Mosaic screens

Reading: pages 702-707 lecture notes

white can be used as cell autonomous marker to monitor the loss of sev.

Approaches to identifying genes involved in development.

1. Direct screens: will often fail to identify essential genes required earlier in development (exception-hypomorphic mutations).
2. Sensitized screens: enhancer screens.
3. FLP/FRT mosaic screens.

Yeast 2 micron plasmid encodes a FLP recombinase and two FRT sites.

FLP recombinase stimulates recombination between two FRT sites.
Since replication origin fires only once during cell cycle. Intramolecular recombination is thought to increase copy number of 2 micron plasmid.

Expression of FLP recombinase can stimulate mitotic recombination at FRT sites.

FLP recombinase expressed from the eyeless promoter results in recombination just in the developing eye.

A digression
Mutations in two types of genes can lead to cancer
1. Oncogenes
   Positive regulators of the cell proliferation
   Activating mutations
2. Tumor suppressor genes
   Negative regulators of cell proliferation
   Loss-of-function mutations

Tumor suppressor genes can either inhibit cell proliferation or promote cell death.

Retinoblastoma is cancer of cone cells that is inherited as an autosomal dominant trait.

Sporadic Rb-cancer in one eye
Inherited Rb-cancer in both eyes
3% inherited cases have deletion in 13q14

In 1971 Knudson proposed that in inherited forms of Rb a second mutation occurred spontaneously in the normal gene. In other words, while Rb is inherited as a dominant trait, it is recessive at the cellular level.
How would I identify a tumor suppressor gene in *Drosophila*?

**To screen for tumor suppressor genes, mutagenize and look for mutants with excessive white tissue.**

**EMS**

- Mutagenized chromosome
- **F1**
- **F2 progeny w/o balancer**

If *m* is in tumor suppressor gene, white cell will produce more cells than red cell
Screen for mutations on each chromosome (FRT near centromere for each chromosome arm)

Mutations define 23 genes

Some were known tumor suppressor genes that had been identified in humans.

Others were new genes, and their human homologs were found to be mutated in cancer cells.