How scientific teams develop new anti-cancer drugs
BLOSSOMS Video Teacher's Guide

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Learning Objectives: Students will learn how all different kinds of people (& robots, too!) work together in the process of discovering anti-cancer drugs. Students meet Broad Institute employees during this lesson, who have many different careers, including: cancer doctors, experimental & computational biologists, synthetic & medicinal chemists, and a science writer. The students watch the process of drug discovery happen, from start to finish, and see how these sorts of "high-throughput" large-scale research projects are performed in highly inter-disciplinary and collaborative ways. The specific cancer type that is used as an example in this lesson is CML, a leukemia caused by a translocation between chromosomes #9 and #22. This translocation leads to production of the fusion protein Bcr-Abl. A drug that inhibits Bcr-Abl is an effective treatment of CML leukemia.

NOTE: We recommend that this lesson be the last BLOSSOMS lesson on cancer, that the students use (i.e. they should use "**From teenage to old age: How cancer develops over time**" first – and then also possibly "**Making it personal: Using DNA to tailor cancer treatments**" – before using this lesson).

Prerequisite Knowledge: The students need to know the following, going into this lesson:

- DNA is composed of four bases (A, C, T, G), and it encodes all RNAs & proteins in a cell.
- DNA can be mutated in cancer cells, and the effects of these mutations are carried over into the RNA and the protein encoded by that stretch of DNA.
- Each human has two versions of every piece of DNA in their genome: one version from their mom and one version from their dad. Thus 50% of the DNA of a child comes from the mom, and 50% from the dad.

Necessary Supplies: Only paper and writing utensils are necessary, and the ability to print out or display the provided handouts. This lesson is intended to take 1-2 class periods.

Lesson Outline:

Segment #1: The students are introduced to two cancer patients, one who is undergoing general chemotherapy, and another who has CML and is being treated with a targeted drug with few side effects. Twenty years ago, the CML patient would have had the same treatment & harsh side effects of the other patient, but recent research has changed that.

What occurs after Segment #1: Students turn to their neighbors and discuss how cancer has impacted the people around them.

Segment #2: A cancer doctor walks us through a history of cancer treatment, starting with Egyptians in 3000 BC. He reveals when the mutation that causes CML was discovered.
What occurs after Segment #2: Students are shown photos of the chromosomes from a normal white blood cell and a white blood cell from a CML patient. They are asked to analyze these photos and describe what large chromosomal rearrangement has occurred.
Note: There is also a more extensive timeline of cancer research (available as a handout that could also be printed poster-sized) that teachers can distribute as a reference material, at the end of this segment. This handout is for reference only, and is not associated with an activity.

Segment #3: The narrator explains what a translocation is, and how this sort of large chromosomal rearrangement causes two genes (Bcr and Abl) to fuse to each other, in the DNA from patients with CML.
What occurs after Segment #3: The students are asked to draw what the chromosomes and protein would look like, that is produced from a fusion gene of Bcr to Abl.

Segment #4: We begin to describe the process of performing a "chemical screen" to find drugs that halt growth of cancer cells. This process starts with Jen, a synthetic chemist whose group at the Broad synthesizes hundreds of thousands of chemical compounds. A big yellow robot then performs the experiment, in which each chemical is tested for its ability to inhibit growth of cancer cells. We then meet Aaron, a computational biologist who analyzes the data. We also hear from Kristina, an experimental biologist who explains how we can tell if the chemical-treated cancer cells are alive or dead.
What occurs after Segment #4: Students are shown photos of cancer cells treated with a promising anti-cancer drug, a positive control, and a negative control. They are asked to describe what they see in these photos, that leads them to believe the drug is promising.

Segment #5: Once a promising chemical is discovered through a chemical screen, we return to the chemistry lab, where Jen synthesizes a large batch of that one chemical. Chris (a medicinal chemist) synthesizes many "analogs" (or versions) of this chemical, to find out which one is most "potent" (i.e. effective in inhibiting cancer cell growth).
What occurs after Segment #5: Students examine a dose response curve, showing the potency of an original chemical compound, and two analogs of that compound. They are asked to determine which of the compounds is most effective (i.e. "potent").

Segment #6: The next steps of the drug discovery process – clinical trials, and then communication of the findings to the general public – are discussed by a

cancer doctor, and a science writer.
What occurs after Segment #6: Students do an activity where they are each assigned a science career, and they have to figure out which kind of scientist does that career, where they would work, and where in the process of drug discovery they would work. Detailed instructions for this activity are included in the packet of teacher materials.

Segment #7: All of the steps we just learned about, were used in sequence, to discover a drug that is now used to treat CML. The main problem with this drug is that patients can acquire resistance to it, over time. We see drug resistance developing quickly, when new cancer treatments are utilized. But we can go through the cycle of drug discovery again, to find treatments for patients resistant to the initially discovered drugs.
What can occur after Segment #7: An optional extension activity, that is a science career project about a career of each student's choosing. Detailed instructions are provided.