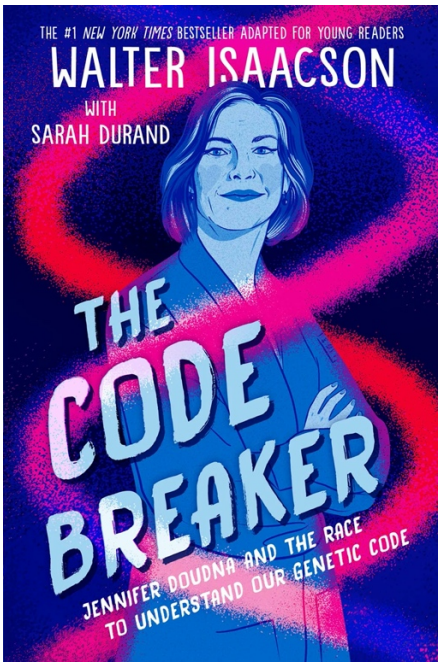

A Curriculum Guide to

The Code Breaker—Young Readers Edition:

Jennifer Doudna and the Race to Understand Our Genetic Code

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About the Book

In 2020, Jennifer Doudna and her research partner, Emmanuelle Charpentier, were awarded the Nobel Prize in Chemistry for the development of a method for genome editing. Their "genetic scissors" revolutionized life science by giving scientists a tool to precisely change the DNA of living things in order to better understand life's inner workings. This tool created great possibilities for plant research and crop development that could positively affect agriculture in our changing climate. It also created new opportunities for curing inherited diseases in people. The opportunity to use this tool for medical progress came in early 2020 when COVID-19 spread rapidly through countries worldwide. Doudna and collaborators quickly focused their work on addressing the pandemic by removing barriers to collaboration and establishing a clinical testing laboratory institute to develop new types of COVID-19 diagnostics.

Doudna's passion and progress in this field go back to her childhood when she was in sixth grade and her dad gave her a paperback titled *The Double Helix*. She was excited by the book's story of a competitive race to discover the code of life. Her passion also led her to defy the high school counselor who told her girls didn't become scientists, when she followed her curiosity to Pomona College in Claremont, California. There she was encouraged to pursue science. She earned a bachelor's degree in chemistry and then went to Harvard University where, in 1989, she finished a biochemistry doctorate.

Completing her education put Doudna at the beginning of a long career with the chemistry underlying RNA and the clues it could provide about the origins of life. Her career has involved universities, laboratories, collaboration, competition, and ingenuity. She turned her discovery into invention when her work and the work of other scientists led to CRISPR—an easy-to-use tool that can edit DNA. Just as CRISPR brings to light the inner workings of life, this book shines a light on leaders in science and previously unheard-of scientists whose discoveries have benefited us and whose work raises interesting ethical questions for future generations to ponder.

Discussion Questions

The following discussion questions may be used for individual writing prompts or to guide robust classroom discussion. Several may also serve as debate or research topics. (A Research and Debate section follows.) Questions are also formulated to allow students to personally reflect and relate to Doudna's experiences so that they may more meaningfully connect with the text.

Introduction

1. In *The Code Breaker*'s introduction, we learn about Victoria Gray, who had sickle cell anemia and with CRISPR gene editing found herself improving. Gray said, "'High school graduations, college graduations, weddings, grandkids—I thought I wouldn't see none of that, now I'll be there to help my daughters pick out their wedding dresses.'" What is it like when you suddenly have a different life? We often celebrate people's fortitude in loss or diminished abilities, but

what about unexpected healing and expanded abilities? How do you think Gray's approach to life changed? Why is Gray's story at the beginning of the book?

Part One: The Origins of Life

2. During her elementary years in Hawaii, Doudna felt alone and isolated. From chapter one:

> In the third grade, she was so unloved by her classmates that she had trouble eating, and she developed all sorts of digestive problems that she later realized were stress related. Kids teased her every day—especially the boys, because unlike them she had hair on her arms. To protect herself, she escaped into books and developed a defensive layer.

There are many ways to escape hurt, stress, and discomfort. What are some ways that you have watched people escape and how do you escape? Was Doudna's escape into books good for her, or should she have spent her energy working things out with her classmates? How did this information in the book help you understand Doudna?

3. Doudna drew inspiration from and developed curiosity about her natural surroundings in Hawaii.

> We all see the wonders of nature every day, whether it be a plant that moves or a sunset that reaches its pink finger rays into a sky of deep blue. The key to true curiosity is pausing to think about the causes. What makes a sky blue or a sunset pink or a leaf of sleeping grass curl?

Review Chapter One: Hilo, and then imagine you are new to your town or neighborhood. What are the natural things in your environment that stand out to you? What inspires you? What are you curious about?

4. After learning about James Watson and Francis Crick, who are credited with discovering the double helix structure of DNA, we learn a bit about Rosalind Franklin, a structural biologist and

crystallographer whose work making clear X-rays of DNA molecules allowed Watson and Crick to make their discovery. Watson and Crick used Franklin's data without permission and did not credit her in their discovery. In fact, as the book points out, they and the larger scientific community were dismissive of women in science. Why did Watson and Crick believe they did not have to credit Franklin and her data in their discovery? How should Watson and Crick have credited Rosalind Franklin for aiding in their discovery?

5. Review Chapter Two: Genes and DNA. Notice that discoveries about genes and DNA are happening simultaneously in different places around the world. Throughout history we see this with inventions and discoveries as well as with political, social, and cultural movements. This was true before the internet and the access to global information we have today. What is something that has happened or is happening in your lifetime that seems to be a global occurrence? Think about discoveries, cultural and political movements, or social changes.

6. When Doudna told her high school counselor she wanted to study chemistry, he told her that "Girls don't do science." (Chapter three) Has anyone ever told you that you can't do something or are incapable of doing something? Did that discourage you or inspire you? How did you react when you were told you couldn't do something?

7. Doudna was struck by the diversity in modern science, and during her career she collaborated and communicated with diverse scientists around the globe. Why is diversity important in progress, scientific or otherwise?

8. From early in her career, Doudna worked collaboratively and always asked permission to use other people's work. Why was this important? Should all scientists ask permission? What could be the reasoning for scientists not to share their findings?

9. Doudna completed her PhD (Doctor of Philosophy) research under a scientist named Jack Szostak. Szostak's guiding principle was *Never do something that a thousand other people are doing*. What do you think is the purpose of this principle? Does it expand or limit possibilities? Why did it appeal to Doudna?

Part Two: CRISPR

10. Doudna and her colleagues publish papers on their discoveries when they deem them important enough to share. Think about a process you went through that resulted in an outcome you were proud to announce. Do not limit this to school. Think about volunteer or paid work, home projects, creative projects, and extracurricular activities. What discovery or accomplishment would you publish a paper about?
Extension: Write your paper.

11. Review Chapter Nine: Restless, in which Doudna reaches a point in her career when she thinks about focusing on applying knowledge rather than gaining it. What experiences have you had in which you gained knowledge and then applied it? At which points in your education were you focused on gaining knowledge and at which points were you focused on using that knowledge?

12. Collaboration is a constant in Doudna's story. At the end of Chapter Twelve: Making Connections around the World, that collaboration is described: "Jinek and Chylinski soon connected, and the rest is history. Theirs was a meeting that would bring about great things, because—together—Jinek, Chylinski, Charpentier, and Doudna would soon make one of the most important advances in modern science." Collaboration seems very important to Doudna. Why is collaboration important in science in general? What about in other fields? What are the benefits and challenges of collaboration?

Part Three: Gene Editing

13. Jennifer Doudna was willing to take risks. This does not mean she did foolish or dangerous things, but she was willing to try new things and risk failing at them in order to learn and find success. This is an essential part of having a growth mindset. If you believe talent can be developed through hard work and trial-and-error exploration, then you also have a growth mindset. What are the advantages to having a growth mindset? Are there disadvantages, and if so, what are they?

14. As already noted, this story is full of collaboration, as well as healthy competition. It is also about ideas and discoveries and who owns them. Did Watson and Crick steal Rosalind Franklin's work? Did Feng Zhang steal Doudna's work? Did Doudna steal Charpentier's work? Can you steal ideas and discoveries?

15. Review Chapter Twenty-One: Commercializing CRISPR, in which Doudna develops a bad feeling about Feng Zhang and loses trust in him. She tells him, "'I'm done. I'm not going to work with people I can't trust, people who stab you in the back. You stabbed me in the back.'" Was her mistrust justified, or was she allowing emotions to dictate her decisions? Was she fair to Zhang? Was he fair to her? Explain your reasoning.

Part Four: CRISPR in Action

16. Review Chapter Twenty-Four: Creating Happy, Healthy Babies, and think about the possibilities Doudna is weighing regarding the potential of CRISPR technology for good versus the potential dangers. These feelings are similar to those of scientists that worked on the atomic bomb. Was dropping the bomb to end WWII worth the loss of life? Did it ultimately save lives? Split the class into assigned pro- and con-CRISPR sides, and debate the lifesaving potentials against the dangers.

17. Scientists recognize the possibility of using Cas9 technology to prevent genetic diseases in in-vitro fertilization (IVF). This is when fertilization happens in a lab. Review Chapter Twenty-Four: Creating Happy, Healthy Babies and make a list of pros and cons related to using this technology in IVF.

18. In the book, gene editing is referred to as being "like the Wild West —a huge, promising frontier, but filled with uncertainty and danger." (Chapter 24) Many people talk about the internet this way. Are these comparisons accurate? If so, how? If not, why not, and why are people making them?

Part Five: CRISPR Babies

19. Review Chapter Seventeen: Doudna's First Competitor and Chapter Twenty-Seven: He Jiankui. Compare the childhoods and education of Feng Zhang and He Jiankui. Which do you believe provides a stronger foundation for following your passion: growing up poor and struggling to develop ingenuity, or having material advantages readily available?

Part Six: The Moral Questions

20. Chapter Thirty-One: Doudna's Ethical Journey, concludes with words from Jennifer Doudna. "'We've never seen anything like this before,' Doudna says. 'We now have the power to control our genetic future, which is awesome and terrifying.'" Why is this both awesome and terrifying?

Part Seven: CRISPR and COVID-19

21. COVID-19 created both opportunity and need that dictated the direction of scientists' work. Your lives have been very affected by COVID-19. What ingenuity and inspiration have you taken from your experiences with this global pandemic?

22. During the Cold Spring Harbor Laboratory's annual CRISPR conference in August 2020, Rosalind Franklin's one hundredth birthday was celebrated. Unfortunately, Franklin died young and was not there to celebrate, but the gathered scientists recognized her pioneering work on the structure of DNA.

> The meeting also wove in another strand of this book. It celebrated the hundredth anniversary of the birth of Rosalind Franklin, whose pioneering work on the structure of DNA had inspired Doudna, when she'd read *The Double Helix* as a young girl, to believe that women could do science. The cover of the meeting's program featured a colorized photograph of Franklin peering into a microscope

What strands do you follow? What event in your life do you carry a memory of and how has it informed your interests and pursuits?

23. During the Cold Spring Harbor conference, a discussion was held about Black people's distrust of medical trials, which was traced back to the Tuskegee experiment. This experiment

was ultimately deemed “ethically unjustified.” What makes an experiment ethical or unethical? Why are ethics important in science?

24. In 2020 Jennifer Doudna and Emmanuelle Charpentier were awarded the Nobel Prize in Chemistry. Five separate Nobel Prizes are awarded each year to people that, during the preceding year, have contributed to work that benefits all people. Learn about the Nobel Prize and other recipients over the years. Do you think their work was worthy of the Nobel Prize? Why or why not?

25. According to Chapter Forty-One: The Next Scientific Horizon:

> Most of us someday will have detection devices in our homes that will allow us to check ourselves for viruses and many other health conditions. We will also have clothes or glasses or wristbands that can monitor all our biological functions, and they will be networked so that they can share information and create a global bio-weather map showing in real time the spread of biological threats. All of this has made biology an even more exciting field of study. The proof is in the data: in August 2020, applications to medical school had jumped 17 percent from the previous year.

Should we have independent access to such complete medical information, or is this dangerous as most of us lack medical training? What advantages and disadvantages do you see to this future possibility?

Epilogue

26. Review this quote from the book’s epilogue:

> After millions of centuries during which the evolution of organisms happened “naturally,” we humans now have the ability to hack the code of life. Or, to confuse those who would label gene editing as “unnatural” and “playing God,” let’s put it another way: nature and nature’s God, in their infinite wisdom, have evolved a species that is able to modify its own genome, and that species happens to be ours.

Just because we *can* do something, should we do it?

Research and Debate

The following topics can be used for argument papers (https://science.nasa.gov/citizenscience) or classroom debates (https://science.nasa.gov/citizenscience). For argument papers, students take a position, use evidence from the text and another source or sources, and use a classic format. For debates, choose the topic as a class, and divide the class into groups, randomly assigning positions to each group. Allow students time to research and prepare for their debate. Both of these options are great opportunities for students to engage in a close reading of the book and to practice research skills as well as writing or speaking skills. Please remember that students should be able to argue both sides in a debate so be careful about assigning debate topics in which students have to argue for things that are inhumane or offensive.

- Watson, Franklin, and Crick: Watson and Crick should receive all the credit versus Franklin should be credited for her role in the discovery of the double helix.
- Ethics in Science: Using other scientists' work with versus without permission; Using other scientists' work with versus without giving them credit.
- Ethics in Science: Using Cas9 technology to prevent genetic diseases in in-vitro fertilization is ethical versus it is unethical to use this technology in this way.
- Ethics in Science: Gene editing technology should only be used when medically necessary (there are no other medical approaches) versus gene editing should be used even when other medical options are available so that the technology can be perfected.
- Human Development: Being poor and lacking resources develops creativity and ingenuity versus creativity and ingenuity come from access to the best resources.

Extension Activities

Below are science experiments, projects, and collaborative classroom activities designed to enhance engagement and understanding as well as spark further curiosity.

1. Let's Look at DNA!

Using simple ingredients and procedures, you can extract and observe the building blocks of life.

Materials	**Steps**
• Strawberries • Zip-closure sandwich bag • Measuring cup • Measuring spoons • 1/2 tsp salt (Salt ensures that the proteins in the cell are kept separate from the DNA.) • Water • Liquid dishwashing detergent (The dishwashing liquid bursts open the cells of the strawberries, releasing the DNA.) • Small glass bowl or cup • Coffee filter • Rubber band • Pipette • Test tube • 1/2 cup isopropyl rubbing alcohol, 70%, chilled in the freezer (Insoluble molecules clump together and become visible. DNA is not soluble in alcohol; therefore, it makes the DNA strands clump together and become visible to the naked eye.) • Bamboo skewer or other thin rod	1. Remove the stem from the strawberry, place the berry in a zip-closure bag, and remove most of the air before you seal the bag. 2. Smash the strawberry (through the bag) with your hand. Do not hit against the table or be too rough as this may damage the DNA. 3. Mix 1/2 teaspoon of salt, 1/3 cup of water, and 1 tablespoon of dish soap in another bag. Shake to mix well. This is your DNA extraction solution. 4. Add two tablespoons of your solution to your strawberry bag. Continue mashing. 5. Place your coffee filter over the bowl or cup and secure it with a rubber band. 6. Slowly pour the strawberry mixture onto the coffee filter, catching solids with the filter. 7. Use the pipette (or a small measuring spoon) to take a spoonful of the liquid that dripped into the glass container and place it in the test tube. 8. Without tilting the tube, add a spoonful of the chilled alcohol to the test tube. 9. The strawberry DNA will clump together and float to the top of the

Why are we using strawberries? Our cells have two copies of their DNA while strawberry cells have eight. They are called octoploids. This makes it easier for us to extract enough DNA to be able to see it with the naked eye.	alcohol. It should look like a white, stringy cloud. 10. You can use your skewer to collect the DNA. 11. Document your findings with a sketch, photograph, or description.

CCSS.ELA-LITERACY.RST.6-8.3; CCSS.ELA-LITERACY.RST.6-8.9; This is an adapted version of an NGSS high school lab.

2. Citizen Science

Jennifer Doudna was very influenced by her natural surroundings in Hawaii. She has also stressed the importance of collaboration throughout her career. Discussion question #3 asks students to become aware of the natural environment around them. This experience can be applied through a citizen science project, which is a collaborative way for people to share observations and information. Citizen scientists are curious people that are not professional scientists, but who use their observations to collaborate with professional scientists.
Sources for finding Citizen Science projects are citizenscience.gov, zooniverse, scistarter, and NASA Science.

Zooniverse: https://www.zooniverse.org/

SciStarter: https://scistarter.org/citizen-science

NASA Science: https://science.nasa.gov/citizenscience

3. Adaptations

1. Ask students to review Chapter Two: Genes and DNA.
2. As a class, discuss adaptations. Adaptations are the adjustment of organisms to their environment to improve their chances at survival in that environment. Adaptations can be divided into three types: Behavioral, Physiological, and Structural.
3. **Behavioral Adaptations** are organism responses that help it to survive and reproduce. Migration and hibernation are examples of behavioral adaptation.

4. **Physiological Adaptations** are body processes that help an organism survive and reproduce. Temperature regulation and production of poison are examples of physiological adaptations.
5. **Structural Adaptation**s are physical features that help an organism survive and reproduce. The thickness and type of fur and the structure of a beak are structural adaptations.
6. Next discuss our changing climate and warmer temperatures, extreme weather events, less access to water, wildfires, and rise in sea level.
7. Now ask students if gene editing can engineer plants and animals to survive in a changing climate. Discuss this as a class before giving students the individual or small group assignment.
8. Assignment: Ask students to brainstorm a list of adaptations that could aid humans in withstanding climate change. They should explain the purpose of each adaptation and categorize it as behavioral, physiological, or structural. They may make a sketch or sketches to accompany these explanations.

4. Feeding Microorganisms

In Chapter Three: Education of a Biochemist, Doudna worked with yeast because "Yeast cells can easily take up pieces of DNA and incorporate them into their genetic makeup." In small groups, conduct your own yeast experiment.

Materials (per group)	**Steps**
• 3 packets of dry yeast (or 6 ¾ tsp) • 3 recycled plastic water bottles of the same size • 3 balloons • 1 funnel • 1 spoon • Water: access to refrigerated, room temperature, and means of boiling water	1. Mark the three bottles: 1. Chilled, 2. Room temperature, 3. Boiling 2. Using the funnel, measure 7 ounces of the temperature-type of water into each bottle. Be very careful with the boiling water. 3. Use the thermometer to take the temperature of the water in each bottle. (Depending on thermometer and bottle

- Measuring cup
- Thermometer
- Sugar
- A permanent marker to mark the bottles
- Ruler
- A notebook for your observations in words and sketches

Variation:
This experiment uses water temperature as a variable. You can conduct the experiment a second time using the same water temperature for all three, but using different amounts of sugar, with one bottle receiving no sugar. What happens in this variation?

Science:
Yeast, a fungus, needs a source of energy for life and growth, so it eats the sugar. As it does this, it releases carbon dioxide. The CO_2 gas escapes the bottle and fills the balloon.

openings, you may have to do this step before pouring the water in the bottles.) Record this on the bottles and in your notes.

4. Add a tablespoon of sugar to each bottle and gently swirl to dissolve the sugar.
5. Add one packet, or 2 ¼ tsp, of yeast to each bottle.
6. Now stretch a balloon over the neck of each bottle. Write the time on the bottles. (Try to cover each bottle at similar times so three group members should attach the balloons simultaneously.)
7. This is a good time for group discussion about the experiment as you observe the bottles and wait for the balloons to expand.
8. Record the time as each balloon rises.

Questions to Consider:

- Do all the balloons rise? Why or why not?
- What was the role of yeast, sugar, and temperature in each bottle?
- What caused the balloons to rise?

CCSS.ELA-LITERACY.RST.6-8.3; NGSS: **MS-PS1-2 Matter and its Interactions**

5. Classroom Science Conference

Jennifer Doudna presented at, attended, and organized conferences. An academic conference is an event during which researchers present their work to one another. They can be one-day or multiday events. Work may be presented in oral and/or visual presentations, papers, or posters. This is a way for people in a field to form and maintain connections and learn about new developments and discoveries. For your classroom conference, establish goals and parameters. You may want to use the extension from discussion question #10. You may want to use other topic guidelines. Next, decide on the presentation format: Is everyone using the same format or are there options? Finally, plan your day or days and give students a time limit or expectation for their presentations. Alternatively, invite another class or staff members and invite them to walk through the displayed student work and ask students questions about their research and findings. A poster session conference is a great way to give students the opportunity to better understand DNA, RNA, and CRISPR-Cas9 gene editing by explaining and visually creating models of these things.

6. Crystals and Temperature

In Chapter Five: Twists and Folds of Structural Biology, Doudna discovers the role of temperature in obtaining crystals of the RNA molecule. This experiment is an opportunity to explore the role of temperature in crystal formation.

Epsom Salt Crystals

Materials	**Steps**
Materials: • ½ cup Epsom salts divided in half • Two small shallow cups or bowls • Hot tap water • (optional) Food coloring • (optional) Coffee filter or paper towel **Crystal Science:**	1. In each cup or bowl, stir 1/4 cup of Epsom salts with 1/2 cup of very hot tap water until the solid salt is fully dissolved. If you are adding food coloring, do so now. 2. If you have some sediment, or undissolved solid, you may pour your liquid through a coffee filter or paper towel. Be very careful since the water is hot.

Epsom salt is an inexpensive, nontoxic salt. Epsom salt is another name for the chemical magnesium sulfate ($MgSO_4$), but the crystals incorporate water to form magnesium sulfate heptahydrate ($MgSO_4 \cdot 7H_2O$). The temperature of the water determines how much magnesium sulfate it can hold; it will dissolve more in hotter water. As the solution cools, the magnesium sulfate atoms run into each other and join together in a crystal structure. It forms monoclinic crystals that can assume a variety of shapes, but most often look like crystal shards or needles. Left undisturbed, your crystals should last for a few months or more.	3. Place one cup or bowl with the liquid in it in a sunny location and the other in the fridge. 4. The shape and size of the crystals depends on their growing conditions. Larger crystals should grow in a sunny location, where the temperature is warm and evaporation concentrates the liquid. These crystals may take a few hours to a couple of days to grow. Quick crystals, which are smaller and delicate-looking, grow when the liquid cools quickly in a refrigerator. Quick crystals usually grow within 30 minutes to a couple of hours.

NGSS: **MS-PS1-2 Matter and its Interactions**

7. Acronyms

There are many acronyms in this book. An acronym is formed from the initial letter or letters from a longer phrase.

1. Discuss the book, and as a class group, identify the acronyms. List these on the board or a piece of poster paper.
2. Next, ask everyone to practice by turning their name into an acronym. They will use the letters from their names to write down adjectives that describe them. Example: JENNIFER (Justice, Enthusiasm, Notable, Nobel winner, Ingenious, Friendly, Engaging, Remarkable)
3. Ask some students to share their name acronyms with the class.
4. Finally, assign everyone the task of creating an acronym from a frequently used phrase. For example, the phrase “students are dismissed” becomes SAD. Ask students to think about daily announcements or phrases that a coach, band director, or teacher might use frequently, and make an acronym of that phrase.

8. Timeline Slideshow

Ask students to use a slide program such as PowerPoint or Google Slides to create a time line of significant events in the book that led to the development of CRISPR-Cas9. Begin with the work of Franklin, Watson, and Crick and conclude with COVID-related advancements. Establish parameters such as the number of slides, amount of text, number of images, etc. Students may hand these in or present them to the class.

9. Inventory

Lead a classroom discussion about research, discovery, and advancement. Talk about the changes in your lifetime versus those in your students' lifetimes. Look toward the future and reflect on the book. Ask students to choose an environment (home, school, community center, parent workplace, etc.) that they are able to take time to slowly walk through. As they do this, they should make a list of inventions, discoveries, and technological advancements that they see. Lists will vary greatly as some people will look far back in time and note things like glass windows, wheels, or gears while others may focus on modern technology. That's okay. Accept all perspectives, and use the lists to guide a classroom discussion that evaluates the effectiveness of technological solutions and scientific advancements.

10. Crossword Puzzles

Students may use the vocabulary list at the end of the book and an online crossword puzzle creator to create puzzles. Once all puzzles are created, distribute them randomly. Remind them to use the book for reference as they write the clues.

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