

Making it personal: Using DNA to tailor cancer treatments

BLOSSOMS Video Teacher's Guide

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Learning Objectives: Students will learn that different mutations in DNA can lead to the same general category of cancer (e.g. lung cancer), and that choosing specific treatments – based on which mutations have occurred – can lead to improved outcomes for the patient. This video will emphasize that incorporating laboratory work into the clinic – to determine which mutations have occurred in the DNA of the cancer cells – can direct decisions about how to treat different cancer patients. Mutations can lead to over-active mutant forms of different proteins present in cancer cells, which make them divide out of control.

Therefore the drug that most selectively inhibits the specific protein that is mutated and over-active in a certain patient's cancer cells, should be chosen as the treatment for that patient.

NOTE: We recommend that this lesson be used after the basic concepts of cancer biology are covered in the lesson “**From teenage to old age: How cancer develops over time**”. (The lesson “**How scientific teams develop new anti-cancer drugs**” works well as an extension to the lesson discussed in this Teacher's Guide.)

Prerequisite Knowledge: It would be helpful (but not necessary) if the students know:

- DNA is composed of four bases (A, C, T, G). It encodes all RNAs & proteins in a cell.
- DNA can be changed in the context of cancer, and the effects of these mutations are carried over from DNA to RNA to protein.
- 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: Students will receive information about three lung cancer patients, all with Stage III lung adenocarcinoma (a type of lung tumor), including their age, gender, ethnicity & number of years as a smoker. Though they all have the same general category of cancer, they will be recommended different treatments, by the end of the lesson.

What occurs after Segment #1: Students do a worksheet, in which they compare and contrast images (taken by a pathologist) of the lung tumor tissue from the 3

patients. They then answer the question: “What would you want to know next about each patient, before you make treatment decisions for each of them?”

Segment #2: Some common cancer treatments will be described, including surgery, radiation and drugs (including chemotherapy and targeted therapies).

An example of a chemotherapy drug, and a targeted therapy, will be given.

What occurs after Segment #2: Students will discuss the question: “Which treatment do you think will have the fewest side effects, and why?”

Segment #3: The students are introduced to an analogy of a cancer cell, namely, a kitchen with multiple appliances. In each kitchen, one appliance is spiraling out of control (either the coffee maker’s nozzle is dripping continuously, or the blender is spewing liquid out of its top).

What occurs after Segment #3: The students are asked which treatments would work for which out-of-control kitchens: a rubber stopper, or a lid (both of which are analogous to targeted therapies), or turning off the power to the whole kitchen (which is analogous to chemotherapy).

Segment #4: Students will be instructed on how to analyze images of the chromosomes of normal & cancerous cells. These images are of cells at metaphase, so the chromosomes have been replicated (i.e. both “sisters” are visible). We explain that there is a set of sisters in each cell, one from the person’s father & one from the person’s mother (i.e. “homologs”).

What occurs after Segment #4: The students look at images of the chromosomes in the lung cancer cells of each of the 3 patients. They are asked to determine whether large chromosomal rearrangements have occurred, in the tumor cells.

Segment #5: Not all changes to DNA are large rearrangements, like those seen in the last section. Some are single letter changes (e.g. a “T” to a “G”). Students will be introduced to DNA sequencing as a tool to investigate which genes are mutated at the single-letter level.

What occurs after Segment #5: Students will analyze DNA sequencing data (in the form of “chromatograms”), showing the sequences of two genes commonly mutated in cancer, in each patient. They are asked to find any mutations, in the two genes, in any of the patients.

Segment #6: We will summarize the lesson at this point, showing the students that they have now seen 3 different types of data for each cancer patient (images of the cells, images of the chromosomes, and DNA sequencing chromatograms of 2 genes in the genome). They are asked to compile the results of analyzing all of these data, to determine what mutations exist in each of the 3 patients, and then suggest a treatment for each patient.

What occurs after Segment #6: Students complete a worksheet, aimed at those two goals. This worksheet contains a chart, showing drug response statistics for patients whose cancer cells contain different mutations.

Segment #7: The segment ends with a discussion of how the incorporation of molecular medicine into the clinic has changed the way doctors treat patients today versus 10 years ago – i.e. targeted therapies versus generalized therapies such as chemotherapy. Cancer is a complicated series of diseases, with no “one treatment fits all” solution. Therefore future research, like that currently ongoing at the Broad, focuses on finding treatments for individual sub-types of cancer. DNA sequencing is playing an increasingly larger role in cancer research; with the benefits of DNA sequencing, however, come many ethical issues.

What can occur after Segment #7: An optional discussion activity is provided, which focuses on the bioethics behind people having access to their genome sequences.