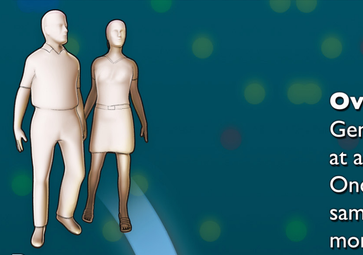
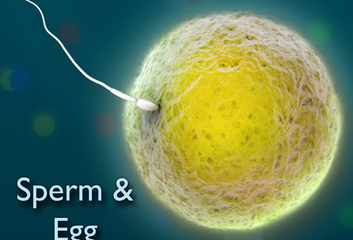
Genetic Mutations and Disease

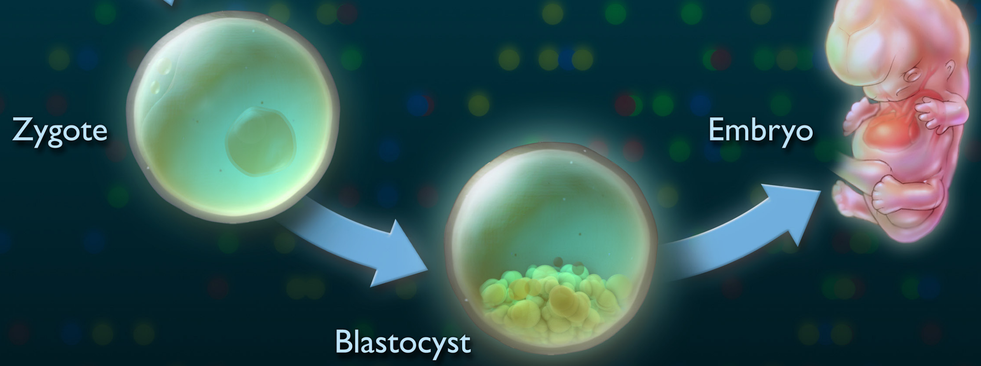
hhmi | BioInteractive

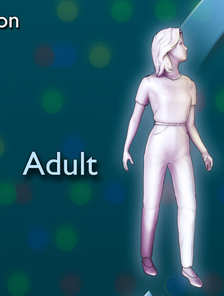


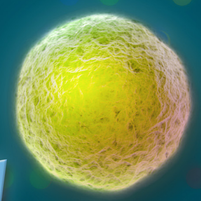
Overview
Genetic mutations are changes in a DNA sequence that can occur at any time in an individual's life and in many different cell types. Once a mutation occurs in a cell, its daughter cells will carry that same mutation. A mutation that occurs early in development is more likely to affect a greater portion of the body than a mutation occurring later in life. Only some mutations cause disease depending on where in the genome they occur.



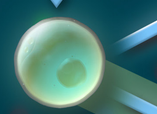
Development
In development, one fertilized cell becomes many different types of cells through repeated cycles of cell division and differentiation.



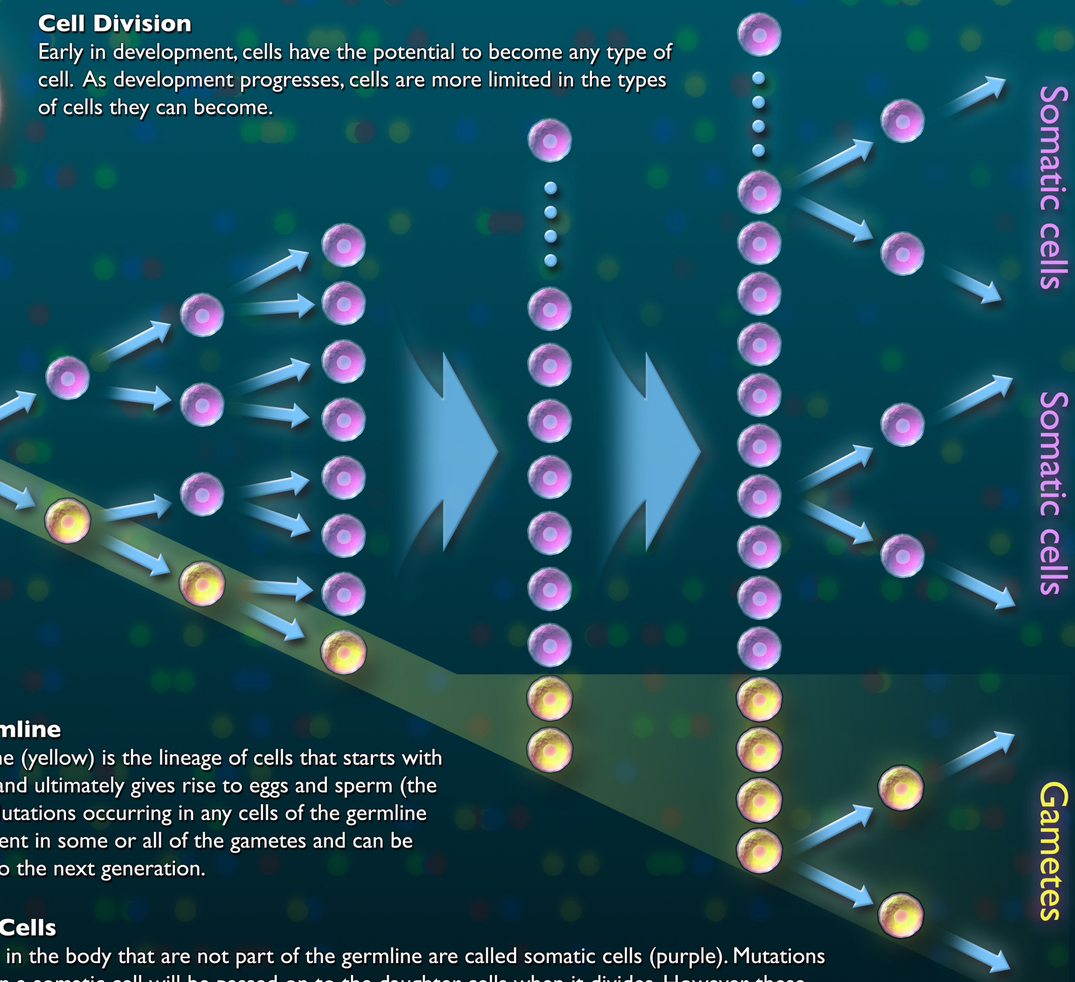




Fertilization



Cell Division
Early in development, cells have the potential to become any type of cell. As development progresses, cells are more limited in the types of cells they can become.

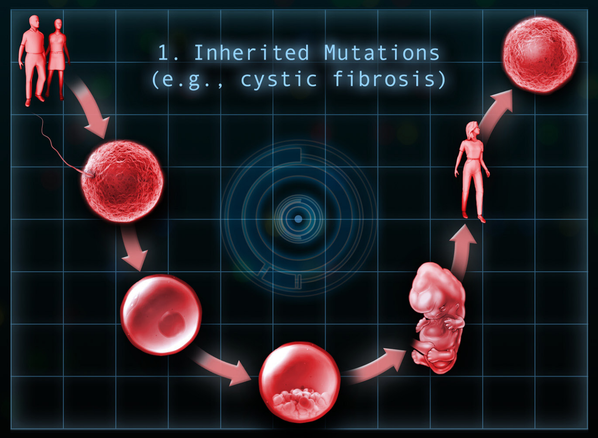


The Germline
The germline (yellow) is the lineage of cells that starts with the zygote and ultimately gives rise to eggs and sperm (the gametes). Mutations occurring in any cells of the germline will be present in some or all of the gametes and can be passed on to the next generation.

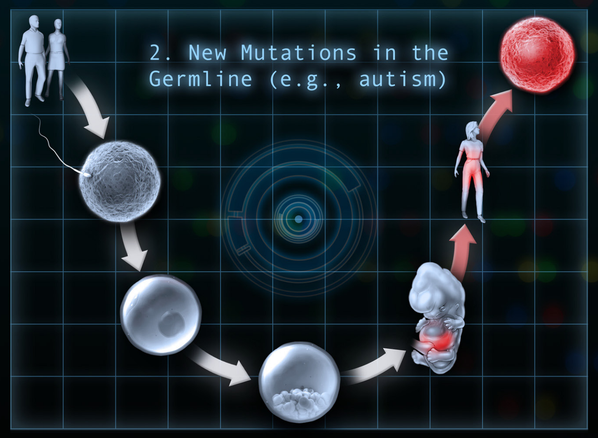
Somatic Cells
All the cells in the body that are not part of the germline are called somatic cells (purple). Mutations that occur in a somatic cell will be passed on to the daughter cells when it divides. However, these mutations are not inherited by the individual's offspring since they do not occur in the germline.

When and Where Mutations Occur Matters

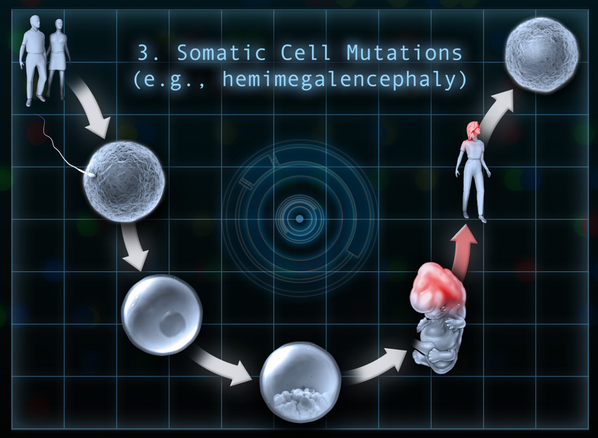
Cells and tissues with disease-associated mutations are highlighted in red



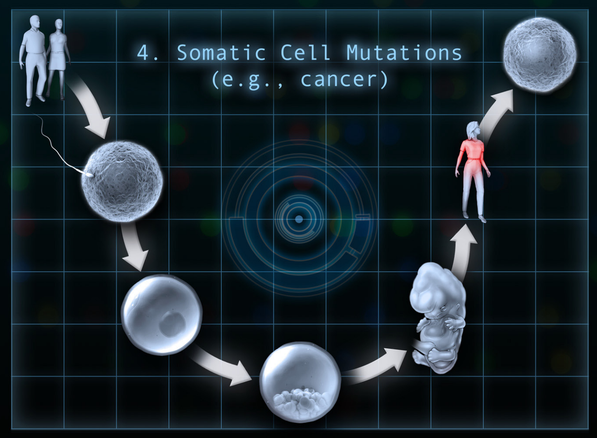
When a mutation is inherited from parent to offspring, all the cells of the offspring will carry the mutation including the germline. Therefore, the mutation can be inherited by subsequent generations. Cystic fibrosis (recessive) and Huntington disease (dominant) are well-studied examples.



If a disease mutation occurs late in the germline lineage, during gamete production, offspring may inherit the mutation from the unaffected individual. This is an example of a new (*de novo*) mutation. Some cases of autism have been shown to involve *de novo* mutations.



Hemimegalencephaly is a genetic disorder in which part of the brain grows larger than normal. It is caused by a mutation that arises in a somatic cell early in brain development. The mutation can typically only be detected in the affected parts of the brain and nowhere else.



Cancer results primarily from somatic mutations. While cancer is not inherited, mutations associated with higher risk of cancer can be. For example, people who inherit certain mutations in the *BRCA1* gene are more likely to develop breast and ovarian cancer.