Targeting Cancer

Objectives

Students will:

- Identify happens to cellular machinery in a cell that becomes cancerous and factors that can cause cancer.
- Explore how targeted cancer therapies can be more effective and have fewer side effects for patients than other types of treatments, such as chemotherapy.
- Discover that next generation sequencing can reveal important information about cancer-related mutations that can lead to better cancer-related treatment plans.
- Create a presentation and 3-D model that will explain the cellular mechanism of targeted therapies and the benefits and risks for cancer patients.

OVERVIEW

In this lesson bundle, students will show how targeted therapy is changing the treatment for cancer patients by using gene sequencing to look for cellular changes, chromosomal abnormalities, and gene mutations that can help doctors to design personalized treatment plans that can save lives. Students will first learn what causes cancer; that it can be caused by both genetic and environmental factors and the cellular machinery failures that occur in a cancer cell. They will explore various types of targeted therapy and how they can improve or be used in combination with other types of more invasive treatments, such as chemotherapy and radiation. Students will then be asked to form teams that will be tasked with giving a presentation on targeted cancer therapy at a fictional cancer innovations conference. They will be presenting a specific type of targeted therapy to the class; each being becoming an expert on one type of targeted therapy. As a part of their presentation, groups will need to use classroom materials (clay, hot glue, paper, craft supplies) to create a 3-D model that can be used to demonstrate how their targeted therapy works to stop or prevent the growth of cancer cells. Student groups will have time to research their subject and create their presentation and model, then all groups will participate in the conference where they will share their presentation.

The accompanying presentation was created with PowerPoint so that it can be used in a variety of classrooms. If you are using a laptop with an LCD projector, simply progress through the PowerPoint by clicking to advance. All of the interactive aspects of the presentation are set to occur on click. This includes images, text boxes, and links to outside videos, which will appear in your web browser. If you are using an interactive whiteboard, tap on each slide with your finger or stylus to activate the interactive aspects of the presentation. It does not matter where you tap, but you can make it appear as if you are making certain things happen by tapping them. In the notes for each slide, there will be information for the instructor.

CONTENT AREAS

Genetics, Genomics, Cancer, Medicine

ACTIVITY DURATION

4 class sessions (45-50 minutes each)

GRADE LEVEL

Grades 9–12

ESSENTIAL QUESTIONS

- What goes wrong in a cell that causes cancer?
- What types of therapies are used to treat and prevent cancer?
- What is targeted therapy?
- How are scientists using next generation sequencing to learn more about cancer?
- How do targeted therapy drugs affect a cancer cell's machinery to slow or stop the division of cancer cells?

MATERIALS

All days:

- Device with the ability to project
- Student 1-1 devices (laptop, iPad)

Day 1

- Think-Pair-Share: Cellular Causes of Cancer student sheet (1 per student)

Day 2

- Card Sets for the Types of Targeted Therapy sorting activity

Day 3

- Targeted Therapy Research Sheet (1 per group)

Materials for creating drug action models including (but not limited to)

- Play-Doh or modeling clay
- pipe cleaners
- hot glue and glue sticks
- cardboard
- craft sticks
- scissors, craft knife
- paint or markers
- construction paper
- dried pasta of various shapes
- Styrofoam balls and sheets
- poster board

Day 4

- Copy of the article "First U.S. Patients Treated with CRISPR As Human Gene-Editing Trials Get Underway" (1 per student)

BACKGROUND

Nearly everyone has a story about cancer impacting their life. Whether it's a story about a friend, family member, or a personal story, cancer is the second leading cause of death in the U.S. and affects millions of people every year. It has been difficult to treat and cure, but genetic and medical innovations are paving the way for new cancer-fighting methods, drugs, and treatment plans. By looking deep into cancer cells through next generation sequencing, scientists and doctors are gaining a better understanding of the link between genetics and cancer. They are learning how these genes can predispose people to cancer or help explain how cancer cells can grow, divide, spread and are able to evade treatment. In this lesson, students will learn about how the treatment of cancer is changing and improving through technology, such as Next-Generation Sequencing (NGS) in an ever-increasing quest to understand how cancer cells work and can how they can be stopped.

This guide gives educators a collection of resources designed to help students investigate what happens in the genomes of cancer cells, and how NGS can be used to discover the mutations that are causing cancer in patients, allowing them to determine the most effective type of treatment for the patient. It provides slide-by-slide instructions to ensure educators are prepared to explain, discuss, and facilitate the hands-on content in the presentation. The presentation is designed to cover four class sessions, but it can be flexible depending on the students' needs and the time available. Additional extension ideas are included at the end of the manuscript.

This lesson plan follows an inquiry-driven 5E instructional model: Engage, Explore, Explain, Elaborate, and Evaluate. Over the course of four class periods, students will work together to understand what happens in a cancerous cell, discover how targeted therapy is changing the way we treat cancer and research how targeted therapy drugs work on cells and proteins. Finally, they will work in teams to create a presentation and working 3-D model to inform the public how a specific targeted therapy works to slow and stop cancer cells from dividing and spreading as they participate in a fictional cancer innovations conference in their classroom.

Engage | Slides 1–7

OVERVIEW

Instructor will open with a slideshow that gives facts and statistics about cancer and asks students to guess the topic that they will be studying in this lesson as the information is revealed. Students have the opportunity to share their own experiences with cancer and things they know about cancer and its impact on human health.

DAY 1 | SLIDES 1–6

Begin class by asking students to guess the topic that this lesson will focus on by reading some facts and statistics you will display on the overhead screen. (https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2019.html)

- Click through the slides one at a time, allowing students to guess what the topic is as you go through the slides.

DAY 1, SLIDE 7

- Reveal that the topic is cancer. Click and ask students to stand if they have been impacted by cancer in their lives. Do they know someone who has had cancer? (Likely most, if not all, students will stand) Encourage students to look around and see how common cancer is in the lives of people. Allow students to share their stories of their connection to cancer briefly, if time allows.

Engage | Slides 8–12

OVERVIEW

Students will participate in a Think-Pair-Share activity, where they will brainstorm what they think causes cancer: what happens in a cell that becomes cancerous? After recording their initial ideas, they will pair up with another student and each pair will be assigned one term that relates to what happens in a cell that becomes cancerous. Pairs will research how their term relates to cancer, and each pair will report their findings to the whole group, for each student to record. They will then use the information they have learned to write or draw a summary of what events happen in a cancerous cell. Student can share their summaries with the whole group and the class can agree on a timeline of events that lead to cancer on a cellular level.

DAY 1, SLIDE 8

- Explain to students that next they will be participating in a Think-Pair-Share activity.
- Give each student a copy of the Think-Pair-Share sheet
- Ask them to write down their answers to the questions: What causes cancer? What happens in a cell that becomes cancerous? (2–4 min)
- Ask students to share their ideas with the class. The instructor should make a list on the front board or overhead screen of students' initial thoughts about the causes of cancer.

DAY 1, SLIDE 9

- Next, students should pair up with a person sitting beside them. Assign each pair one of the terms pertaining to cancer.
- TERMS: **cell cycle, oncogenes, proto-onco genes, tumor supressors, p53, metastasis, angiogenesis, contact inhibition, cell cycle checkpoints, cyclins, cyclin-dependent kinase, apoptosis, neoplasm**
- Students should find their term on the Think-Pair-Share student sheet and use their device (iPad or laptop) to record a working definition of the term and how it relates to cancer. **When doing a search, students may find it helpful to search their term along with the words "and cancer".*

DAY 1, SLIDE 10

- Once students have completed their research and written down a definition of their assigned term, students should share their definitions with the class. Each group should record all definitions on their Think-Pair-Share sheet.

DAY 1, SLIDE 11

- Once all definitions have been recorded, ask students to work with their partner to create an explanation (in the "Share" box of their sheet) that describes in as much detail as possible what happens in a cancerous cell using the information and definitions they now have.

- They should include terms in their explanations.
- When pairs have finished, ask a few students to share the explanation they created with the class. The class can give feedback on explanations presented.

DAY 1, SLIDE 12

- First ask students to go to the Eukaryotic Cell Cycle and Cancer interactive and click through, (media.hhmi.org/biointeractive/click/cellcycle/) making revisions and additions to the SHARE section of their student sheet.
- Then, play the video link that explains the basics of cancer for students on the overhead screen (~12 min)
- Students should make any final revision to their explanation of what is happening in a cancerous cell.
- To end the lesson, the instructor should go back to the initial list that students created (Slide 8) to discover any misconceptions they had about cancer and analyze new information they have learned.

EXPLAIN | Slides 13–20

OVERVIEW

Now that students have learned about the mechanisms in a cell that causes it to become cancerous, they will discuss how cancer has historically been treated using chemotherapy and radiation in a 1-solution-for-everyone method. They will compare the benefits and drawbacks of these traditional treatments and think about how this might be improved. Students will then be introduced to targeted therapy that is being used to treat cancer patients through genetic sequencing and personalized medicine through a short video clip. They will then learn about various types of targeted therapies used to treat cancer by completing a card sort activity. In this, students will form groups of 2-3 and be given a card set. They will read about the mechanism of action of each type of therapy and attempt to classify them as being either a small-molecule drug or monoclonal antibodies, two of the major groups of targeted therapy.

DAY 2, SLIDE 13

- Begin class by explaining to students that, now that they have an understanding of what happens in a cell to cause cancer, today they will be looking at past, current, and future treatments that scientists are developing to fight cancer.
- Ask students to share what they know about treatments that patients typically have when diagnosed with cancer. They will likely mention chemotherapy and radiation.
- Click to play the following video (from 4:51– 6:06) that explains how these treatments work to get rid of cancerous cells: https://www.youtube.com/watch?v=7tzaWOdvGMw

- Ask students to think about the pros and cons of chemotherapy and radiation treatments and share their ideas with the class.

  (Students should mention the side effects and that the treatment is targeting all cells, not just cancer cells)

- Next ask students if they can think of ways that treatment could be improved and share any ideas that they have. (Ideas may include finding a way to kill only the cancer cells—not healthy cells, which could help lessen side effects for patients.)

DAY 2, SLIDE 14

- Introduce the term "targeted cancer therapy" to students. Read the information on the slide
- Click to play the video clip (https://www.youtube.com/watch?v=PrE30zRPAqE) that introduces a type of targeted therapy used to treat melanoma, the most dangerous type of skin cancer.
- Ask students to compare how this treatment differs from what they learned about chemotherapy and radiation. What benefits could this have for the patient over other types of treatments?

DAY 2, SLIDE 15–16

- Read the information on the slides to students. Allow students to ask questions as they have them.

DAY 2, SLIDE 17

- Students will learn that scientists gather the information about the genetic makeup and anomalies in cancer cells by using Next-Generation sequencing. Read the information about NGS to students and play the video that will allow them to see the process of next generation sequencing and how the information it provides can be incredibly valuable to create targeted therapy plans for cancer patients. (Start at 2:20) (https://www.youtube.com/watch?v=_a6_Sf_-_BU)

DAY 2, SLIDE 18

- Click to play the video (https://www.youtube.com/watch?v=uhk-da20VMo) for students that explains what a game-changer genomic sequencing was for Bryce Olsen, a man who has been battling metastatic prostate cancer.

DAY 2, SLIDE 19

- Read the information on the slide to students. Allow students to ask questions as they have them.

DAY 2, SLIDE 20

- Students will now participate in a card sorting activity, where they will read descriptions of types of targeted therapy treatments for cancer and try to determine if they are small molecule drugs (SMD) (designed for targets inside cells) or if they are monoclonal antibodies (MCA) (designed for targets outside or on the surface of cells.

- Students should get into pairs or small groups and work together to try to correctly sort out the cards according to their type. They should use the SMD and MCA cards as headings for the two main groups.
- The instructor may want to return to slide #18 to remind students of the purpose of the two different types of therapies.
- Students may also want to use their devices (iPad, laptops) to do research about each of the types of targeted therapies to help them discover how to sort them.
- Students should have the instructor check for accuracy when they think they have sorted the cards correctly.

ELABORATE, Slides 21–26

OVERVIEW

In this culminating activity, students will form small groups and play the role of a team of cancer biologists who will be presenting at a fictional Lung Cancer Sequencing and Treatment Conference. Each team will be assigned a specific type of targeted cancer therapy drug that is used to treat non-small cell lung cancer and that will be the subject of their presentation. The team will need to do research to identify the mutation in the cell detected through sequencing that is connected to their drug, and how their drug works to combat cancer. They will construct a 3-D model that can be used to demonstrate the drug's mechanism of action on the cell, and use their research to create a brief google slideshow or PowerPoint (to accompany the presentation of their model). Once the presentations and models are completed, the mock conference will begin, and groups will take turns presenting information about their drug, including how it works in the cell, what type of targeted treatment it is, what patients can expect from the treatment, and a demonstration of their model.

DAY 3, SLIDE 21

- Explain to students that they will form small groups and play the role of a team of cancer biologists who will be presenting a type of targeted therapy cancer drug at a fictional Lung Cancer Sequencing and Treatment Conference. Each team will create a presentation and 3-D model that will show how their drug works to reduce cancer growth and cancer cell division. Presentations will be no more than 5 minutes.
- Ask students to form small groups
- Targeted Therapy Drugs that may be assigned to groups include:
    1. Tarceva
    2. Gilotrif
    3. Iressa
    4. Tagrisso
    5. Portrazza

6. Xalkori
7. Zykadia
8. Alecensa
9. Tafinlar
10. Mekinist

DAY 3, SLIDE 22

- Assign each team one targeted therapy from the slide.

DAY 3, SLIDE 23

- Read the instructions and tips on the slide and give each team a copy of the Targeted Therapy Research Sheet.

  NOTE: Information about each of the drugs can be found here: https://www.cancer.org/cancer/non-small-cell-lung-cancer/treating/targeted-therapies.html

  It may be helpful to give this link to students to get them started in their research.

DAY 3, SLIDE 24

- Read the instructions and tips on the slide for building the 3-D model that can show the targeted therapy's mechanism of action. There is an example video (https://www.youtube.com/watch?v=7ZMVQ1Vbb7Y) for a drug called Gleevec that students can view to help them understand the mechanism of action–or how their drug interacts with the cancer cell.
- Allow student groups the remainder of the class period to begin their research and slide show and begin the construction of their model.

DAY 4, SLIDE 25

- Instruct students to rejoin their teams from Day 3 and explain that they should use the beginning of the class period for final preparations of their presentations.
- Review the instructions for presentations with the class, and answer questions as needed before allowing student groups to begin working.
- Give students approximately 15-minutes of a 50-minute class period to finish any part of and prepare for their conference presentation.

DAY 4, SLIDE 26

- It's time to present for the Lung Cancer Sequencing and Treatment Conference! Reiterate that the goal of this conference is to educate people in the medical profession about how specific targeted cancer therapies work so that doctors may be able to add them to their patient's treatment plans when appropriate.
- Explain that each group will be given no more than 5 minutes to present their slideshow and 3-D model. There will be an opportunity for questions and feedback after presentations have concluded.

EVALUATE | Slides 27–28

OVERVIEW

Students have learned how various types of targeted therapy drugs work to inhibit the growth and reproduction of cancer cells, but what are some of the ethical and societal dilemmas that we will face as we gain more and more information through cancer gene sequencing? Students will read the following article (https://journalofethics.ama-assn.org/article/cancer-gene-sequencing-ethical-challenges-and-promises/2012-11) and participate in a whole class discussion on the idea of the promise and potential ethical dilemmas of cancer gene sequencing, and if they think they would want to have preventative cancer gene sequencing themselves.

DAY 4, SLIDES 27–28

- Give students the link to the article on cancer gene sequencing or print off a hard copy for each student. Give students time to read through the article.
- Display the reflection questions on Slide 28 for the students to think about as they read.
- When students are finished, engage students in a discussion centered on the questions about the medical promise and potential ethical dilemmas that may come from cancer gene sequencing.

EXTENSION, Slide 29

- If you have additional time and/or would like to further challenge your students, consider the following extension options:
    - You may have heard of the microbiome, but did you know that scientists are finding the connection between the microbes in your body and your immune system—and these microbes may be able to influence cancer growth and other diseases? Check it out here!

      https://www.youtube.com/watch?time_continue=12&v=Q5PgPUvOBzo

      https://www.youtube.com/watch?v=A-IqdPch9t0

      Go to the following website to get started:
      learn.genetics.utah.edu/content/microbiome/simulator/
    - What are the other applications of Next Generation Sequencing? Explore videos and interviews on Illumina's website!
    - https://www.illumina.com/science/education/adventures-in-genomics.html

LINKS:

https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet

https://www.khanacademy.org/science/biology/cellular-molecular-biology/stem-cells-and-cancer/a/cancer

https://www.mayoclinic.org/diseases-conditions/cancer/in-depth/monoclonal-antibody/art-20047808

https://www.cancerresearch.org/immunotherapy/what-is-immunotherapy

https://www.cancer.gov/about-cancer/treatment/types/precision-medicine/tumor-dna-sequencing

https://www.cancerquest.org/patients/treatments/targeted-therapies

https://www.illumina.com/areas-of-interest/cancer/research/sequencing-methods.html

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5956085/

https://www.genomicsengland.co.uk/understanding-genomics/

https://www.cancer.gov/publications/dictionaries/cancer-terms/def/parp-inhibitor

https://journalofethics.ama-assn.org/article/cancer-gene-sequencing-ethical-challenges-and-promises/2012-11

NEXT GENERATION SCIENCE STANDARDS (NGSS)

Next Generation Science Standards:

- HS-ETS1-3. Evaluate a solution to a complex real-world problem based on prioritized criteria and trade-offs that account for a range of constraints, including cost, safety, reliability, and aesthetics, as well as possible social, cultural, and environmental impacts.
- HS-LS1-2 Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms.

COMMON CORE STATE STANDARDS FOR ENGLISH LANGUAGE ARTS

Common Core ELA Standards:

Grades 9–10

- CCSS.ELA-LITERACY.RST.9-10.2. Determine the central ideas or conclusions of a text; trace the text's explanation or depiction of a complex process, phenomenon, or concept; provide an accurate summary of the text.
- CCSS.ELA-LITERACY.SL.9-10.1.D Respond thoughtfully to diverse perspectives, summarize points of agreement and disagreement, and, when warranted, qualify or justify their own views and understanding and make new connections in light of the evidence and reasoning presented.
- CCSS.ELA-LITERACY.SL.9-10.5 Make strategic use of digital media (e.g., textual, graphical, audio, visual, and interactive elements) in presentations to enhance understanding of findings, reasoning, and evidence and to add interest.

Grades 11–12

- CCSS.ELA-LITERACY.RST.11-12.2. Determine the central ideas or conclusions of a text; summarize complex concepts, processes, or information presented in a text by paraphrasing them in simpler but still accurate terms.
- CCSS.ELA-LITERACY.SL.11-12.1.D. Respond thoughtfully to diverse perspectives; synthesize comments, claims, and evidence made on all sides of an issue; resolve contradictions when possible; and determine what additional information or research is required to deepen the investigation or complete the task.

ITEAA STANDARDS FOR TECHNOLOGICAL LITERACY

Technology and Society, Standard 3: Students will develop an understanding of the relationships among technologies and connections between technology and other fields of study.

J. Technological progress promotes the advancement of science and mathematics.

Technology and Society, Standard 4: Students will develop an understanding of the cultural, social, economic, and political effects of technology.

I. Making decisions about the use of technology involves weighing the trade-offs between the positive and negative effects.

THINK

PAIR

Cell Cycle	Neoplasm
Oncogenes	Cell cycle checkpoints
Proto-onco genes	Cyclins
Tumor supressors	Cyclin-dependent kinases
P53	Contact inhibition
Metastasis	Apoptosis
Angiogenesis	

SHARE

Is it SMD or MCA: Sorting Targeted Therapies?

Instructors should individually cut out the cards below. The first two cards (all in caps) represent the two main types of targeted therapies—small molecule drugs (SMD) and monoclonal antibodies (MCA). Students should lay these out first to create the groups for the card sort. Next students should read through the descriptions of each of the types of therapy and try to decide which type they are, laying the card under the heading card—classifying them as either SMD or MCA. Have the instructor check to see if they are sorted correctly!

SMALL

MONOCLONIAL

MOLECULE

ANTIBODIES

DRUGS

HORMONE THERAPIES

slow or stop the growth of hormone-sensitive tumors, which require certain hormones to grow. Hormone therapies act by preventing the body from producing the hormones or by interfering with the action of the hormones.

SIGNAL-TRANSDUCTION INHIBITORS

block the activities of molecules that participate in signal transduction, the process by which a cell responds to signals from its environment. During this process, once a cell has received a specific signal, the signal is relayed within the cell through a series of biochemical reactions that ultimately produce the appropriate response(s).

GENE EXPRESSION MODULATORS

modify the function of proteins that play a role in controlling gene expression.

APOPTOSIS INDUCERS

cause cancer cells to undergo a process of controlled cell death called apoptosis. Apoptosis is one method the body uses to get rid of unneeded or abnormal cells, but cancer cells have strategies to avoid apoptosis. Apoptosis inducers can get around these strategies to cause the death of cancer cells.

ANGIOGENESIS INHIBITORS

block the growth of new blood vessels to tumors (a process called tumor angiogenesis). A blood supply is necessary for tumors to grow beyond a certain size because blood provides the oxygen and nutrients that tumors need for continued growth.

IMMUNOTHERAPY

triggers the immune system to destroy cancer cells. Some immunotherapies recognize specific molecules on the surface of cancer cells. Binding of the drug to the target molecule results in the immune destruction of cells that express that target molecule. Others bind to certain immune cells to help these cells better kill cancer cells.

PARP INHIBITORS

block an enzyme in cells called PARP that's helps repair DNA when it becomes damaged. DNA damage may be caused by many things, including exposure to UV light, radiation, certain anticancer drugs, or other substances in the environment. In cancer treatment, blocking PARP may help keep cancer cells from repairing their damaged DNA, causing them to die.

PROTEOSOME INHIBITORS

block the action of proteasomes, large protein complexes in the cell that help destroy other cellular proteins when they are no longer needed.

KINASE INHIBITORS

blocks enzymes called kinases that help control important functions, such as cell signaling, metabolism, division, and survival. Certain kinases are more active in some types of cancer cells and blocking them may help keep the cancer cells from growing. Kinase inhibitors may also block the growth of new blood vessels that tumors need to grow.

Yellow cards are **SMALL MOLECULE DRUGS** and Green cards are **MONOCLONICAL ANTIBODIES**

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RESEARCH SHEET: TARGETED CANCER THERAPY

Directions: Use the space below to record notes from your research that you will use in your presentation. As you perform your research, do your best to find reputable news sources, and focus on quality over quantity! Your notes do *not* have to be in complete sentences.

Name of your targeted therapy drug (pharmaceutical and medical names):

What gene mutation is associated with this treatment?

What category of targeted therapy is this? (small molecule drugs? monoclonal antibodies?)

What part of the cancer cell does your drug target?

Explain the mechanism of action of your drug.

Create a sketch of how your drug works in the cell. (You can use this to guide you as your build your 3-D model.)

What are the side effects or drawbacks of this drug? Is there any resistance over time seen in patients?

Can your drug be used in combination with other types of treatments?

What is the greatest benefit from this type of targeted therapy for lung cancer patients?