Steps in the discovery of new cancer treatments

Discovering which protein is altered in one type of cancer

Synthesizing small amounts of thousands of different chemicals

Examining cancer cells treated with these chemicals to see their effects

Analyzing all of the data to determine which chemicals are most promising

Synthesizing large batches of each promising chemical

Making analogs of each chemical, & measuring their potencies

Testing each potential new treatment in a clinical trial

Sharing findings with the scientific community & the general public
Please take a moment to discuss with your neighbor how cancer has impacted those around you.
What has changed about the DNA in the cancer cell, that may have led to the disease?

All of the chromosomes in a non-cancerous cell

Chromosomes #9 & #22 in a non-cancerous cell

All of the chromosomes in a “CML” cancer cell

Chromosomes #9 & #22 in a “CML” cancer cell
DNA
Gene
Cell
Chromosome
Nucleus
The Basic Structure of DNA

- Base pairs
- Sugar Phosphate Backbone
- Adenine Thymine
- Guanine Cytosine
A translocation is when two chromosomes swap their ends.
The translocation present in CML cancer patients
The genes encoding *Bcr & Abl* in a non-cancerous cell:

![Diagram of chromosome 9 and chromosome 22 with Bcr and Abl genes](image)

The proteins Bcr & Abl in a non-cancerous cell:

![Diagram of Bcr and Abl proteins](image)

**If a translocation occurs between chromosomes 9 & 22...**

Draw what the Bcr & Abl genes would look like in a “CML” cancer cell.

Draw what the Bcr-Abl fusion protein would look like in a “CML” cancer cell.
Normal cells with no translocation:

Chromosome 9  
\[ \text{Abl} \]

Chromosome 22  
\[ \text{Bcr} \]

CML cancer cells with a translocation:

Translocated Chromosomes 9 & 22

Bcr-Abl Fusion Protein

Bcr Protein

Abl Protein
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Background for this experiment:
Cancer cell samples have been treated with a negative control, a positive control, and a promising new anti-cancer drug “Chemical A.” The DNA in the cells has been stained, so that each nucleus appears as a bright spot. Photographs of the cells were taken and are shown here.

1) What does it mean about what has happened to the cancer cells, when there are lots of bright dots in an image (versus very few bright dots)?

2) How and why would cancer researchers conclude from these photos that “Chemical A” is indeed a promising new anti-cancer drug?

3) What do you think might have been used as a positive control and a negative control in this experiment? Explain your answer.
Photos of cancer cells treated with:

- a negative control
- a positive control
- a promising new anti-cancer drug “Chemical A”

Many cancer cells are alive.
Few cancer cells are alive.
Few cancer cells are alive.
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Initial compound

Reverse the atoms = improved potency

Remove lower region = improved solubility but lower potency

Add nitrogen = improved stability but lower potency

Add chlorine = even better potency!
This graph is called a “dose response curve,” and it shows the amount that a chemical compound inhibits the activity of the cell/protein that it targets.

Which of these three chemical compounds is the most potent?
The chemical compound “Gleevec” binds to & inhibits the Bcr-Abl fusion protein.
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A clinical trial shows us how well patients respond to a new treatment
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Evolution of drug resistance in cancer cells can occur because of changes in the protein target of the drug. Drug A binds to the protein target. The protein target is altered, causing resistance to Drug A. Drug B is discovered and can treat cancers resistant to Drug A.