FUTURELAB+

BIOMED

Behind the Scenes of Scientific Breakthroughs

Senolytics: Our War Against Aging!

Developed in partnership with:

Discovery Education and Ignited

In this Lesson Plan:

Print the **Teacher Section** →

Print the **Student Section** →

This document is separated into two sections, For Teachers [T] *and* Student Resources [S]*, which can be printed independently.*

Select the appropriate printer icon above to print either section in its entirety.

Follow the tips below in the Range field of your Print panel to print single pages or page ranges:

Single Pages (use a comma): T3, T6

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Cover Image
This is a conceptual illustration of genetic engineering.

BIOMED / BEHIND THE SCENES OF SCIENTIFIC BREAKTHROUGHS

Senolytics: Our War Against Aging!

ACTIVITY DURATION

Five class sessions
(45 minutes each)

DRIVING QUESTION

How can we improve the quality of life for the aging population?

ESSENTIAL QUESTIONS

In which part of the cell cycle are aged cells?

Are senescent cells harmful to the body?

Why do cells become senescent?

OVERVIEW

Senescent research and recent advances in the field have propelled its therapeutic possibilities. Discovering the causes of senescence, including telomere erosion, DNA damage, mitochondrial dysfunction, and epigenetic factors, could help scientists discover the various connections among these characteristics and how they play a role in cellular aging. Understanding the hallmarks of senescence assists biomedical researchers and other scientists with identifying biomarkers for the diagnosis of ailments connected to senescence. Lastly, all of this knowledge is necessary to determine possible drug targets to prevent cellular aging. As a result, senolytics is a popular field in the future of medicine for aging and any diseases associated with it.

In this lesson, students will review the most recent evidence on senescent cells. They will build models of the causes of senescence. Ultimately, they will summarize information to describe the potential benefits of senolytics.

OBJECTIVES

Students will be able to:

Discuss the process through which cells become senescent in the body.

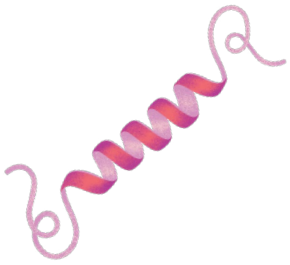
Explain why removing senescent cells would benefit an organism.

Define senolytic drugs as those that use small molecules to target and remove these cells from the body.

Summarize the potential benefits of senolytics.

BACKGROUND INFORMATION

In 1800, the average life expectancy of an American male was 41.7 years old. Today, it is 78.9 years. That's an increase of over 37 years—virtually another lifetime! In another 200 years, will the life expectancy of the average American male double again to be closer to 150? Some scientists think so. That's because scientists are learning more and more about what causes cells to age and die. This process, called senescence, could potentially be reversed through genetic engineering. As with other biomedical advances, there are ethical issues associated with reversing cell senescence. Would only wealthy people be able to avoid aging by paying for expensive medical treatments? What would happen to our planet if it got more and more crowded? Could we inadvertently direct a cell to replicate forever and cause cancer? Students will discuss these issues as they learn the biomarkers associated with cellular aging and examine the process of cell senescence.



Materials

- **Causes of Senescence Model Capture Sheet**
- **Causes of Senescence Model Rubric**
- **Museum of Senescence Capture Sheet**
- **Signs of Cellular Senescence Capture Sheet**
- **Senescent Cell Removal Capture Sheet**
- **Senescent Cell Removal Rubric**
- **Senolytic Drugs Presentation Guidelines**
- **Senolytic Drugs Presentation Rubric**
- **Applications of Senescence Capture Sheet, Parts 1, 2, and 3**
- **Senolytics Infographic Guidelines**
- **Senolytics Infographic Rubric**
- **Ruler**
- **Scissors**
- **Glue or Tape**
- **Colored Pencils**
- **2–3 Cardboard Boxes Per Group**
- **Tissues**
- **Wooden Craft Sticks**
- **Aluminum Foil**
- **Cotton Swabs or Cotton Balls**
- **Foam Cups and Plates**
- **Beads**
- **Chenille Stems**
- **Modeling Clay**
- **Design Journal**

Pedagogical Framing

Instructional materials are designed to meet national education and industry standards to focus on in-demand skills needed across the full product development life cycle—from molecule to medicine—which will also expose students and educators to the breadth of education and career pathways across biotechnology.

Through this collection, educators are equipped with strategies to engage students from diverse racial, ethnic, and cultural groups, providing them with quality, equitable, and liberating educational experiences that validate and affirm student identity.

Units are designed to be problem-based and focus on workforce skill development to empower students with the knowledge and tools to be the change in reducing health disparities in communities.

SOCIAL-EMOTIONAL LEARNING

During Day 3, students will research various ailments, such as kidney disease, liver disease, and cardiovascular disease, that are related to cell senescence. Students may have had experience with these ailments and, therefore, may react more emotionally compared to other students. It is important to ensure that students are aware and remain empathetic toward each other. On Day 4, students will discuss social justice challenges that the introduction of senolytic drugs may cause. The importance of choice and right to well-being are topics that students will realize are not always aligned or guaranteed.

CULTURALLY AND LINGUISTICALLY RESPONSIVE INSTRUCTION

Students will brainstorm social justice challenges that the commercialization of senolytic drugs may present. They will discuss what challenges BIPOC and people of low income have with access to these through insurance or with being able to afford the medicine. Instructional strategies are used to provide culturally responsive options for peer interaction and validation of diverse cultures. The lesson offers opportunities for the growth of critical consciousness of self and community, while encouraging students to bridge the learning to their real-world experiences.

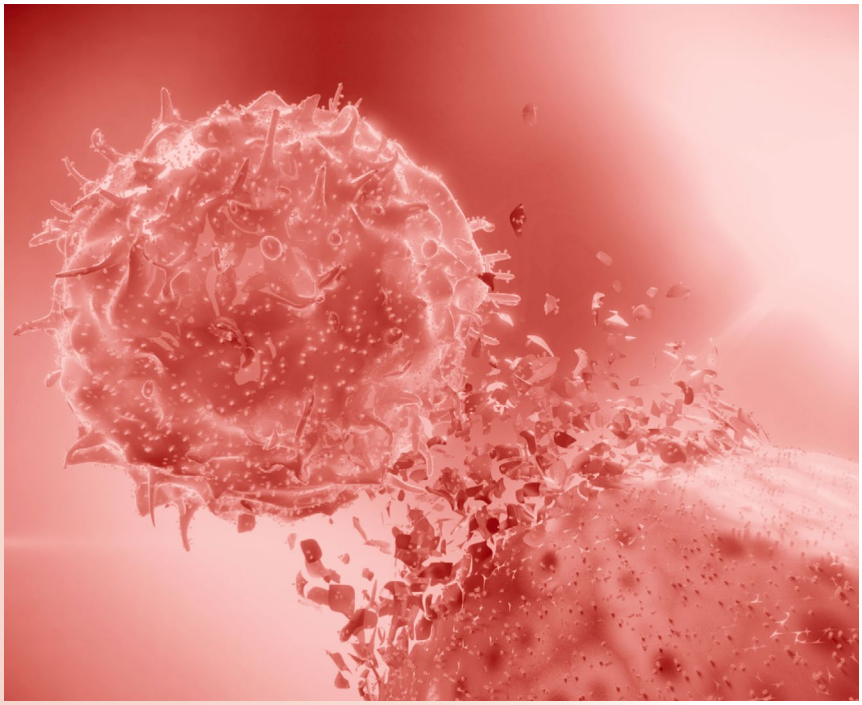
COMPUTATIONAL THINKING PRACTICES

Students apply the computational thinking practice of decomposing problems as they research one of the four factors that contribute to factors that cause senescence. They identify data that can be used to support the claim that removing senescent cells provides benefits to organisms. Finally, students summarize information learned throughout this lesson in order to create an infographic for someone with a non-science background.

CONNECTIONS TO THE PRODUCT LIFE CYCLE

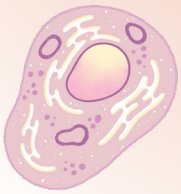
During Days 1 and 2, students discuss the **discovery** phase of the product cycle of medicine. Through research, students will discover information that could be used as possible biomarkers or drug targets. On Day 5, students will create an infographic to introduce a new commercial drug that will be available to consumers, highlighting the **commercial** phase of the product life cycle of medicine.

Have you ever wondered…



How many times can a cell divide?

The cell cycle is the process through which a cell copies its nucleus (chromosomes) and divides into two cells. Cells can divide between 40–60 times depending on the type of cell. The Hayflick Limit is known as the maximum number of times a human cell can undergo mitosis before undergoing cell death.



What are the factors that contribute to cells no longer being able to divide?

The cell cycle is an essential process for cells and organisms to ensure proper functioning of the body. Due to its significance, certain checkpoints in the cycle establish whether or not cells continue to divide or exit the cell cycle to eventually become destroyed.

How do scientists know cells have become old or aged?

Through research, scientists have discovered biomarkers of cellular aging. Certain tests can be performed to determine the absence or presence of a certain molecule or even the functioning or lack of a protein associated with cell senescence.

MAKE CONNECTIONS!

How does this connect to the larger unit storyline?

Identifying how cell senescence works is essential to ensuring proper drug targets and understanding how cells age. Removing senescent cells has been shown in lab animals to extend lifespan, and may soon be adapted to allow humans to live longer.

How does this connect to careers?

Pharmacokinetic scientists are responsible for studying the process of how drugs and chemicals react and move through the body. They play an important role in the discovery, development, and commercialization of safe drugs to be used to treat ailments and disease.

Biomedical researchers are responsible for assisting with researching various topics in the lab in order to help further understand certain processes and their connections with larger scientific concepts. They plan and perform science experiments and analyze the results in order to learn more about a particular research focus in humans.

Molecular biologists are scientists that study the action of molecules and how they affect organisms. They are responsible for investigating the structure and function of various molecules, and often work with cells. Molecular biologists often perform routine protocols, such as gel electrophoresis, western blotting, or protein expression and purification.

How does this connect to our world?

Several diseases are characterized by certain features of aging. From cancer cells to inflammatory diseases such as diabetes, aspects of senescence can be identified. This growing field requires scientists who are detail oriented and can break down larger processes into more manageable amounts of information. From discovering causes of cellular aging to identifying drug targets to treat senescence, research in this field will lead to discovery of the key to human longevity.

Day 1

LEARNING OUTCOMES

Students will be able to:

Understand the causes of senescence at the cellular level.

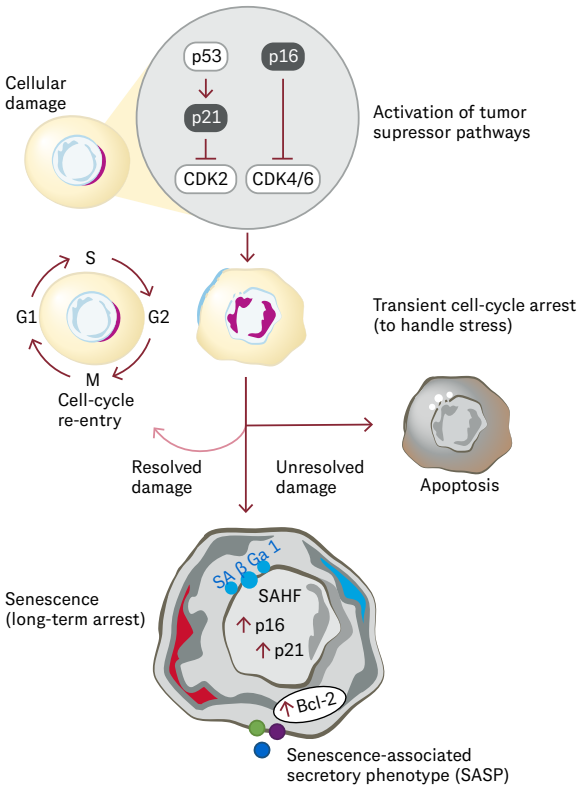
List the effects or the results of cell senescence.

Prepare a physical model depicting a chosen cause for cell senescence.

Procedure

Teacher Note > *Ask students if they remember when they discussed Henrietta Lacks in a previous unit. If time permits, the video also provides examples of research and medical advances that have been performed using HeLa cells. The Henrietta Lacks Video Capture Sheet, including questions related to the video, can be used.*

Whole Group (10 minutes)	
1	Let students know that during the next few days, they will talk about senescence, a cellular process in which aged or damaged cells stop dividing.
2	Tell them it has to do with the cell cycle, a concept previously discussed. Remind them of the steps of the cycle (G1, S, G2, M).
3	Let students know that cellular damage causes cells to react in different ways in order to handle the stress. If the DNA damage is fixed, then cells can enter back into the cell cycle. If not, then it has two possible outcomes, enter apoptosis or a process known as senescence.



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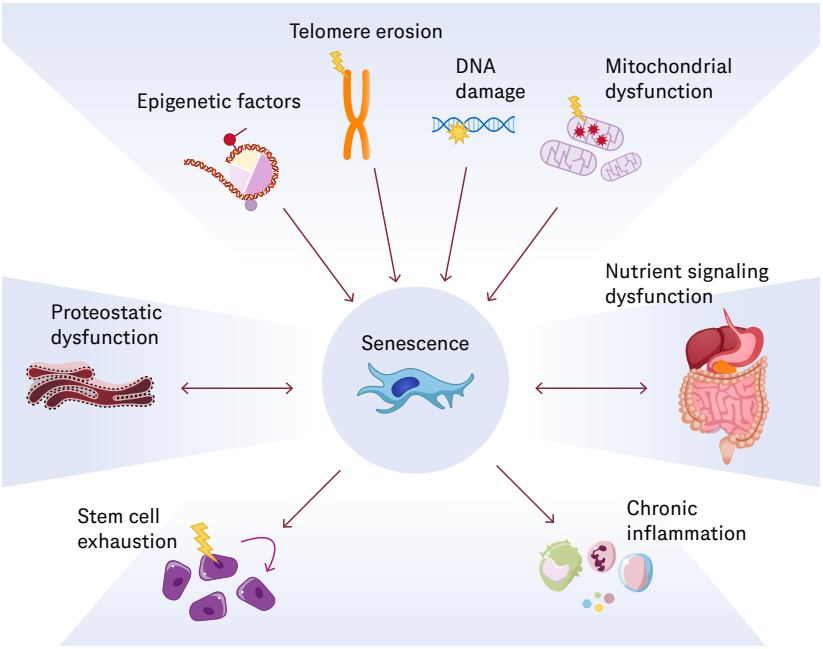
Day 1

Continued

Procedure

4	Show students the image:



5	Ask students to turn and talk with a partner about how they would interpret the model shown.
6	Let students know that arrows pointing in indicate the causes of senescence, and arrows pointing out indicate the results of senescence.
7	Ensure students understand how to read the model in the image. Allow students to practice providing examples of what the model demonstrates. Answer: "Telomere erosion can cause senescence, which can result in chronic inflammation" or "mitochondrial dysfunction can cause senescence, which can lead to stem cell exhaustion."
8	Call on volunteers to explain the two double-headed arrows. Answer: Senescence can cause those actions and those actions are a result of senescence.
9	Let students know that today they will be learning more about the arrows pointing into the center model, or the causes of senescence.

Continues next page >

Day 1

Continued

Procedure

10	Tell students that during the discovery phase of the product cycle of medicine, scientists research more information about organisms in order to find specific drug targets that can be used as drug therapies.
11	Hand out the *Causes of Senescence Model Capture Sheet* and *Causes of Senescence Model Rubric*. Review components of the assignment.
12	Divide students into groups of three to four.
13	Ensure that groups assigned the same topic do not select the same concept from the scientific journal article. Be sure to assign the factor *proteostasis* to more advanced students because more explanation will be required. The telomere erosion can be assigned to a less advanced group as it is more familiar because it was discussed at the beginning of the unit.

COMPUTATIONAL THINKING IN ACTION

Students take on the role of molecular biologists tasked with providing information to the public regarding a particular topic in senescence. Because the information researched is often so abstract, molecular biologists have to be able to explain small details to others with basic to no science background. Students work in groups to create a model demonstrating how epigenetic factors, telomere erosions, DNA damage, or mitochondrial dysfunction can cause senescence.

Small Group (25 minutes)	
1	Monitor students as they work.
2	Let them know when they have 15, 10, and 5 minutes remaining to complete their models.

INDUSTRY AND CAREER CONNECTION

Emphasize to students that major soft skills needed as a molecular biologist are being detail oriented and a motivated learner. In this lesson, students will be creating a cellular model, and so will need to ensure they include all necessary components of the model. For this to be successful, students will need to utilize all of the resources and thoroughly read and understand the topic. Because students will not have the opportunity to choose their topics for the senescence model, they may not be fully interested. However, students must realize the importance of being a motivated learner. Let students know that the overall goal of scientists is to make new discoveries that will help improve the well-being of humans.

Whole Group (10 minutes)	
1	Let students know that they will spend the last portion of class completing a museum guide that will help them tomorrow. Hand students the *Museum of Senescence Capture Sheet*.
2	Have them complete the first row with their assigned topics.

Day 2

LEARNING OUTCOMES

Students will be able to:

Describe characteristics of cells in senescence.

Collate relevant information about various models of cell senescence.

Procedure

Teacher Note > *Because most of the information students will learn is abstract, strategies that help students visualize the processes are helpful. If necessary, show additional pictures, animations, or videos of SASP. In addition, brainstorm various analogies or examples to support student understanding.*

Whole Group (5 minutes)	
1	Let students know that they will view the models created in the last class and complete a graphic organizer.
2	Have students take out their *Museum of Senescence Capture Sheet*.
3	Let them know that they will participate in a *Gallery Walk* in the Museum of Senescence. They will view each different model as a group and have three minutes to complete the graphic organizer.

Small Group (20 minutes)	
1	Monitor student groups to ensure they are completing the capture sheet.
2	Note any challenges students have with understanding the models.

Whole Group (20 minutes)	
Let students know that today they will learn about the details of senescence. In particular, they will learn about the characteristics of cells that are in senescence.	
1	Ask students why it would be important to be able to identify the characteristics of senescent cells. Answer: To be able to use them as biomarkers to diagnose senescence or to identify possible drug targets, which is part of the product life cycle.
2	Let students know that they will now take a few notes in their **Design Journal**. Give them a choice as to whether they want to write their notes Cornell Style or using bullet points.
3	Tell students to title their notes, “Characteristics of Senescent Cells.”

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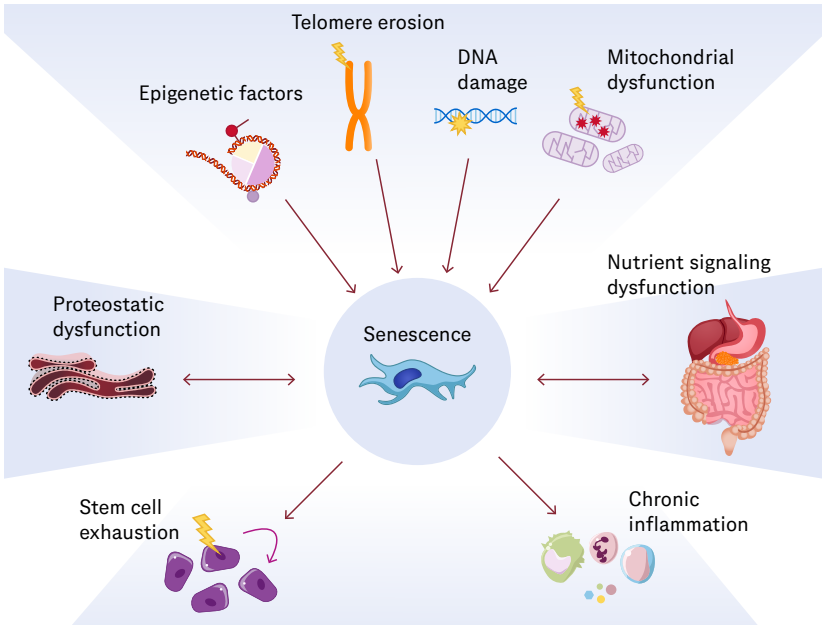
Day 2

Continued

Procedure

4 Ask students what they would expect cells in senescence to "look" or "act" like.

5 Show students the following diagram:



a. Ask students which arrows would depict how senescence cells "look" or "act."

Answer: arrows pointing away from senescence cell

b. Ask students to use this diagram to discuss with the person next to them what cells in senescence to "look" or "act" like.

c. Let students know that greater number of senescent cells is an indication of aging and is characteristic of certain diseases, including cancer, neurodegenerative disease, Type II diabetes, and atherosclerosis.

d. Ask students to pull out their notebook or paper to write notes during the lecture.

e. Let students know that you will model Cornell Note Style of note taking during the lecture on today's topic. Let students know that the question side of their notes may vary depending on the question that they create.

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Day 2

Continued

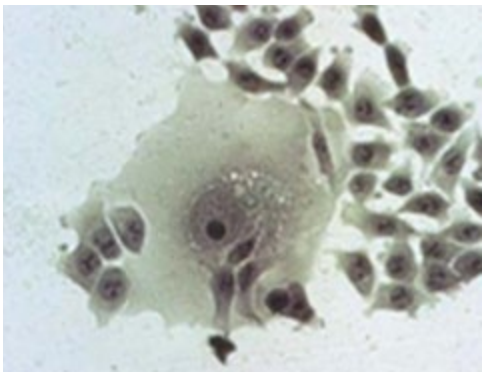
Procedure

f. Throughout the lecture, be sure to define any technical terms that may be unfamiliar to students.

Teacher Note > *You may also use a station rotation model and have different artifacts at each station that student groups use to respond to each question.*

g. Use an analogy to help students understand the role of SASP in senescence. Just as a volcanic eruption has a cause, which is shifting tectonic plates, senescence has a cause, which can be mitochondrial dysfunction, telomere shortening, epigenetic factors, etc. When a volcano erupts, it releases lava. SASP is like lava, the various molecules that are produced are spread to other cells, or trigger other effects to happen (tissue remodeling or immune cell recruitment).

h. Begin writing:

Question	Notes
What are the two types of characteristics?	Phenotype and Function(process)-based
What is a phenotype?	Phenotype: Changes to the cell's morphology, which include its size, shape, and texture.
What does a cell in senescence look like?	Cell Size Changes: Enlarged Cell Shape Changes: Cells are less circular and more irregularly shaped. 

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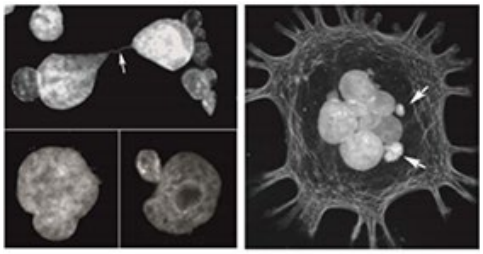
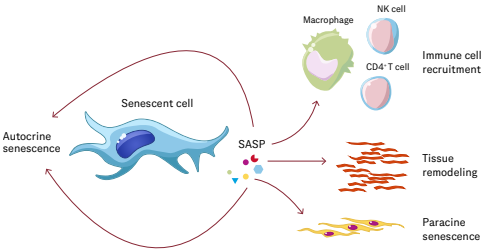
Day 2

Continued

Procedure

Why are senescent cells polyploidy?	Cell look changes: Cells are Polyploidy (more than two sets of chromosomes)—uneven cell division.  Left: shows nuclei Right: 1 cell with multiple nuclei Function (process) Based (how the cell acts)
What are other signs of senescence?	Other signs of cell senescence: increased lysosomal activity, expression of anti-proliferative proteins, resistance to apoptosis, activation of damage-sensing signaling routes
What is the SASP?	SASP: senescence-associated secretory phenotype secretion of mixture of interleukins (ILs), inflammatory factors, chemokines, proteases and growth factors 

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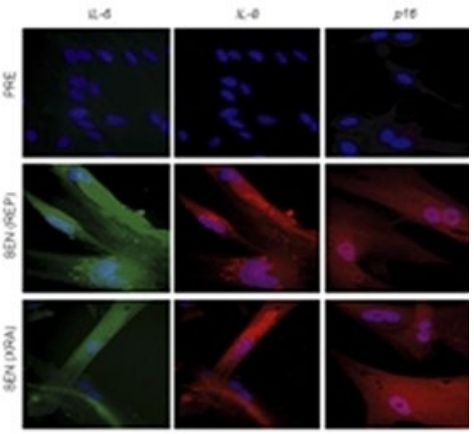
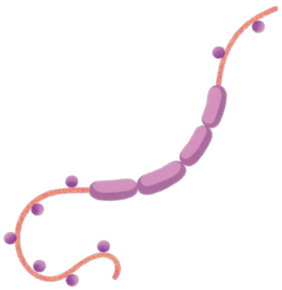
Day 2

Continued

Procedure

What is the evidence for the SASP?	Evidence of the SASP: Presence of interleukin in cells in senescence (red & green); blue stain is dapi, a dye used to identify the nucleus 
What types of diseases exhibit characteristics of senescent cells?	Diabetes Type II, Atherosclerosis, Cancer, Fibrosis, Glaucoma
Summary: Write a two paragraph summary of today's notes.	Answers will vary.

6 Save a few minutes for students to take few notes in their **Design Journal**. They should capture how content learned in this lesson connects to the information they are investigating and to the creation of their final product.



Day 3

LEARNING OUTCOMES

Students will be able to:

Identify characteristics of senescent cells.

Explain why removing senescent cells would benefit an organism.

COMPUTATIONAL THINKING IN ACTION

Students must identify the data from the scientific studies that can be used to support their claim.

Procedure

Whole Group (5 minutes)	
1	Provide students with the *Signs of Cellular Senescence Capture Sheet*.
2	Let students know that for this assignment, they will work in groups and use their notes to complete the capture sheet.
3	Divide students in groups of three to four.

Small Group (20 minutes)	
1	Have students complete the capture sheet.
2	Ensure students are monitoring and managing their time.
3	Note any challenges or misconceptions students may have.

Whole Group (5 minutes)	
1	Provide students with the *Senescent Cell Removal Capture Sheet*.
2	Let them know that they will be reading through scientific studies to find proof of the benefits.
3	Review the assignment criteria. Remind students to reference the *Senescent Cell Removal Rubric* when writing their paper.

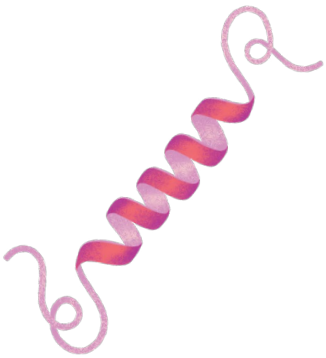
Individual (15 minutes)	
1	Have students work on the assignment for the rest of class.
2	Let students know they will need to complete whatever they did not finish for homework.
3	Be sure students understand the difference between a description and explanation for the CER assignment. Students should describe the "what" of the graph and save the "why" for the reasoning section.

Day 4

LEARNING OUTCOMES

Students will be able to:

Define senolytic drugs.



Procedure

Teacher Note > *Depending on the size of the class, you may want to divide paragraphs up differently from what is stated in the instructions. Ensure groups of paragraphs are cohesive and do not end in the middle of a story.*

Whole Group (10 minutes)	
1	Tell students that today they will be learning about senolytic drugs.
2	Ask students what they think senolytic drugs are? Answer: Drugs that remove cells that are in senescence.
3	Let them know that senolytic drugs are small molecules used to target and remove senescent cells from the body.
4	Ask them which part of the product cycle of medicine relates to senolytic drugs. Answer: commercialization
5	Let them know that they will work in groups and play the role of a pharmacokinetic scientist for this assignment by researching information on senolytic drugs.
6	Let students know they will read the first two paragraphs of the paper *Can Destroying Senescent Cells Treat Age-Related Disease?* together.
7	Begin reading a few sentences and then pass it to a student.
8	Repeat until the end of paragraph two.

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Day 4

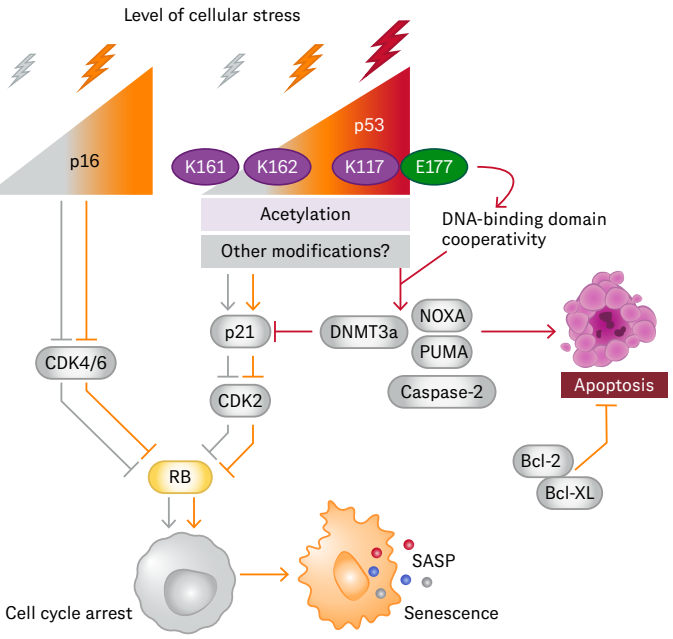
Continued

Procedure

COMPUTATIONAL THINKING IN ACTION

Students work in groups of scientists who are responsible for presenting a section of the information during a shared group presentation. They must abstract as they read in order to summarize the content into a smaller chunks and practice their presentation to deliver it succinctly within the given timeframe.

9 Show students the image here:



10 Review the diagram being sure to point out the differences and similarities between apoptosis and senescence. (Orange arrows lead to senescence; red arrows lead to apoptosis; larger lightning bolts indicate increased levels of cellular stress.)

- **a.** Both apoptosis and senescence are caused by cellular stress.
- **b.** p53 is an important gene in determining whether a cell will go through apoptosis or senescence (low level = senescence and higher levels = apoptosis).
- **c.** Senescence is a result of cell cycle arrest, while apoptosis is a result of the expression of certain genes due to DNA damage.

11 Provide students with *Senolytic Drugs Presentation Guidelines* and *Rubric*.

12 Review the requirements of the assignment. Emphasize to students that they use the *Senolytic Drugs Presentation Rubric* to guide their work.

13 Split students up into pairs.

Continues next page >

Day 4

Continued

Procedure

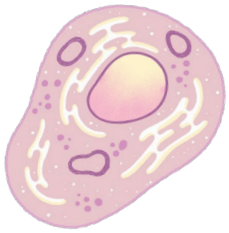
INDUSTRY AND CAREER CONNECTION

Emphasize to students that two major soft skills needed as a pharmacokinetic scientist are being organized and being a motivated learner. In this lesson, students will be creating two slides to represent their assigned information from the article. Students have to synthesize their own material in a way that flows with the information of the pairs in front and behind. Students will need to carefully review the topic and understand it well enough to create a presentation that helps tell a story. Because students will not have the opportunity to choose their topics for the senescence model, they may not be fully interested. However, students must realize the importance of being a motivated learner. Let students know that the overall goal of scientists is knowledge and it is only through that knowledge that the health of humans will improve.

Small Group (20 minutes)	
1	Assign each pair four paragraphs (depending on size of groups).
2	Be sure to assign one pair of students the sidebar section titled "The bright side of senescence."
3	Have students begin to silently read to themselves.
4	After five minutes, let students know they have 15 more minutes to summarize the section and create a presentation to share with the class.

Small Group (15 minutes)	
1	Have each student pair present the summary of its section in 1–1:30 minutes (depending on the number of groups).
2	Ensure student pairs present in order of the information in the article.
3	For homework, have students write a reflection about their experience working in pairs.
4	Let them know the reflection needs to include at least six sentences and discuss something that went well when working with their partners, something they would improve with working with their partners, and a summary of how well they displayed the soft skills of the molecular biologist.

Teacher Note > *Remind students to update their **Design Journal** to capture how content learned in this lesson connects to the information they are investigating and to the creation of their final product.*



Day 5

LEARNING OUTCOMES

Students will be able to:

Describe the potential of generating stem cells from reprogrammed senescent cells.

Summarize the potential benefits of senolytics.

Procedure

Teacher Note > *In order to hear the audio, use the link in the instructions and then click on "Full Text Link" Nature Publishing Group towards the top of the page and to the right of the title. Once on that page, scroll down and you will see the audio clip on page 6.*

Whole Group (20 minutes)	
1	Provide students with all parts of the *Applications of Senescence Capture Sheet*. Tell students that today they will complete an assignment that will help them summarize and review what they learned the past few days. Let them know they will first discuss applications that have to do with senescent cells.
2	Tell students that they will now listen to an audio of a scientist researching zombie cells.
3	Ask students what they think zombie cells are. Accept all answer at this time.
4	Play the audio found in the *Nature article*. The audio portion can be found midway through the article.
5	Pause the recording every 1.5 minutes to allow students to answer the questions in Part 1. Call on students to answer questions. Then, give students five minutes to complete Part 2 of the assignment with the person sitting next to them.
6	Use a *Stand and Share* protocol for a few pairs to come up to the board to draw their proposed models. Tell students that scientists use models all the time, from planning an experiment to describing the connection of the results to a particular scientific concept.
7	Let students know that additional studies have been conducted in which senescent cells have been reprogrammed into induced pluripotent stem cells or IPSCs. Show and describe the *image of the IPSCs*.
8	Ask for five volunteers to read aloud portions of the abstract located on the *Applications of Senescence Capture Sheet*, Part 3 while the rest of the class follows along silently.
9	Allow students one minute of silent time to answer the questions related to the abstract.

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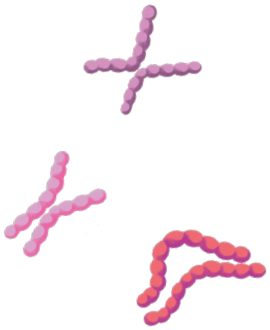
Day 5

Continued

Procedure

10	Call on students to answer, using a random calling strategy such as *Pick a Stick*.
11	Continue until all questions have been answered.
12	Ask students to provide an example or explain the significance of using cells in senescence as IPSCs. Explanation: Using cells in the brain of Alzheimer's patients and reprogramming them back to new brain cells; Essentially all cells that exhibit senescence, whether it be due to old age or disease, can be reprogrammed and made 'new.'
13	Ask students to stand. Let them know that they have to make a decision about the best approach to treating cellular aging. Tell them to sit if they believe that research should focus more on reprogramming senescent cells and to stay standing if they believe that research should focus on creating senolytics.
14	Choose two students standing and sitting to share their thoughts on their decisions. Enhance the conversation by telling students to think about such factors as cost, labor, time, etc.
15	Let students know that they will spend the rest of class working on their senolytics infographic.
16	Hand out the *Senolytics Infographic Guidelines*.
17	Review the assignment criteria.



Individual Group (25 minutes)	
1	Have students work on the infographic for the rest of the class period.
2	Let students know that they will need to complete what they did not finish for homework. Emphasize that the assignment is due next class.

National Standards

Next Generation Science Standards

LS1.A: Structure and Function
All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins.

Science and Engineering Practices

Developing and using models
Develop, revise, and/or use a model based on evidence to illustrate and/or predict the relationships between systems or between components of a system.

Obtaining, evaluating, and communicating information
Communicate scientific and/or technical information or ideas (e.g. about phenomena and/or the process of development and the design and performance of a proposed process or system) in multiple formats (i.e., orally, graphically, textually, mathematically).

Crosscutting Concepts

Structure and Function
Investigating or designing new systems or structures requires a detailed examination of the properties of different materials, the structures of different components, and connections of components to reveal its function and/or solve a problem.

Systems and System Models
Models (e.g., physical, mathematical, computer models) can be used to simulate systems and interactions—including energy, matter, and information flows—within and between systems at different scales.

Career and Technical Education (CTE)

A3.1
Define and describe the structure and function of DNA ribonucleic acid (RNA) and proteins, explain the consequences of DNA mutations on proteins.

A4.1
Use electronic reference materials to gather information and produce products and services.

Continues next page >

National Standards

CTE *Continued*	**A4.3** Use information and communication technologies to synthesize, summarize, compare, and contrast information from multiple sources.
	A5.1 Use the Internet and World Wide Web to collect and share scientific information.
	A5.4 Interpret information and draw conclusions, based on the best analysis, to make informed decisions.
	A5.6 Read, interpret, and extract information from documents.

The Museum of Senescence Capture Sheet

ANSWER KEY **Do not share with students**

Welcome to the Museum of Senescence.
Today you will view several different models that depict the causes of senescence. Complete this capture sheet and use it as an informational keepsake for years to come!

	Model Name	Description of Model	Cellular Result
1	Epigenetic Factors Cause Senescence in Cells	Alterations in DNA methylation patterns, post-translational modification of histones, and chromatin remodeling can cause aging.	These alterations block the transcription of genes.
2	Telomere Shortening Causes Senescence in Cells	Telomeres protect the DNA at the ends of chromosomes. Telomere shortening would expose the DNA which could be damaged.	The DNA Damage Response (DDR) arrests cell division in cell cycle.
3	DNA Damage Causes Senescence in Cells	Mutations or increased expression of genes that damage DNA are causes of DNA damages. DNA damage accumulates with age due to an increase in production of reactive oxygen species (ROS) and a decline in DNA repair capacity.	Causing apoptosis or cellular senescence can lead to tissue homeostasis through stem cell depletion and/or disrupted tissue structure. Ultimately organ function declines and phenotypical features of ageing manifest at organismal level.
4	Mitochondrial Dysfunction Causes Senescence in Cells	Aging-associated mtDNA mutations, reduced mitochondriogenesis, destabilization of the electron transport chain (ETC) complexes, altered mitochondrial dynamics, or defective quality control by mitophagy can cause aging.	Reduction of mitochondrial function, which can generate ROS, at high or continued levels can contribute to aging.
5	Nutrient Signalling Dysfunction Causes Senescence in Cells	Growth hormone (GH) and another molecule produced in response to GH, IGF-1, are involved in eliciting a dietary response. The insulin and IGF-1 (IIF) pathways inform cells of the presence of glucose. It is also the most conserved aging-controlling pathway. Levels of IGF-1 and GH decline with age. Decreased IIF is common in aging cells.	Expression of genes may be down-regulated; IIS decrease causes a decrease in cell growth and metabolism.
6	Proteostasis Causes Senescence in Cells	Proteostasis involves mechanisms for the stabilization of correctly folded proteins, most prominently, the heat-shock family of proteins, and mechanisms for the degradation of proteins by the proteasome or the lysosome. Stress and aging cause a decline in the efficiency of proteostasis.	Chronic expression of misfolded proteins can lead to Alheimer's disease, Parkinson's disease, and cataracts; no intracellular protein renewal.

Signs of Cellular Senescence Capture Sheet

ANSWER KEY — **Do not share with students**

Directions
Work in groups and use your notes to answer the questions.

1. Write each of the following terms in the category of changes in cells during senescence with which they are most closely associated.

enlarged cell	lysosomal activity
growth factors	no apoptosis
interleukin	polyploidy
irregular shape	SASP

Phenotypic Changes	Functional Changes
polyploidy enlarged cell irregular shape	no apoptosis interleukin lysosomal activity growth factors SASP

Continues next page >

Signs of Cellular Senescence Capture Sheet

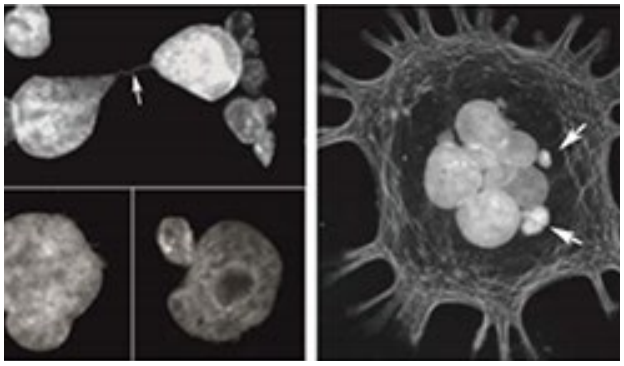
ANSWER KEY **Do not share with students**

Continued

2. For the past two class periods we have been reviewing the model shown to the right.

   For each of the descriptions (a–c), draw a picture of the senescence model described. If the description includes information about a phenotypic change, be sure to include a picture. Otherwise words, arrows, shapes are fine. For the descriptions without the pictures, use the example below as your guide and include specific terms associated with the information in each description.

   a. Cells are polyploid.



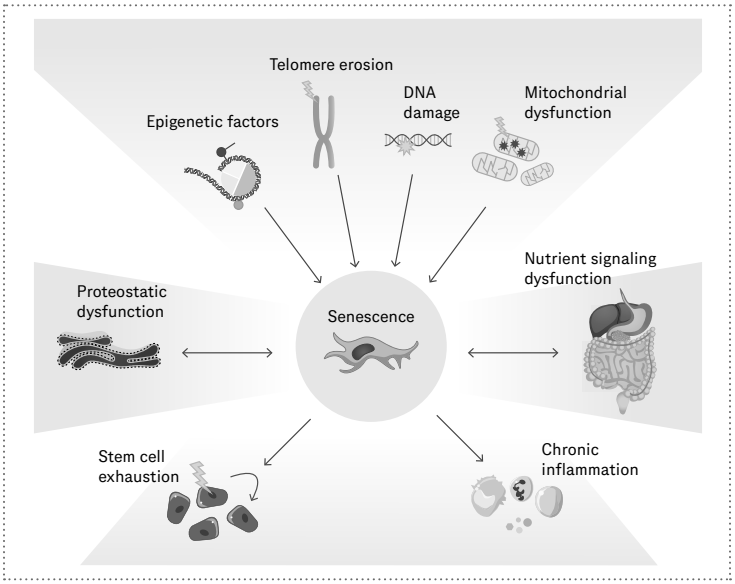
   b. Other signs of cell senescence: increased lysosomal activity, expression of anti-proliferative proteins, resistance to apoptosis, activation of damage-sensing signaling routes

   Factor(s) Causing → cell senescence → increased lysosomal activity,→ expression of anti-proliferative proteins, → resistance to apoptosis, → activation of damage sensing signaling routes

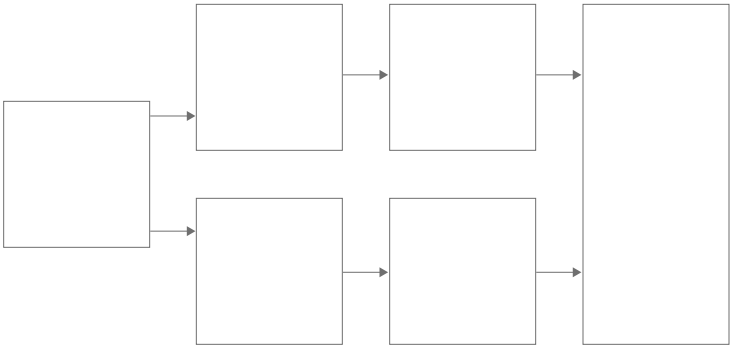
   c. SASP

   SASP → secretion of a mixture of interleukins, inflammatory factors, chemokines, proteases and growth factors can result in → inflammation, compels other nearby cells to go into senescence.

Senescence Model



Senescence Descriptions



Applications of Senescence Capture Sheet, Part 1

ANSWER KEY — **Do not share with students**

Directions
Answer the questions as you listen to the audio of two scientists being interviewed for their cell senescent research published in the journal Nature.

1. What are zombie cells?

Cells in senescence—stop replicating and dividing, but are still alive and can be very hard to kill.

2. What is the name of the "complex variety of molecules" that have profound effects on neighboring cells?

SASP

3. What is the dark side of senescence?

As the organism ages, there are more and more senescent cells. Secretion from cells can now attract the immune system cells, which can be destructive, and factors that can enhance inflammation or even tumors.

4. What did the scientist discover when performing cell senescent studies in mice?

Geriatric mice in senescence developed cataracts, were humpback; blocked a certain protein involved senescence, removed senescent cells, and reversed any and all ailments in the geriatric mice.

5. What are senolytic agents?

Drugs that kill senescent cells

6. List two issues of social justice associated with the use of senolytic drugs.

Price of medicine (insurance)

Access to medicine

Knowledge or education about medicine

Applications of Senescence Capture Sheet, Part 2

ANSWER KEY **Do not share with students**

Directions

Read the article and create a conceptual model on paper of the scientist's experiment as described in the article. Include important vocabulary and ensure steps are sequential. Think about the various types of models, including the one you made, that have been reviewed over the past few days. Models must include inputs and outputs, which can be represented by arrows pointing up and down.

4 month old mice + SEN → 2 weeks → impaired physical endurance (maximum walking speed), daily activity, food intake and body weight + >SEN

4 Month old mice + CON → 2 weeks → normal physical endurance, daily activity, food intake, and body weight

SEN mice + D +Q → 3 days → SEN(cells) + slowed deterioration in walking speed, endurance, and grip strength

CON mice + D + Q → 3 days → normal physical endurance, daily activity, food intake, and body weight

20 month old mice + D + Q → 4 months → alleviated normal age-related physical dysfunction, higher walking speed, treadmill endurance, grip strength, and daily activity

4(Control) 20 month old mice → 4 months → normal age-related physical dysfunction, normal walking speed, treadmill endurance, grip strength, and daily activity

24–27 month old mice + D + Q → 2 weeks → 36% higher average life span and lower mortality

(Control) 24–27 month old mice → 2 weeks → average life span and mortality

Applications of Senescence Capture Sheet, Part 3

ANSWER KEY — **Do not share with students**

Directions
Read and annotate the abstract. Answer the questions that follow.

Rejuvenating senescent and centenarian human cells by reprogramming through the pluripotent state

Abstract

Direct reprogramming of somatic cells into induced pluripotent stem cells (iPSCs) provides a unique opportunity to derive patient-specific stem cells with potential applications in tissue replacement therapies and without the ethical concerns of human embryonic stem cells (hESCs). However, cellular senescence, which contributes to aging and restricted longevity, has been described as a barrier to the derivation of iPSCs. Here we demonstrate, using an optimized protocol, that cellular senescence is not a limit to reprogramming and that age-related cellular physiology is reversible. Thus, we show that our iPSCs generated from senescent and centenarian cells have reset telomere size, gene expression profiles, oxidative stress, and mitochondrial metabolism, and are indistinguishable from hESCs. Finally, we show that senescent and centenarian-derived pluripotent stem cells are able to redifferentiate into fully rejuvenated cells. These results provide new insights into iPSC technology and pave the way for regenerative medicine for aged patients.

1. What has been a barrier for scientists in obtaining iPSCs?

Cellular senescence

2. What do the authors claim?

By using an optimized protocol that cellular senescence is not a limit to reprogramming and that age-related cellular physiology is reversible.

3. What is the evidence?

iPSCs generated from senescent and centenarian cells have reset telomere size, gene expression profiles, oxidative stress, and mitochondrial metabolism, and are indistinguishable from hESCs. Senescent and centenarian derived pluripotent stem cells are able to redifferentiate into fully rejuvenated cells, have reset telomere size gene.

4. Draw a model that would accurately depict the results of this study. (Can just use words and arrows; up or down showing increase or decrease; in or out showing inputs and outputs.)

Senescent Cells + Optimized Protocol → iPSCs
Centenarian Cells +Optimized Protocol → iPSCs

5. Create a new title for this research study for a population of individuals with no background in science.

Answers will vary.
"Changing Old into New"
"The Case of Benjamin Button Cells"

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Causes of Senescence Model Capture Sheet

Directions

For this assignment, you will play the role of a molecular biologist and provide the public with information regarding a particular topic related to senescence. Because the information researched is often so abstract, molecular biologists have to be able to explain small details to others with basic to no science background. In your groups, you will create a model demonstrating how epigenetic factors, telomere erosions, DNA damage, or mitochondrial dysfunction can cause senescence.

Your model may be made using a variety of supplies, including chenille stems, modeling clay, cotton balls, aluminum foil, paper, tissues, cotton swabs, wooden craft sticks, foam cups, plates, and beads.

Each model should include:

1. A title that includes the below phrase completed in your own words.

   "_____ *causes senescence in cells.*"

2. A depiction of the:
   a. Cause of Senescence
   b. Result
3. Labels of the components
4. A legend or key
5. A written step-by-step description of the process
   a. Causes
   b. Results

Resources

1	**General**	This *article* includes information that will provide an overview of each of the topics.
2	**Epigenetic Factors**	Using the *article* from resource 1, choose two epigenetic factors to include in your model and describe. Use Figure 1 from this article as a guide to create your model. Note: Your model will not include all of the pictured parts, only the parts included from your chosen factors.
3	**Telomere Erosions**	Use this *article*, sections 1.2, 2, 3, 4, and Figure 1, as a guide to create your model. For your model, choose the natural and one of the stress-induced forms of senescence.
4	**DNA Damage**	Use this *article*, and particularly Figure 3, as a guide to create your model. For your model, choose one of the contributing factors to DNA damage (ROS Production or DNA Repair).
5	**Mitochondrial Dysfunction**	Use this *article*, including Figure 2, as a guide to create your model. For your model, choose one of the examples of mitochondrial dysfunction (mitochondrial biogenesis increases, mitophagy decrease, or mitochondrial network fusion).
6	**Nutrient Signaling Dysfunction**	Use this *article*, particularly Figure 2, as a guide to create your model. Your model should reflect the connection between nutrient availability and senescence.
7	**Proteostasis**	Use this *article*, especially Figure 4, as a guide to create your model. Your model should reflect the connection between proteostasis and aged or diseased cells. Note that this factor is both a cause and result of senescence. Be sure your model and written description depicts this.

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Causes of Senescence Model Rubric

Score	4	3	2	1
Model Aesthetic	The model includes labels and a key, is artistic, and demonstrates creative use of the supplies.	The model includes labels and a key, but is not very artistic and does not demonstrate creative use of the supplies.	The model includes labels, but no key, is not artistic and does not demonstrate a creative use of the supplies.	The model is missing labels, a key, artistry, and a creative use of the supplies.
Model Accuracy	The model clearly and accurately depicts the cause of senescence and its result.	The model correctly depicts the cause of senescence, although one to two portions are unclear or inaccurate.	The model correctly depicts the cause of senescence, but not its result.	The model does not correctly depict the cause of senescence or its result.
Model Description	Correct and specific vocabulary terms are used to describe the cause of senescence and results specific to cell are included.	Correct vocabulary terms (although not specific) are used to describe the cause of senescence and results specific to cell are included.	Vocabulary terms used to describe the cause of senescence and results specific to cell are inaccurate.	A model description was not included.
Final Score				

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Museum of Senescence Capture Sheet

Welcome to the Museum of Senescence.
Today you will view several different models that depict the causes of senescence. Complete this capture sheet and use it as an informational keepsake for years to come!

	Model Name	Description of Model	Cellular Result
1			
2			
3			
4			
5			
6			

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Signs of Cellular Senescence Capture Sheet

Directions
Work in groups and use your notes to answer the questions.

1. Write each of the following terms in the category of changes in cells during senescence with which they are most closely associated.

enlarged cell	lysosomal activity
growth factors	no apoptosis
interleukin	polyploidy
irregular shape	SASP

Phenotypic Changes	Functional Changes

Continues next page >

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Signs of Cellular Senescence Capture Sheet

Continued

2. For the past two class periods we have been reviewing the model shown to the right.

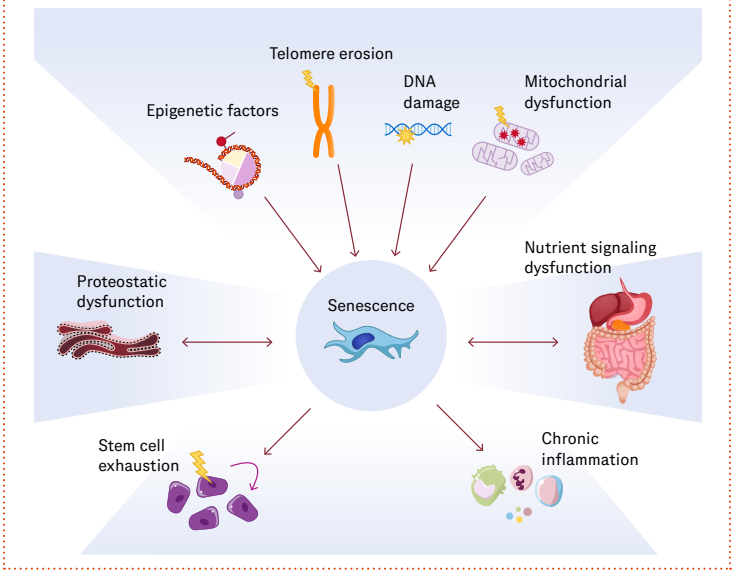
   For each of the descriptions (a–c), draw a picture of the senescence model described. If the description includes information about a phenotypic change, be sure to include a picture. Otherwise words, arrows, shapes are fine. For the descriptions without the pictures, use the example below as your guide and include specific terms associated with the information in each description.

   a. Cells are polyploid.

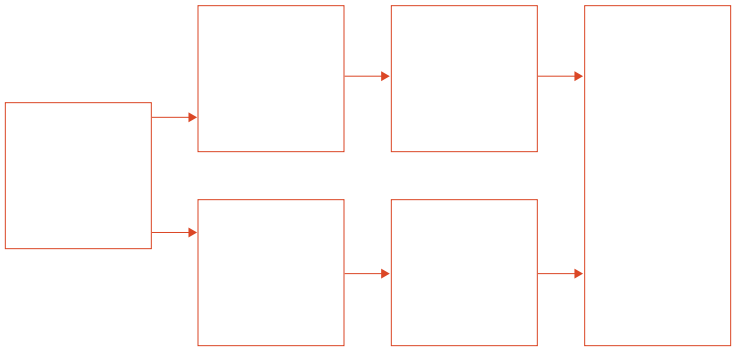
   b. Other signs of cell senescence: increased lysosomal activity, expression of anti-proliferative proteins, resistance to apoptosis, activation of damage-sensing signaling routes

   c. SASP

Senescence Model



Senescence Descriptions



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Senescent Cell Removal Capture Sheet

Directions

For this assignment, you will be completing a CER paper on a particular ailment caused by senescence. CER stands for Claim, Evidence, and Reasoning. The claim has already been created: removing Senescent Cells Will Benefit Organisms. You will be responsible for identifying evidence that supports this claim and providing a reason that this evidence can be used to support the claim. The reasoning portion of the paper will include scientific terminology and concepts that will help explain how the evidence supports the claim.

Choose any of the disease types listed (except Type 2 Diabetes and Neurodegenerative Diseases). Type a page CER paper including the following components:

1. Name of Disease
2. Description of Disease
3. Incidence Rate
4. Special Groups Affected (Ethnic, Gender, etc.)
5. Evidence
    a. Data displaying evidence of before or after removal of senescent cells
    b. Description (not explanation) of what the data shows
6. Reasoning
    a. Vocabulary associated with disease and senescence
    b. Identification of biomarker(s) of senescence
    c. Description of the purpose of the biomarker
    d. At least two benefits that occur due to the removal of the senescent cells, including an explanation of before or after

Resource

Targeting senescence cells: approaches, opportunities and challenges

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Senescent Cell Removal Rubric

Score	4	3	2	1
Claim	Disease name, description, incidence rate, and any special ethnic, racial, or gender groups identified.	Disease name, description, incidence rate identified (no special ethnic, racial, or gender groups identified).	Disease name and description (no incidence rate or special ethnic, racial, or gender groups identified).	Only the disease name included.
Evidence	Graph, figure clearly show evidence of before and after removal of cells and description is clear.	Graph, figure clearly show evidence of before and after removal of cells; description is not very clear.	Graph, figure clearly show evidence of before and after removal of cells; no description is included.	No graph or figure included.
Reasoning	Correct and specific vocabulary is used, biomarker(s) identified and described, and specific benefits are included.	Correct vocabulary is used, biomarker(s) identified and described, and benefits are included, but are not specific.	Correct vocabulary is used, but biomarker(s) are not identified or described and benefits are not included.	Reasoning section is not included.
Final Score				

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Senolytic Drugs Presentation Guidelines

Directions

You are a part of a larger group of scientists and are responsible for presenting a section of the information from the article for a presentation. The information you gather will be included in a larger class Google Slides presentation. Everyone will work from the same Google Slide Show and create their two specific slides from there. Each student pair is responsible for two slides, which must include:

1. Summary of your information
2. How it fits into the bigger picture of senescence
3. A smooth transition from and into other topics
4. Text to image ratio 3:1

Include a reflection with your assignment. The reflection needs to be at least six sentences and discuss:

1. Something that you learned
2. Something that went well when working with your partner
3. Something you would improve about working with your partner
4. Summary of how well you displayed the soft skills of the molecular biologist

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Senolytic Drugs Presentation Rubric

Score	4	3	2	1
Content	The information is clearly and accurately summarized and not copied; images used were relevant to the content.	The information is accurately summarized, but may be slightly unclear; information is not copied and most images used were relevant to content.	The information is summarized, but some portions are unclear; information is not copied and some images used were relevant to content.	The information is copied or no images were included.
Aesthetics	Font is easy to see and the text was large enough to see. Text to image ratio was 3:1.	Font is easy to see and the text was large enough to see. Text to image ratio is not 3:1; too many words or not enough pictures.	Font is consistent, but not large enough to see. Text to image ratio is not 3:1; not enough words and too many pictures.	Font or text is not easy to see. Information is lacking in quantity and quality.
Presentation	Both partners demonstrate a clear understanding of the topic.	Both partners demonstrate understanding of the topic.	Only one partner demonstrates understanding of the topic.	Neither partner demonstrates understanding of the topic.
Final Score				

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Applications of Senescence Capture Sheet, Part 1

Directions
Answer the questions as you listen to the audio of two scientists being interviewed for their cell senescent research published in the journal Nature.

1. What are zombie cells?

2. What is the name of the "complex variety of molecules" that have profound effects on neighboring cells?

3. What is the dark side of senescence?

4. What did the scientist discover when performing cell senescent studies in mice?

5. What are senolytic agents?

6. List two issues of social justice associated with the use of senolytic drugs.

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Applications of Senescence Capture Sheet, Part 2

Directions

Read the article and create a conceptual model on paper of the scientist's experiment as described in the article. Include important vocabulary and ensure steps are sequential. Think about the various types of models, including the one you made, that have been reviewed over the past few days. Models must include inputs and outputs, which can be represented by arrows pointing up and down.

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Applications of Senescence Capture Sheet, Part 3

Directions
Read and annotate the abstract. Answer the questions that follow.

Rejuvenating senescent and centenarian human cells by reprogramming through the pluripotent state

Abstract

Direct reprogramming of somatic cells into induced pluripotent stem cells (iPSCs) provides a unique opportunity to derive patient-specific stem cells with potential applications in tissue replacement therapies and without the ethical concerns of human embryonic stem cells (hESCs). However, cellular senescence, which contributes to aging and restricted longevity, has been described as a barrier to the derivation of iPSCs. Here we demonstrate, using an optimized protocol, that cellular senescence is not a limit to reprogramming and that age-related cellular physiology is reversible. Thus, we show that our iPSCs generated from senescent and centenarian cells have reset telomere size, gene expression profiles, oxidative stress, and mitochondrial metabolism, and are indistinguishable from hESCs. Finally, we show that senescent and centenarian-derived pluripotent stem cells are able to redifferentiate into fully rejuvenated cells. These results provide new insights into iPSC technology and pave the way for regenerative medicine for aged patients.

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Applications of Senescence Capture Sheet, Part 3

Continued

1. What has been a barrier for scientists in obtaining iPSCs?

2. What do the authors claim?

3. What is the evidence?

4. Draw a model that would accurately depict the results of this study. (Can just use words and arrows; up or down showing increase or decrease; in or out showing inputs and outputs.)

5. Create a new title for this research study for a population of individuals with no background in science.

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Senolytics Infographic Guidelines

Directions

For this final lesson assignment, you will create an infographic to introduce a new senolytic that will soon be available for consumers to purchase. Because this infographic is for someone with a non-scientist background, be sure to include information on senescence. You are free to use any of the notes from previous lessons. You have the choice of creating this infographic using Canva or Piktochart.

The infographic should include:

1. Model of senescence (include a description)
2. Senescence Information
   a. Description
   b. Experimental evidence
   c. One related image
3. Senolytics
   a. Description
   b. At least two possible applications that demonstrate benefits
   c. One related image
4. Name of the drug (use an example of an actual senolytic)
5. Mechanism of action (how does the drug work? Use your knowledge of the causes of cell senescence)
6. At least two references

Resource

Senolytics: A New Weapon in the War on Aging

Advancements in Therapeutic Drugs Targeting of Senescence

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Senolytics Infographic Rubric

Score	4	3	2	1
Senescence Background	The information is organized, thorough and clear; includes experimental evidence.	The information is organized and thorough, but lacks in clarity; includes experimental evidence.	The information is organized, but lacking in depth and clarity, or does not include experimental evidence.	The information is not organized, lacks depth and clarity, or experimental evidence is missing.
Senolytics	The information is organized, thorough and clear; the image is relevant and the benefits are specific.	The information is organized and thorough, but lacks in clarity; the image is relevant and the benefits are specific.	The information is organized, but lacking in depth and clarity, or does not include an image or the benefits are not specific.	The information is not organized, lacks depth and clarity, and does not include an image or the benefits are not specific.
Drug Information	Accurately describes the mechanism of action with specific and general terms and demonstrates a clear knowledge of senescence.	Accurately describes the mechanism of action with specific and general terms, demonstrates knowledge of senescence.	Describes the mechanism of action using only general terms or does not demonstrate a clear knowledge of senescence.	Does not accurately describe the mechanism of action and does not demonstrate a clear knowledge of senescence.
Final Score				

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United States of America—Place Explorer