

Mutations and the Birth and Death of Genes

Author

Ann Brokaw
Rocky River High School
Ohio

About This Activity...

These slides provide examples of different mutations and their effects on the organism and populations.

Answer the questions on the student handout when prompted.



Mutations and Evolution

A **mutation** is a change in an organism's genetic information, or DNA.

Mutations occur at random, at any time, and in the DNA of any type of cell.

When mutations occur in genes, they may result in new phenotypes that natural selection acts upon.

*Student Handout:
Answer Question 1.*

Heritability of Mutations

Mutations that occur in somatic (body) cells only affect the individual in which they occur.

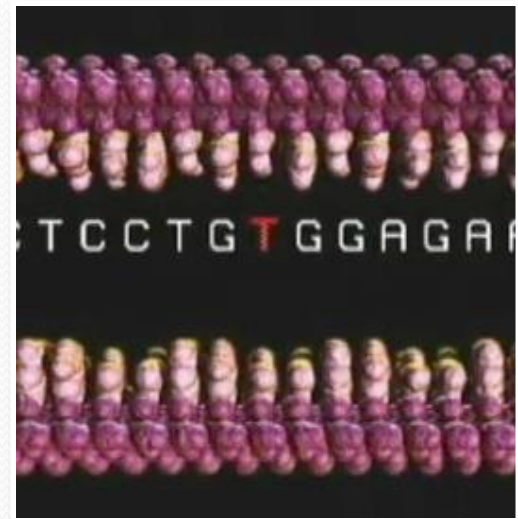
Mutations that occur in gametes (egg and sperm) can be passed on to the next generation.

*Student Handout:
Answer Question 2.*

Types of Mutations

Mutations can occur on a small scale, most often affecting one or two nucleotides of DNA, or they can involve large segments of a chromosome or an entire chromosome.

Any mutation in a gene's DNA can alter the function of the protein encoded by the gene.



Point Mutations

Most mutations are **point mutations**, or changes in a single nucleotide of an organism's DNA.

They include **substitutions**, **insertions**, and **deletions**.

Insertions and deletions also can involve two or more nucleotides.

*Student Handout:
Answer Questions 3–4.*

Substitution Mutations

A substitution is the replacement of a single nucleotide with another. It is classified by its effect on the protein produced:

- **Silent mutations** have no effect on the protein.
- **Missense mutations** result in a single amino acid change in the translated sequence.
- **Nonsense mutations** result in an amino acid codon being replaced by a “stop” codon. Nonsense mutations end translation prematurely and result in a truncated protein.

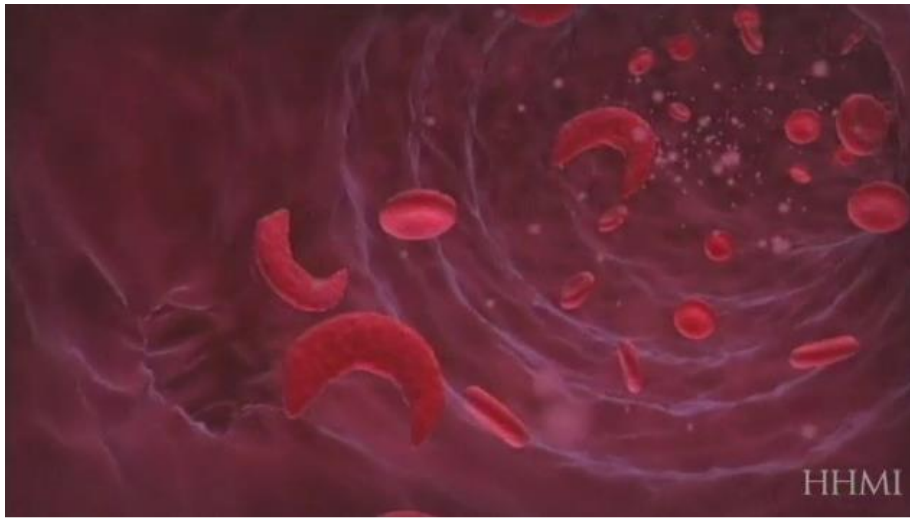
Substitution Examples

Location	Wild-Type (unmutated)	Silent Mutation	Missense Mutation	Nonsense Mutation
DNA	GTC	GTT	GTG	ATC
Messenger RNA (mRNA)	CAG	CAA	CAC	UAG
Amino acid	Glutamine	Glutamine	Histidine	Stop

*Student Handout:
Answer Questions 5–6.*

Sickle Cell Anemia

Sickle cell anemia (or sickle cell disease) is caused by a point mutation that affects the shape of red blood cells. People with sickle cell anemia experience frequent pain, infections, and other symptoms.



Click on the image to view an animation on sickle cell anemia.

<http://www.hhmi.org/biointeractive/sickle-cell-anemia>

*Student Handout:
Answer Question 7.*

Rett Syndrome

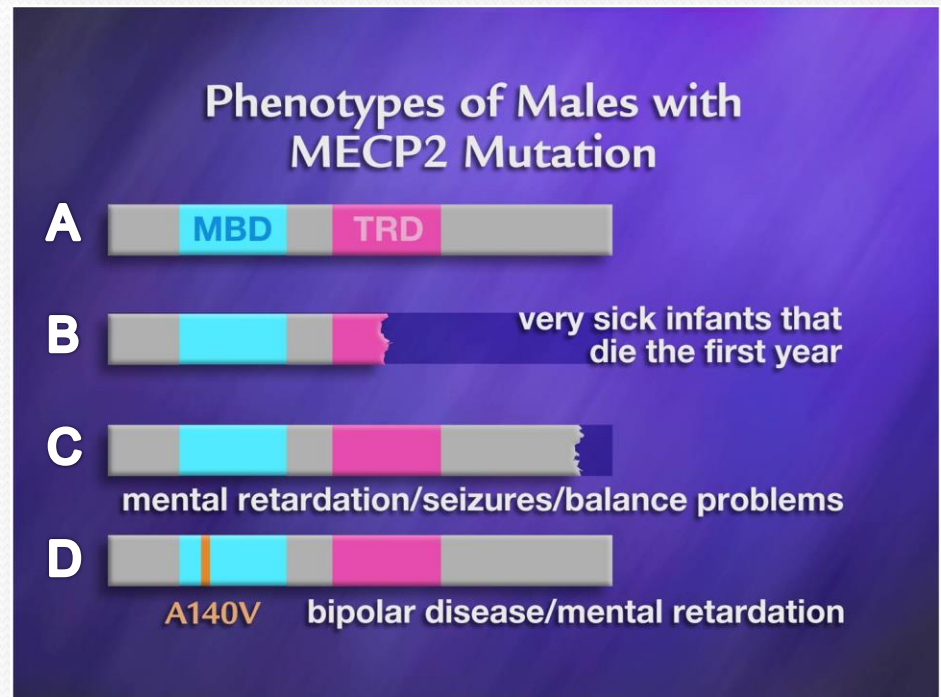
Rett syndrome primarily affects girls and causes severe learning, communication, and coordination problems. Its most common cause is mutations in the *MECP2* gene on the X chromosome. These mutations include changes in single base pairs, insertions or deletions of DNA in the gene, and changes that affect how the gene is processed into a protein.

Click to view a lecture clip on Rett syndrome.



<http://www.hhmi.org/biointeractive/rett-syndrome>

*Student Handout:
Answer Question 8.*



Insertions and Deletions

Insertion and deletion mutations occur when one or more base pairs are inserted into or deleted from the DNA sequence.

mRNA is translated three nucleotides at a time. Insertions and deletions that do not involve three nucleotides or multiples of three nucleotides change the translation of all the mRNA downstream of the mutation. These **frameshift mutations** almost always result in a nonfunctional protein.

*Student Handout:
Answer Question 9.*

Repeat Expansion

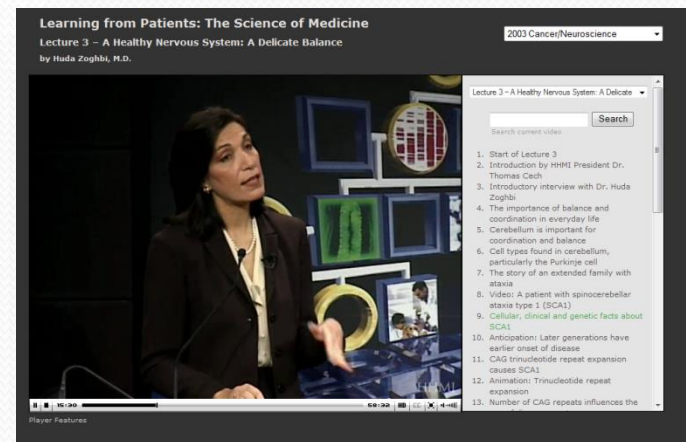
Some protein-coding genes contain **trinucleotide repeats**, or sequences of three nucleotides repeated several times. The number of repeats can increase, or expand, due to an error during DNA replication. The repeat expansion creates a new allele, but the protein still functions. However, when the number of repeats exceeds the “normal” threshold for the gene, the protein no longer functions properly.

*Student Handout:
Answer Question 10.*

Spinocerebellar Ataxia Type 1

Spinocerebellar ataxia type 1 (SCA1) is caused by a trinucleotide repeat expansion. SCA1 is an inherited disease of the central nervous system. The mutations cause malfunctioning of the nerve fibers that carry messages to and from the brain. Consequently, the cerebellum (the coordination center of the brain) degenerates.

Click to view a lecture clip on SCA1.



Learning from Patients: The Science of Medicine
Lecture 3 - A Healthy Nervous System: A Delicate Balance
by Huda Zoghbi, M.D.

2003 Cancer/Neuroscience

Lecture 3 - A Healthy Nervous System: A Delicate Balance

Search current video

1. Start of Lecture 3
2. Introduction by HHMI President Dr. Thomas Cech
3. Introductory interview with Dr. Huda Zoghbi
4. The importance of balance and coordination in everyday life
5. Cerebellum is important for coordination and balance
6. Cell types found in cerebellum, particularly the Purkinje cell
7. The story of an extended family with ataxia
8. Video: A patient with spinocerebellar ataxia type 1 (SCA1)
9. Cellular, clinical and genetic facts about SCA1
10. Anticipation: Later generations have earlier onset of disease
11. CAG trinucleotide repeat expansion causes SCA1
12. Animation: Trinucleotide repeat expansion
13. Number of CAG repeats influences the

<http://media.hhmi.org/hl/03Lect3.html?start=12:26&end26:16>

*Student Handout:
Answer Question 11.*

Are All Mutations “Bad”?

A common misconception is that “all mutations are bad.” We learned that some mutations in genes have no effect, such as silent mutations, whereas others cause disease. But mutations can also benefit an organism. Here is an example.



**Click to view the short film
*The Making of the Fittest:
Natural Selection and
Adaptation.***

<http://www.hhmi.org/biointeractive/making-fittest-natural-selection-and-adaptation>

*Student Handout:
Answer Question 12.*

Chromosomal Alterations

Changes to the number or structure of chromosomes can affect an organism's phenotype.

Such large-scale changes most often occur during the S phase of interphase, when DNA is replicating; during prophase I of meiosis, when crossing-over occurs; or upon exposure to damaging agents, such as radiation.

*Student Handout:
Answer Question 13.*

Types of Chromosomal Alterations

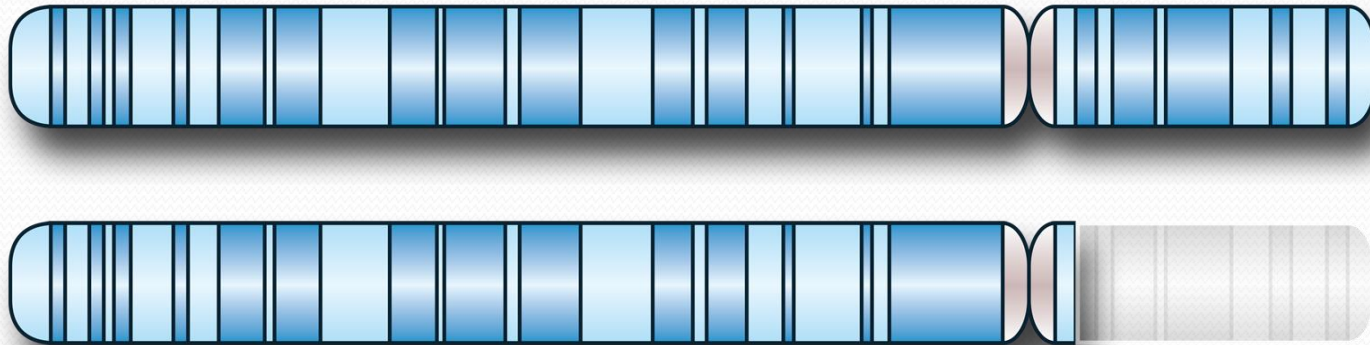
There are four main alterations in chromosome structure:

- **Chromosomal deletions** occur when part or all of a chromosome is lost.
- **Chromosomal inversions** occur when a segment of a chromosome breaks off and reattaches in the reverse orientation.
- **Chromosomal translocations** occur when a part of a chromosome breaks off and attaches to a nonhomologous chromosome.
- **Chromosomal duplications** occur when part or all of a chromosome is repeated.

*Student Handout:
Answer Questions 14–15.*

Cri-du-Chat Syndrome

Cri-du-chat is a rare disorder caused by a chromosomal alteration on chromosome 5. Infants with this condition often have a high-pitched cry that sounds like a cat's. The drawing below shows an affected individual's chromosome 5.

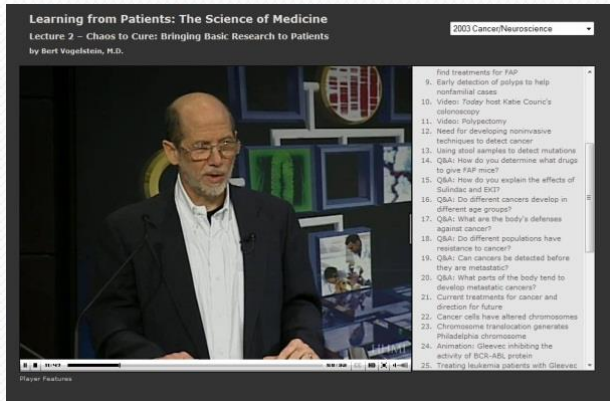


*Student Handout:
Answer Question 16.*

Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a rare cancer caused by a chromosomal alteration in somatic cells. It is characterized by increased and unregulated growth of myeloid cells in the bone marrow, which then accumulate in the blood.

Click to view a lecture clip on CML.



Learning from Patients: The Science of Medicine
Lecture 2 – Chaos to Cure: Bringing Basic Research to Patients
by Bert Vogelstein, M.D.

2003 CancerNeuroscience

Find treatments for FAP
9. Early detection of polyps to help nonfamilial cases
10. Video: Tuley host Katie Couric's interview
11. Video: Polypectomy
12. Need for developing minimally-invasive techniques to detect cancer
13. Using stool samples to detect mutations
14. Q&A: How do you determine what drugs to give FAP mice?
15. Q&A: How do you explain the effects of Sulindac and EVT?
16. Q&A: Do different cancers develop in different age groups?
17. Q&A: What are the body's defenses against cancer?
18. Q&A: Do different populations have resistance to cancer?
19. Q&A: Can cancers be detected before they are metastatic?
20. Q&A: What parts of the body tend to develop metastatic cancers?
21. Current treatments for cancer and direction for future
22. Cancer cells have altered chromosomes
23. Chromosome translocation generates Philadelphia chromosome
24. Animation: Gleevec inhibiting the activity of BCR-ABL protein
25. Tracking leukemia patients with Gleevec

<http://media.hhmi.org/hl/03Lect2.html?start=32:20&end=36:11>

Click to view an animation on CML and Gleevec.



<http://www.hhmi.org/biointeractive/cml-and-gleevec>

*Student Handout:
Answer Question 17.*

A Closer Look at Duplications

Chromosomal duplications result in two copies of a gene or genes.

Two genes are **paralogous** if they exist at different chromosomal locations in the same organism and if they arose from a common ancestral gene.

Gene duplication can lead to new traits, and it plays a major role in the evolution and diversification of life.

*Student Handout:
Answer Question 18.*

Gene Duplication Outcomes

When an entire gene is duplicated

- one of the two gene copies can lose its function by accumulating mutations over generations;
- one of the two gene copies can gain a novel function through subsequent mutation (this only happens if the original gene duplication event does not severely affect the organism and persists over generations); or
- the two copies of the gene split the total function of the ancestral gene into two unique but related functions for more-efficient expression.

*Student Handout:
Answer Question 19.*

Duplicated Genes in Animals

Lysozyme is an enzyme in animals that protects against bacterial infection. Alpha-lactalbumin is a nonenzyme protein that plays a role in mammalian milk production.

Both proteins have similar amino acid sequences and three-dimensional structures. They are both present in mammals, but only lysozyme is present in birds.



*Student Handout:
Answer Question 20.*

The “Death” of Genes

Genes can lose their protein-producing abilities or stop being expressed. Such genes are called **pseudogenes**. As species have evolved, diverged, and gone extinct, so have their genes.

Genes become pseudogenes when they accumulate mutations over a long time. This only happens if the mutations do not compromise the organism’s survival; otherwise, natural selection would eliminate the mutations.

Student Handout: Answer Questions 21–22.

Examples of Gene Death

These two examples demonstrate the evolutionary significance of genes losing their functions.

- **Olfactory receptor genes in humans and mice:** Mice have about 1,500 olfactory receptor genes, while humans have about 1,000. Only 20 percent of mouse olfactory receptor genes are pseudogenes, compared to about 60 percent in humans.
- **Myoglobin gene in some icefish species:** Myoglobin is an oxygen-binding protein found in muscles, similar to hemoglobin in red blood cells. Myoglobin is absent from muscles, including the heart, of several, but not all, icefish species.

*Student Handout:
Answer Question 23.*

Gene Birth and Death in Icefish

Icefish are an excellent example of both the birth and death of genes.

Click to view the short film *The Making of the Fittest: The Birth and Death of Genes*.



<http://www.hhmi.org/biointeractive/making-fittest-birth-and-death-genes>

*Student Handout:
Answer Questions
24–27.*

Resources

- Campbell, Neil A., and Jane B. Reece. *Biology, AP Edition*. 8th ed. San Francisco: Pearson Benjamin Cummings, 2008.
- Carroll, Sean B. “In Cold Blood: The Tale of the Icefish.” Chap. 9 in *Into the Jungle: Great Adventures in the Search for Evolution*. San Francisco: Pearson Benjamin Cummings, 2008.
- Deng, Cheng, C.-H. Christina Cheng, Hua Ye, Ximiao He, and Liangbiao Chen. “Evolution of an Antifreeze Protein by Neofunctionalization under Escape from Adaptive Conflict.” *Proceedings of the National Academy of Sciences* 107, no. 50 (December 14, 2010): 21593–21598.
- Howard Hughes Medical Institute. DNA animations. 2011. www.BioInteractive.org.
- “Learning from Patients—The Science of Medicine.” 2003 Holiday Lectures on Science presented in Chevy Chase, MD, 2003.
- *The Making of the Fittest: The Birth and Death of Genes*. Chevy Chase, MD: Howard Hughes Medical Institute. 2011. Short film.
- *The Making of the Fittest: Natural Selection and Adaptation*. Chevy Chase, MD: Howard Hughes Medical Institute. 2011. Short film.
- Hurles, Matthew. “Gene Duplication: The Genomic Trade in Spare Parts.” *PLoS Biology* 2, no. 7 (2004): e206. doi:10.1371/journal.pbio.0020206.
- Raven, Peter H., and George B. Johnson. *Biology*. 9th ed. New York: McGraw-Hill, 2011.
- Zhang, Xiang et al. “Gene Duplication Adapts to Changing Environment.” *Nature Genetics* (March 4, 2002). (online)