

Teacher Notes for How Mistakes in Meiosis Can Result in Down Syndrome or Death of an Embryo¹

In this minds-on analysis and discussion activity, students learn how a mistake in meiosis can result in Down syndrome. Students also analyze karyotypes to learn how other mistakes in meiosis can result in the death of an embryo. Finally, students consider how a health problem can be genetic, but not inherited.

We recommend that, before your students begin this activity, you have them complete the analysis and discussion activity "[Understanding How Genes are Inherited via Meiosis and Fertilization](#)" or the hands-on activity "[Meiosis and Fertilization – Understanding How Genes Are Inherited](#)".

Learning Goals

In accord with the [Next Generation Science Standards](#)²:

- This activity helps to prepare students for the [Performance Expectations](#):
 - HS-LS3-1, "Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring."
- Students will gain understanding of several [Disciplinary Core Ideas](#):
 - 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."
 - LS3.A: Inheritance of Traits – "Each chromosome consists of a single very long DNA molecule, and each gene on the chromosome is a particular segment of that DNA. The instructions for forming species' characteristics are carried in DNA."
- Students will engage in the [Scientific Practices](#):
 - "Constructing Explanations – Apply scientific ideas, principles and/or evidence to provide an explanation of phenomena..."
 - "Developing and Using Models – Develop and/or use a model... to support explanations, predict phenomena, analyze systems..."
- This activity provides the opportunity to discuss the [Crosscutting Concept](#)
 - "Cause and Effect: Mechanism and Explanation – ... A major activity of science is to uncover such causal connections, often with the hope that understanding the mechanisms will enable predictions... [Students] suggest cause and effect relationships to explain and predict behaviors in complex natural and designed systems. They also propose causal relationships by examining what is known about small-scale mechanisms within the system."

Instructional Suggestions and Background Information

If your students are learning online, we recommend that they use the Google Doc version of the Student Handout available at <https://serendipstudio.org/exchange/bioactivities/coronavirusprev>. To answer questions 1 and 3, students can either print the relevant pages, draw on those and send

¹ By Drs. Ingrid Waldron, Jennifer Doherty, Scott Poethig and Lori Spindler. Department of Biology, University of Pennsylvania, 2020. These Teacher Notes and the Student Handout are available at <https://serendipstudio.org/exchange/bioactivities/mmfmistakes>.

² Quotations from <http://www.nextgenscience.org/sites/default/files/HS%20LS%20topics%20combined%206.13.13.pdf>

you pictures, or they will need to know how to modify a drawing online. They can double-click on the relevant drawing in the Google Doc, which will open a drawing window. Then, they can use the editing tools to add lines, shapes, and text boxes.³ If you are using the Word version of the Student Handout to make revisions, please check the PDF version to make sure that all figures and formatting are displayed properly in the Word version on your computer.

If you would like to have a key with the answers to the questions in the Student Handout, please send a message to iwaldron@upenn.edu. The following paragraphs provide additional background information and instructional suggestions.

You may want to begin by showing the video “50 Mums | 50 Kids | 1 Extra Chromosome”. In this 4.5-minute video, 50 mothers are shown, each with their child who has Down syndrome. Each mother is signing the words to a song. Children with Down syndrome typically have delayed expressive language acquisition; learning sign language helps toddlers with Down syndrome to develop expressive language. This charming video helps to humanize Down syndrome.

More than 90% of cases of Down syndrome are due to trisomy 21 as the result of meiotic nondisjunction during the first or second meiotic division that produced the gamete. The risk of meiotic nondisjunction increases for older mothers. This type of trisomy 21 is genetic, but it is almost never inherited. You may want to show your students the ~5-minute video, “Chromosome Nondisjunction Animation”, available at <https://www.youtube.com/watch?v=4bzY9e-YQqI>.

Roughly 2% of cases of Down syndrome are due to inheritance of a translocated chromosome 21. A parent may be a carrier of a balanced translocation (i.e. one chromosome 21 free and most of a second chromosome 21 attached to a different chromosome); a person with a balanced translocation does not have symptoms, but does have a propensity to produce gametes with two copies of chromosome 21.

Mosaic Down syndrome is due to mitotic nondisjunction and is of variable severity, depending on how many and which cells have trisomy 21. This condition can be used to illustrate the general point that Down syndrome varies in severity.

Additional information about Down syndrome, including clinical symptoms and testing for

³To draw a line

1. At the top of the page, find Select line and pick the type of line you want.
2. Place the line on your drawing:
 - Line, Elbow Connector, Curved Connector or Arrow: Click to start, then drag across the canvas.
 - Curve or Polyline: Click to start, then click at each point you want the line to bend. Double-click or complete the shape to finish.
 - Scribble: Click to start, then drag across the canvas.

To draw a shape

1. At the top of the page, find and click Shape.
2. Choose the shape you want to use.
3. Click and drag on the canvas to draw your shape.

To insert text

1. At the top of the page, click Insert.
 - To place text inside a box or confined area, click Text Box and drag it to where you want it.
2. Type your text.
3. You can select, resize and format the word art or text box, or apply styles like bold or italics to the text.

When you are done, click Save and Close.

Down syndrome, is available at:

- <https://ghr.nlm.nih.gov/condition/down-syndrome>
- <http://www.mayoclinic.org/diseases-conditions/down-syndrome/basics/tests-diagnosis/con-20020948?p=1>
- <https://americanpregnancy.org/birth-defects/down-syndrome-696>.

You may want to use an analogy to help your students understand why abnormalities result when each cell has an extra copy of one of the chromosomes and therefore has extra copies of the proteins coded for by the genes in that chromosome. For example, you could ask your students what would happen if someone added too much milk when preparing a box of macaroni and cheese or what would happen if there were too many tubas in a marching band. Cells are much more complicated than these examples, and cells cannot function properly when there are too many copies of some types of proteins due to an extra copy of one of the chromosomes.

To answer question 5, students should extrapolate from the explanation for the abnormalities in trisomy 21. Researchers have found that autosomal monosomy is nearly always fatal in utero (<https://chromodisorder.org/wp-content/uploads/2017/08/21ChromosomeChapter.pdf>).

For question 6, students are expected to argue that trisomy for chromosomes 1, 2, 3, 4 or 5 is more likely to be lethal than trisomy for chromosome 21 because the longer chromosomes would be expected to have more genes and a third copy of all of these genes would be more likely to disrupt cellular functions so much that the embryo dies. It should be mentioned that the severity of abnormalities resulting from trisomy is not strictly related to the length of the trisomy chromosome. One reason is that the number of genes on a chromosome is not strictly proportional to the length of the chromosome; for example, chromosome 4 appears to have 1000-1100 genes, while chromosome 11 appears to have 1300-1400 genes (chromosome 21 appears to have 200-300 genes; <http://ghr.nlm.nih.gov/chromosomes>).

The table on the last page of these Teacher Notes summarizes information about mistakes in fertilization, meiosis and mitosis in humans. The 6-minute video, Meiosis (<https://www.biointeractive.org/classroom-resources/meiosis>), reviews meiosis, fertilization and early embryonic development and shows how mistakes in recombination (crossing over) can result in XX males or XY females.

Follow-Up and Related Activities

We recommend that this activity be followed by “Genetics” (https://serendipstudio.org/sci_edu/waldron/#genetics). The final section of the genetics activity discusses how mutations can also result in conditions which are genetic, but not inherited.

These activities are part of an integrated sequence of learning activities for teaching genetics, presented in "Genetics – Major Concepts and Learning Activities" (<https://serendipstudio.org/exchange/bioactivities/GeneticsConcepts>).

Sources for Figures in the Student Handout

- Couple with Down Syndrome Son from https://sl.sbs.com.au/public/image/file/a8eee88d-721f-4836-b373-c579f989881f/crop/16x9_large
- Figure of meiosis on page 1 modified from <https://i.pining.com/originals/50/82/97/50829772227db79c5fb2aaa3a4a77a91.jpg>
- Figure of karyotype on page 2 modified from http://bio3400.nicerweb.com/Locked/media/ch02/02_04-human_karyotype.jpg

This table describes a variety of mistakes in fertilization, meiosis and mitosis and their outcomes in humans. The conditions listed in this table are genetic, but not inherited.

Mistake	Results in	E.g.	Pregnancy outcome	Outcome after birth
Fertilization by more than one sperm	Polyploidy	Triploidy	Almost always fatal in utero; -> ~15% of miscarriages	Fatal within a month
		Tetraploidy	Fatal in utero; -> ~5% of miscarriages	
Meiotic non-disjunction	Aneuploidy	Autosomal trisomy	Usually fatal in utero, but trisomy 8, 13 and 18 sometimes survive until birth and trisomy 21 can survive into adulthood; trisomies -> ~1/3 of miscarriages	Trisomy 8, 13 or 18 severely disabled and do not survive to adulthood; trisomy 21 can survive to adulthood, although heart defects and leukemia relatively common; degree of mental retardation variable
		Autosomal monosomy	Almost always fatal in utero	
		45XO (44 autosomes plus 1 X chromosome) = Turner syndrome	99% die in utero; but this is the only viable monosomy*	Infertile, normal IQ
		47XXY = Klinefelter syndrome	Majority die in utero, but some survive into adulthood*	Very low fertility and learning disabilities common
Mitotic non-disjunction	If occurs very early in embryonic development, can result in polyploidy or aneuploidy or mosaic	Klinefelter syndrome mosaic can have similar symptoms, but some cells have normal chromosome makeup		

(Primary source: Michael Cummings, 2006, [Human Heredity](#))

*In each cell all but one X chromosome is inactivated, so variation in the number of X chromosomes does not produce as severe abnormalities as autosomal trisomy or monosomy. A small part of each X chromosome is not inactivated, which explains why abnormal numbers of X chromosomes result in some abnormalities.