Reading:

pp152-154
Mitotic recombination can produce genetic mosaics
(— and cause cancer)

I’ve asked to reserve a lecture room from 7-9pm Thursday, April 5, for a review session in connection with the midterm on Monday, April 9. I’ll announce where the session will be held as soon as I know myself.
Last Friday:

(1) **genetically sensitize** the system:
    “turn” lof recessives into dominants  (**but** only with respect to one non-essential aspect of their function)

Poising the activity level of “your favorite gene” on a **phenotypic threshold** to make other genes **haploinsufficient**
...**but only with respect to the functioning of “your favorite gene.”**

So that:
(1) we can identify new mutations of interest *in the F1 generation* (first generation after mutagenizing the parents) **AND**
(2) can overcome some **complications of pleiotropy**
...so that we can more easily study the non-vital aspects of the functioning of genes that ALSO have vital functions
(1) **genetically sensitize** the system:

“turn” **lof** recessives into dominants **(but only with respect to one non-essential aspect of their function)**

Based on the **rationale** that:

Wildtype fly must normally have an **excess** of most genes’ activity **as insurance** against fluctuations in the levels of activity of various genes in a pathway during development

...if take away that **cushion** for any **one gene** in a pathway, now make the normal operation of the pathway **...with respect to that one gene...** more **vulnerable** to **reductions** in other gene levels
Another way around the limitations of pleiotropy in genetic screens:

(2) use **targetted genetic mosaics** to screen for recessives in the F1 (homozygous clones **in heterozygotes** …in **non-essential** tissues only!)

…recover new recessives in the F1???

*(without making them dominant?)*
genetic mosaics

according to your text:

“an organism containing tissues of different genotypes”

...all derived from a single initial cell (zygote)

(genetic) chimera: an embryo or animal composed of cells from two or more different organisms

(individuals)

(and that’s what they say in the text)
**genetic mosaics** are extremely useful for determining where a particular gene’s function is needed:

Your text short-changes the key concept of **cell autonomy** in gene function.

Fig 20.4:

(b) Using mosaics to study cell signaling

![Diagram showing cell signaling in genetic mosaics](image-url)
Genetic mosaics are extremely useful for determining where a particular gene’s function is needed:

In what cell type (L2 vs. L1) is ag\(^+\) function needed to elicit normal differentiation of L1?
For \(ag\), the cell whose phenotype is mutant is not the cell whose genotype is mutant. Hence \(ag\) is not cell autonomous with respect to the L1 phenotype.

The “genetic marker” is cell autonomous (that’s why it was chosen), since the cell whose marker phenotype is mutant is the cell whose marker genotype is mutant.

…if a cell’s genotype in the mosaic dictates that cell’s phenotype...
When discussing autonomy/nonautonomy, need to specify the phenotype in question:

...ag is non-autonomous with respect to the L1 differentiation phenotype

...perhaps ag is autonomous with respect to generating the signal in L2. (if we had an assay for the signal, we might see that phenotype directly)
T.H. Morgan published on genetic mosaics in 1914:

First nuclear division of a zygote:

Hence, \(~50\%\) of each set of chromosomes are lost...too large for our purposes.

Do males normally have white eyes?

\[XX, w^+/w^-\]

\[XX, w^-/w^-\]

\[w^-/w^+\]

\[w^-/-\]
Another way around the limitations of pleiotropy in genetic screens:

(2) use **genetic mosaics** to screen for recessives in the F1

...look for **homozygous mutant clones**

in otherwise **heterozygous** animals

...identify (and recover) new **recessives** in the F1

even works for new mutants that are recessive lethal or sterile

provided

-- one generates clones in only a small fraction of all cells

or

-- one generates clones only in **non-essential** tissues
Based on a phenomenon discovered (‘30s) by former chair of U.C. Zoology Dept: mitotic recombination

but improved upon enormously in modern times

...only possible because of a very strange aspect of fly chromosome behavior:

homologous chromosomes pair during mitotic interphase

Another way around the limitations of pleiotropy in genetic screens:

(2) use genetic mosaics to screen for recessives in the F1
...look for homozygous mutant clones in otherwise heterozygous animals
Stern’s observation:

…for fly heterozygous for recessive cell-autonomous l.o.f. alleles of two genes:

\[
\begin{array}{c}
\text{yellow(body)}^- & \text{singed(bristles)}^+ \\
\hline \\
\text{yellow(body)}^+ & \text{singed(bristles)}^-
\end{array}
\]

most flies wildtype

If \textbf{irradiated} (ionizing) during development occasionally saw odd ADULT fly:

\textit{“twin spot”}

deduced: mistake in mitosis, \textbf{not} new mutant alleles
Fig. 5.23 p152

Single yellow spot

Twin spot

Single singed spot
Consider what it is about mitosis that insures daughter cells will have the same genotype as their mother cell:

\[ X_m X_p \]

Then:

If instead:

\[ y^- sn^+ m \]
\[ y^+ sn^- p \]

\[ y^+ sn^- \]
\[ y^- sn^- \]

\[ y^- sn^+ m \]
\[ y^+ sn^- p \]

\[ y^+ sn^- \]
\[ y^- sn^- \]

\[ y^- sn^+ m \]
\[ y^+ sn^- p \]

\[ y^+ sn^- \]
\[ y^- sn^- \]
What if **DNA breaks** and **improper repair** after S phase change relationship between genes and centromeres:

NO CHANGE if instead:

- **yellow**
- **twin-spot**
- **singed**
DNA breaks and improper repair after S phase generate the “twin-spot” of cells homozygous for \( y \) and \( sn \).

\[
\begin{align*}
&y^- sn^+ m \\
&y^+ sn^- p
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ m \\
&y^+ sn^- m
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ m \\
&y^+ sn^- m
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ m \\
&y^+ sn^- m
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ p \\
&y^+ sn^- p
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ p \\
&y^+ sn^- p
\end{align*}
\]

\[
\begin{align*}
&y^+ sn^- m \\
&y^+ sn^- m
\end{align*}
\]

\[
\begin{align*}
&y^+ sn^- p \\
&y^+ sn^- p
\end{align*}
\]

twin-spot: because progeny of the \( y/y \) & \( sn/sn \) original cells tend to stay together.

size of patches depends on when aberrant mitosis occurs.

Growth:

\[
\begin{align*}
&y^- sn^+ m \\
&y^- sn^+ p
\end{align*}
\]

\[
\begin{align*}
&y^- sn^+ m \\
&y^- sn^+ p
\end{align*}
\]
Fig. 5.24 (p152)
What if we had induced a NEW recessive MUTATION on a mutagenized y sn+ chromosome (in the father’s sperm) that affected cell growth parameters?

..appearance of an ABNORMAL homozygous yellow patch next to homozygous singed patch would SIGNAL that the female carried a new mutant allele.