Unit Overview:

Unit Summary, Learning Standards, & Student Learning

FRED HUTCH Frontiers in Cancer Research Science Education Partnership

High School Advanced Unit: Immunotherapy

Unit Summary

This curriculum unit is designed to span approximately three weeks when enacted in Advanced/Honors Biology or Biotechnology courses. This unit focuses on the topic of cancer, leukemia, and immunotherapies as a way to explore concepts such as the cell cycle, cell growth, the immune system, and genetic mutations. Over the seven lessons, students are introduced to a case study featuring Kristin K., a woman diagnosed with a treatment-resistant form of leukemia and for whom a stem cell donor match could not be found. [This case study is based on a real person]. The case study explains how Kristin and her doctors at Seattle Cancer Care Alliance (the clinical arm of Fred Hutchinson Cancer Research Center) harnessed the power of her own immune system to treat her cancer. As the unit unfolds, students develop and revise a conceptual model on the immune system, cancer, and cancer treatments. Students discover that after chemotherapy fails, Kristin decides to enroll in a clinical trial using CAR T-cell therapy and CRISPR-Cas9 gene editing technology. The unit builds toward a wet lab in which students conduct gel electrophoresis focused on in vitro CRISPR Cas-9 on MHC genes in order to identify "self" from "foreign" to reduce the possibility of transplant rejection.

Through lab activities, classroom discussions, and research case studies, the concept of "productive uncertainty" in science is experienced. The prohibitive cost of the therapy and potential uses of CRISPR introduce students to important bioethical, health inequities, and social justice issues. Additional NGSS-aligned nature of science concepts are explored as students learn about the clinical trial process for approval of novel drugs and therapies.

This unit integrates with SEP teaching kits, particularly DNA Lab 2 and CRISPR (in development), both of which enable the exploration of genetic engineering techniques.

Learning Standards Alignment

NEXT GENERATION SCIENCE STANDARDS

Building Toward the NRC Framework & Next Generation Science Standards

The three focal Performance Expectations (PE) for this unit are listed below, along with the three-dimensional connections for each PE. Additional SEPs and CCCs not includes in these PEs, but integrated into the lessons within this unit, are marked with an asterisk (*).

Focal Performance Expectations (PEs):

- **HS-LS1-1**: Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins which carry out the essential functions of life through systems of specialized cells.
- **HS-LS1-2:** Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organizations.
- **HS-LS1-4:** Use a model to illustrate the role of cellular division (mitosis) and differentiations in producing and maintaining complex organisms.

Science & Engineering Practices (SEPs)	Disciplinary Core Ideas (DCIs)	Crosscutting Concepts (CCCs)
Constructing Explanations and Designing Solutions	LS1.A: Structure and Function	Structure and Function
Developing and Using Models	LS1.A: Structure and Function	Systems and Systems Models
Developing and Using Models	LS1.B: Growth and Development of Organisms	Systems and Systems Models
Engaging in Argument from Evidence* Analysing and Interpreting Data*		Nature of Science: • Science Addresses Questions About the Natural and Material World*

		• Science is a Human Endeavor*

NGSS Lead States. 2013. *Next Generation Science Standards: For States, By State*s. Washington, DC: The National Academies Press.

COMMON CORE STATE STANDARDS

Building Toward Common Core State Standards in Mathematics:

- **MP.4:** Model with mathematics. (HS-LS1-4)
- **HSF-IF.C.7:** Graph functions expressed symbolically and show key features of the graph, by hand in simple cases and using technology for more complicated cases. (HS-LS1-4)
- **HSF-BF.A.1:** Write a function that describes a relationship between two quantities. (HS-LS1-4)

National Governors Association Center for Best Practices, Council of Chief State SChool Officers. (2010). *Common Core State Standards (Mathematics*). Washington, DC: National Governors Association Center for Best Practices, Council of Chief State School Officers.

Building Toward Common Core State Standards in English Language Arts:

- **RST.11-12.1:** Cite specific textual evidence to support analysis of science and technical texts, attending to important distinctions the author makes and to any gaps or inconsistencies in the account. (HS-LS1-1)
- **WHST.9-12.2:** Write informative/explanatory texts, including the narration of historical events, scientific procedures/ experiments, or technical processes. (HS-LS1-1)
- **WHST.9-12.9:** Draw evidence from informational texts to support analysis, reflection, and research. (HS-LS1-1)
- **SL.11-12.5:** 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. (HS-LS1-2; HS-LS1-4)

National Governors Association Center for Best Practices, Council of Chief State SChool Officers. (2010). *Common Core State Standards (English Language Arts*). Washington, DC: National Governors Association Center for Best Practices, Council of Chief State School Officers.

Student Learning

Assumptions About Students' Prior Knowledge:
This unit consists of 7 multi-part lessons designed for students who have already taken basic Biology. Students should have already received a general introduction to the central dogma, enzyme function, the basics of DNA, the cell cycle and how it can sometimes go wrong (genetic mutations leading to cancerous cells). Little background knowledge of the immune system is expected, however students should have some basic understanding of the circulatory system and its primary function. It is also assumed that students have little background knowledge of clinical trials.

What Students Figure Out:
See the Lesson Progression below for lesson-level information on student sensemaking, what students find out during each lesson, and how each lesson leads into the one that follows it.

Through this seven-lesson unit, it is anticipated that students will figure out the following key concepts through engagement in scientific practices:

- Normal immune system function includes how the different cells deal with various threats to the body, including cancer.
    - The relevant parts of the immune system involved in leukemia are leukocytes (lymphocytes, granulocytes, monocytes, and macrophages).
    - Students will understand how the different parts of the immune system fit together including bone marrow, various blood cells (rbc's and white blood cells), lymph nodes and lymphatic ducts and glands.

- Normal circulatory system function relates to the immune system and circulation of the immune system cells.
    - The relevant components of the circulatory system involved in leukemia are those involved in the transport of leukocytes (plasma and the cellular components) and those involved in the production of leukocytes (bone marrow).
    - The circulatory and immune system interact to provide response to infection and cancer.

- Leukemia is a group of cancers that involves the immune system (leukocytes). Mutations/ environmental impacts influence whether a person develops this cancer and what type of leukemia they develop.
    - DNA contains instructions for proteins that regulate the cell cycle, including those that increase cell division and slow cell division.

  - Environmental factors such as smoking may increase a person's risk of leukemia by causing mutations. When these mutations occur in oncogenes and tumor suppressor cells, there is an increased risk of cancer

- The emerging field of genetic engineering offers new techniques, such as CRISPR gene editing.
  - CRISPR techniques have impacted doctor's abilities to engage a patient's own immune system to more effectively treat leukemia and potentially other cancers.
  - However, there are complex social and bioethical issues relating to the use of CRISPR, including the misuse of this technology.

- Clinical trials are used to test the safety and efficacy of novel drugs and therapies on humans prior to being approved for clinical use. There are ethical issues involved in enrolling patients for clinical trials for cancer treatments.

Lesson Progression:

Lesson 1: Introduction | Initial Model	Students will create an initial model demonstrating what happens in Kristin's body (a patient diagnosed with Acute Lymphoblastic Leukemia) when she has cancer and during successful Car T-Cell therapy. They will share ideas they already know and generate questions that would be helpful to have answers for through a driving question board.
Lesson 2: Intro to Immunology	In this lesson, students figure out the normal immune response to cancerous cells and how this immune response can be overcome by the cancer cells. New vocabulary terms related to immunology and leukemia are pre-taught through a vocabulary matching exercise.
Lesson 3: What is Leukemia?	Through a cooperative group worksheet, students are guided to understand that the cell cycle is tightly regulated by groups of proteins coded for by proto-oncogenes and tumor suppressor genes. They learn that mutations to these genes contribute to cancer development, and what cell types are affected in leukemia, specifically acute lymphocytic leukemia. In the second part of this lesson, students learn that productive uncertainty is an important experience in science - that engaging in ideas with which the answer is not clear is what leads to new discoveries and understandings. They

	will see that there are multiple risk factors for survival of ALL including those at an individual level and a societal level. They will also give ideas that they think might increase the survival for people with ALL.
Lesson 4: Leukemia Treatments	In this lesson, students figure out how chemotherapy and stem cell (bone marrow) transplantation can each act to treat leukemia. They understand the cause of common chemotherapy side effects and how stem cell donors are matched to recipients. They end by considering the drawback of these treatments and how these drawbacks could potentially be addressed.
Lesson 5: Clinical Trials & Cancer	In this lesson, students are reminded of Kristin K.'s story, specifically that her "last hope" was a clinical trial. They learn what a clinical trial is and address questions about whether one should be encouraged to participate, how clinical trials for cancer treatments differ from other clinical trials, and whether a treatment should be approved.
Lesson 6: CAR T-Cells	Students will figure out how CAR T-cells are made, how they work, and why they don't work to cure all cancers. The question that is likely to emerge is "How do we solve the problems associated with CAR T-cell therapy? This lesson leads into the next lesson, which revolves around how some of the problems may be solved by the creation of Universal CAR T-cells.
Lesson 7: CRISPR-Cas9	In this lesson, students figure out the parts and function of the CRISPR Cas9 system for editing a piece of DNA. They then use a bead model of this tool to cut the same gene that scientists are cutting as they work to create a Universal CAR T cell. Students end the unit with a CRISPR wet lab which allows them to check their understanding of how guide RNA's work in the Cas9 system, and perform agarose gel electrophoresis to check the accuracy of the cut.

Assessment of Learning

Summative Assessment:
In addition to embedded formative assessments in the lesson plans, there are several components to assess student learning for this unit. Lesson 6 challenges students to complete a final version of the

conceptual model that they refine over the course of the unit. Lesson 7 asks students to explore CRISPR Cas-9 technology and design an educational poster summarizing their findings, and then engages students in a wet lab using gel electrophoresis technique.

Unit Calendar

Unit Calendar:

This unit calendar provides an example of how the lessons that make up this unit might progress over a three week period. The calendar assumes one 55 minute class period per day and five days per week of instruction. Differences due to block schedules or remote learning or hybrid schedules will require adaptation.

Color Code

- Classroom activity
- Wet lab activity
- Formative and Summative assessments
- Lessons with possible extension activities are indicated with a diamond (♦).

	Monday	Tuesday	Wednesday	Thursday	Friday
Week 1	Lesson 1: Initial Model (Activity 1.1 & 1.2)	Lesson 2: Intro to Immunology (Activity 2.1)	Lesson 2: Intro to Immunology (Activity 2.2)	Lesson 3: What is Leukemia? (Activity 3.1)	Lesson 3: What is Leukemia? (Activity 3.2)
Week 2	Lesson 4: Leukemia Treatments (Activity 4.1)	Lesson 5: Clinical Trials & Cancer (Activity 5.1 & 5.2)	Lesson 5: Clinical Trials & Cancer (Activity 5.3)	Lesson 6: CAR T-Cells (Activity 6.1)	Lesson 6: CAR T-Cells (Activity 6.2)
Week 3	Lesson 6: CAR T-Cells (Activity 6.3)	Lesson 7: CRISPR-Cas9 (Activity 7.1)	Lesson 7: CRISPR-Cas9 (Activity 7.2)	Lesson 7: CRISPR-Cas9 (Activity 7.3)	Summative Assessment

Alternate Instructional Plans:

Differences due to block schedules or remote learning or hybrid schedules will require adaptation. See the section below on Adaptations for Remote Teaching & Learning.