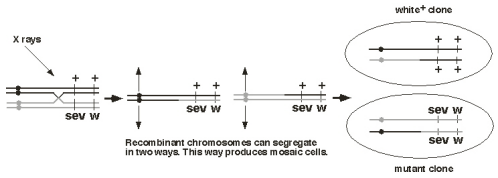
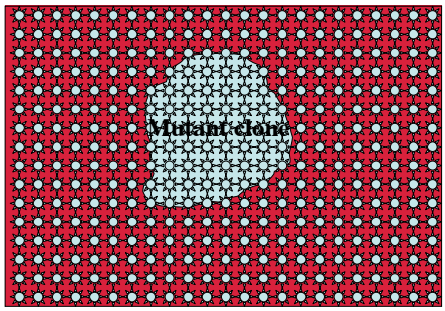
Mosaic screens

Reading: pages 702-707 lecture notes

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



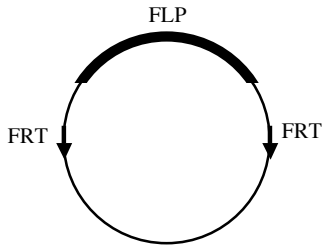
Analyze ommatidia at the periphery of mutant clone. These will be mosaic, containing both wild-type and mutant cells.



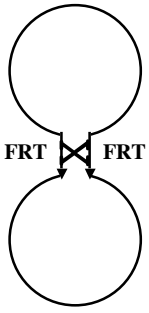
Approaches to identifying genes involved in development.

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.**

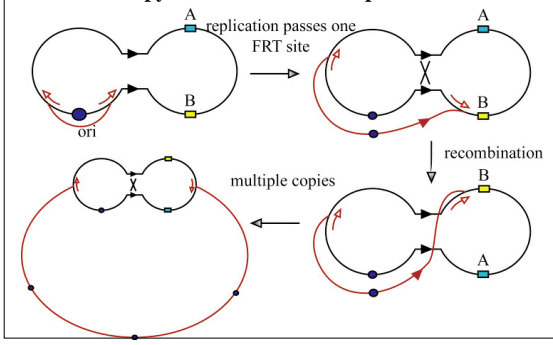
Yeast 2 micron plasmid encodes a FLP recombinase and two FRT sites.



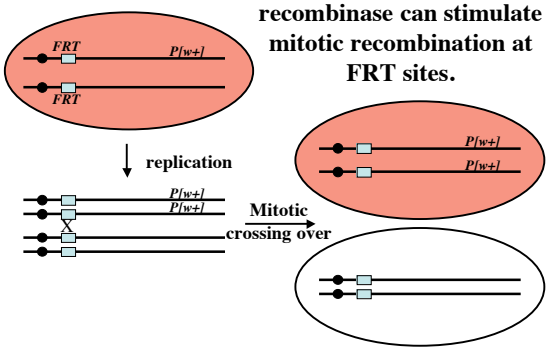
FLP recombinase stimulates recombination between two FRT sites.



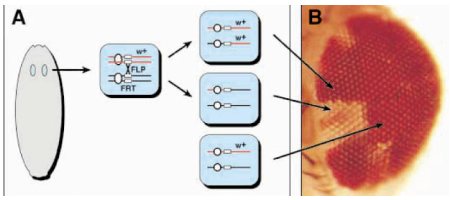
Since replication origin fires only once during cell cycle. Intramolecular recombination is thought to increase copy number of 2 micron plasmid.



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.

Tumor suppressor genes ⊣ **Cell proliferation**

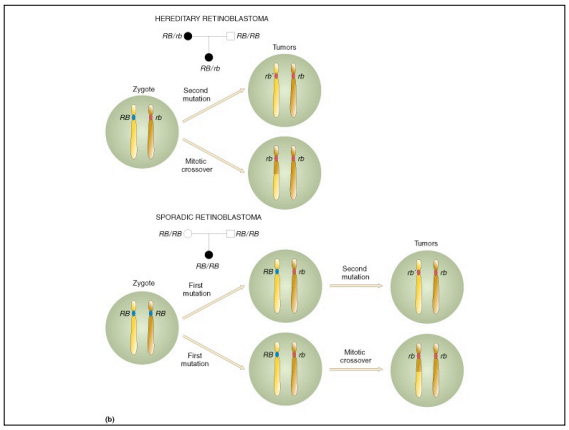
Tumor suppressor genes → **Cell death**

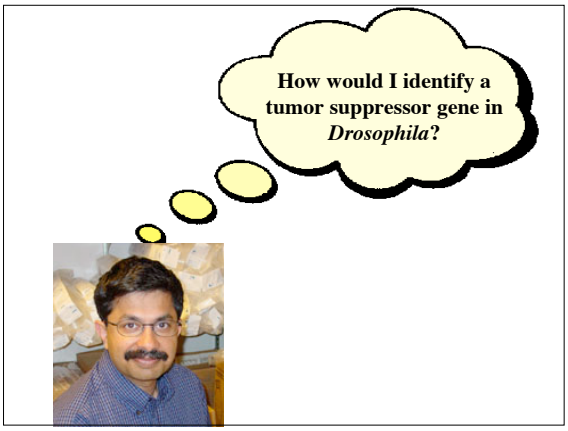
Retinoblastoma is cancer of cone cells that is inherited as an autosomal dominant trait.

Sporadic Rb-cancer in one eye

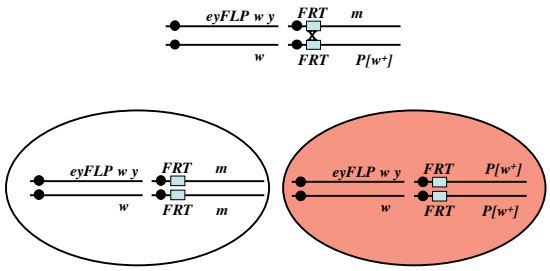
Inherited Rb-cancer in both eyes 3% inherited cases have deletion in 13q14

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.



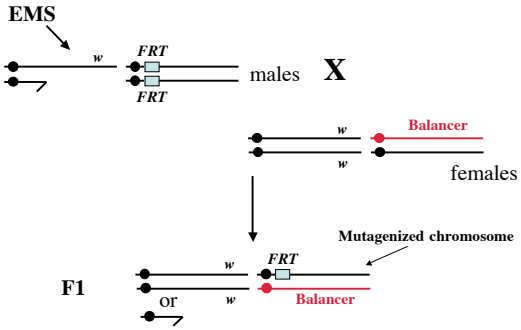


How to identify a tumor suppressor gene in *Drosophila*?

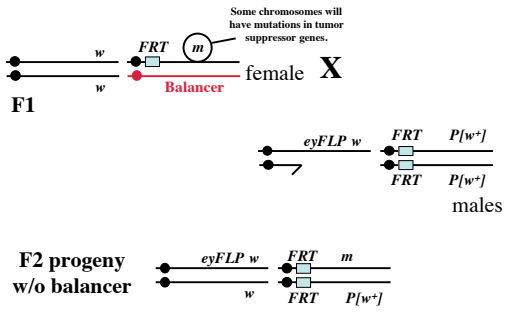


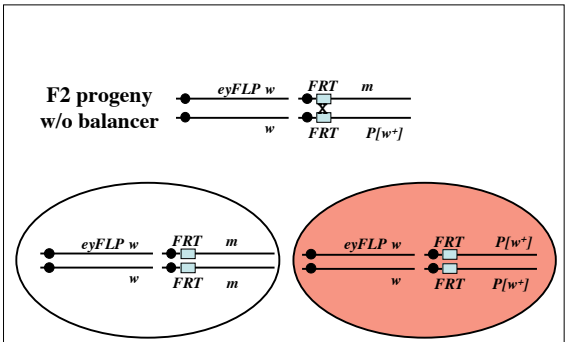
If *m* is in tumor suppressor gene, white cell will produce more cells than red cell

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



Cross individual F1 females





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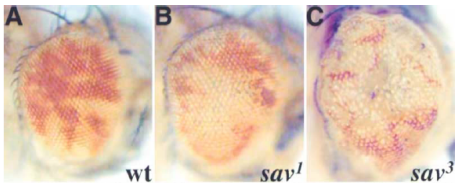

Screen for mutations on each chromosome (FRT near centromere for each chromosome arm)

Mutations define 23 genes

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

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