Lecture 4: Mutant Characterization I

Mutation types (and molecular nature)
Complementation tests

Read: 285-293
Fig. 8.28, 8.29, 8.30, 8.31

Terminologies: Minimal medium, complete medium
    Auxotroph vs. prototroph
    Hot spot, trinucleotide repeats
    ORF
    Silent, nonsense, missense, neutral mutations
    null, hypomorph, hypermorph, neomorph, antimorph
    recessive, dominant, dominant-negative, haploid-insufficient

Homework#1 will be posted today!
Mutations in a gene’s coding sequence can alter the gene product.

- Missense mutations replace one amino acid with another.
- Nonsense mutations change an amino-acid-specifying codon to a stop codon.
- Frameshift mutations result from the insertion or deletion of nucleotides within the coding sequence.
- Silent mutations do not alter amino acid specified.
• Mutations outside of the coding sequence can also alter gene expression.
  – Promoter sequences
  – Termination signals
  – Splice-acceptor and splice-donor sites
  – Ribosome binding sites

![Diagram showing sites of mutation outside the coding sequence that can disrupt gene expression](image)

Fig. 8.28 b
Terminology about different mutations

a) Loss-of-function:
   Null mutation: complete absence of activity
   Hypomorph: reduced activity
b) gain-of-function
   Hypermorph: increased activity
   Neomorph: new function of gene
c) suppressors- compensate for other mutations
d) enhancer- enhances phenotype of a mutation
1: null mutation; 2: hypomorph climtic mutation
Both 1 and 2 are recessive
The underlying nature of recessive or dominant mutations

Recessive
hypomorph: reduced level or a protein with a weak function
Null: complete loss of function

Dominant
hypermorph: increased level or more effective activity
neomorph: new function
dominant-negative: poisonous effect
haploid-insufficient
Ectopic expression

Semi-dominant (incomplete dominant)
Incomplete dominance

\( r^0 \): null; \( r^{50} \): hypomorph; \( R^+ \): wild type
Rarely, loss-of-function mutations are dominant.

- **Haploinsufficiency** – one wild-type allele does not provide enough of a gene product.

Heterozygotes for the null mutation of the T locus in mice have short tails because they have an insufficient amount of protein to produce a wild-type tail.
Rarely, loss-of-function mutations are dominant.

- Dominant-negative mutations – alleles of a gene encoding subunits of multimers that block the activity of subunits produced by normal alleles

Fig. 8.31 b
Kinky: A dominant-negative mutation in mice causing a kink in the tail

Fig. 8.31 c
3: hypermorphic mutation
3 is dominant
Gain-of-function mutations are almost always dominant.

- Rare mutations that enhance a protein function or even confer a new activity on a protein

Antennapedia is a neomorphic mutation causing ectopic expression of a leg-determining gene in structures that normally produce antennae.
Determine recessive or dominant nature of the mutation

\[ C_1C_1 \text{ (Colorless mutant)} \times +/+ \text{ (Red: WT)} \]

\[ \downarrow \]

\[ C_1/+ \text{ (red: recessive)} \]

\[ \text{(colorless: dominant)} \]

\[ \times \text{ (self)} \]

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Complementation tests

Diagram showing the process of complementation tests involving enzymes A and B and genes A and B.
“Complementation group” equals “Gene”

If two mutations failed to complement,
they are alleles of the same gene
they are allelic to each other
they belong to the same complementation group

If two mutations complements each other,
they are alleles of different genes
they are not allelic to each other
they belong to different complementation groups
Determine allelism by complementation tests
Pairwise crosses between homozygotes and examine F1 for phenotype only applicable for recessive mutations

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<th>$c_1c_1$</th>
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Maize kernel mutants:
- $C_1$-$C_6$: colorless, recessive
- wt: red

Three complementation groups:
1. $c_1, c_4$
2. $c_2, c_3$
3. $c_5, c_6$