$: there is color (yellow or green)

P: $Y/Y; W/W$ (true breeding white) $\times$ $y/y; w/w$ (true breeding green)

$F_1$: $Y/y; W/w$ - all white

$F_1 \times F_1$: $W/w$ $Y/y$
white fruit $\times$ $W/w$ $Y/y$
white fruit

$F_2$ – how will it look like?
Epistasis, dominant

Dominant epistasis: a single dominant allele of the epistatic gene (W) is sufficient for the effect on Y or y

F₁ × F₁
W/w Y/y
white fruit
×
W/w Y/y
white fruit

F₂ ratio for W/w × W/w
3/4 W/-
1/4 y/y

F₂ ratio for Y/y × Y/y
9/16 W/- Y/-
3/16 W/- y/y
3/16 white

Combined F₂ ratios
9/16 white
12/16 white

F₂ phenotypic proportions
3/16 white
3/16 yellow
1/16 green
Dominant epistasis: how it works

Y/-; W/- : white
y/y; W/- : white

Y/-; w/w : yellow

y/y; w/w : green
Complementation

\[ P \quad C/C \quad p/p \quad \text{white} \quad \times \quad c/c \quad P/P \quad \text{white} \]

\[ F_1 \quad C/c \quad P/p \quad \text{purple} \]

\[ F_1 \times F_1 \quad C/c \quad P/p \quad \text{purple} \quad \times \quad C/c \quad P/p \quad \text{purple} \]

\[
\begin{array}{c|c|c|c}
\text{F}_2 \text{ ratio for} & \text{F}_2 \text{ ratio for} & \text{Combined } \text{F}_2 \text{ ratios} & \text{F}_2 \text{ phenotypic proportions} \\
C/c \times C/c & P/p \times P/p & \text{} & \text{} \\
\end{array}
\]

\[ \frac{3}{16} \ C/- \quad \frac{9}{16} \ C/- \quad \frac{9}{16} \text{ purple} \]

\[ \frac{1}{16} \ P/- \quad \frac{3}{16} \ C/- \quad \frac{3}{16} \text{ white} \]

\[ \frac{1}{16} \ C/c \quad \frac{3}{16} \ C/c \quad \frac{3}{16} \text{ white} \quad \frac{7}{16} \text{ white} \]

\[ \frac{1}{16} \ P/- \quad \frac{1}{16} \ C/c \quad \frac{1}{16} \text{ white} \]

\[ \frac{1}{16} \ P/- \quad \frac{1}{16} \ C/c \quad \frac{1}{16} \text{ white} \]
Complementation: theory

Mutations in different genes:

\[ p/p; C/C \times P/P; c/c \]

Mutations in the same gene:

- p/p; C/C x P/P; c/c
  - Complementation

- P/p; C/c
  - Mutant phenotype

- P/P; c/c
  - Mutant phenotype

- P/p; C/c
  - No complementation
Complementation

this is a mutant …and this is a mutant

…but are the mutations in the same gene or in different genes?
Complementation

You cross the mutants and if you find that their progeny is wild type... and that means...
Complementation

this is a mutant and this is a mutant

 mutant alleles must belong to different genes!
Normal hands                  Brachydactyly (50-80% penetrance)

The real situation may be very complicated

Neurofibromatosis – highly variable expressivity

Autosomal dominant: B/- brachydactyly, b/b normal fingers
Chi-square analysis of test-cross results

P: A/a; B/b \times a/a; b/b (tester) | F_1 progeny | Observed #
--- | --- | ---
Gametes | AB | ab | A/a; B/b | 140
| ab | ab | a/a; b/b | 135
| Ab | ab | A/a; b/b | 110
| aB | ab | a/a; B/b | 115

Are these results consistent with 1:1:1:1 ratio, as predicted by Independent Assortment?

1. Choose the null hypothesis. In this case the hypothesis is the 1:1:1:1 ratio
2. Determine the **Expected** number of progeny in each class: \( E = 125 \)
3. Calculate chi-square value:
   \[
   \chi^2 = \sum \frac{(\text{Observed} - \text{Expected})^2}{\text{Expected}}
   \]
   \( \chi^2 = 5.2 \)
4. Determine ‘degrees of freedom’ \( df = (\text{number of classes}) - 1 \)
   \( df = 3 \)
5. Use the df and \( \chi^2 \) values and Table 2.5 to determine \( P \). This value is the probability of the observed difference between Observed and Expected being accidental (random or insignificant), that is due to chance alone
6. If \( P > 5\% (0.05) \), this probability is considered high enough to accept that the differences are truly insignificant. Then we accept (cannot reject) the hypothesis
7. If \( P < 5\% (0.05) \), this probability of the difference being insignificant is low; the difference are actually significant, and the ratio is different from the hypothesized. Reject the null hypothesis.
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</table>

 fail to reject | reject at 0.05 level

**Table 2.5** Chi-Square Probabilities
Chi-square analysis of test-cross results

<table>
<thead>
<tr>
<th>Gametes</th>
<th>AB</th>
<th>ab</th>
<th>A/a; B/b</th>
<th>140</th>
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<tbody>
<tr>
<td></td>
<td>ab</td>
<td>ab</td>
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