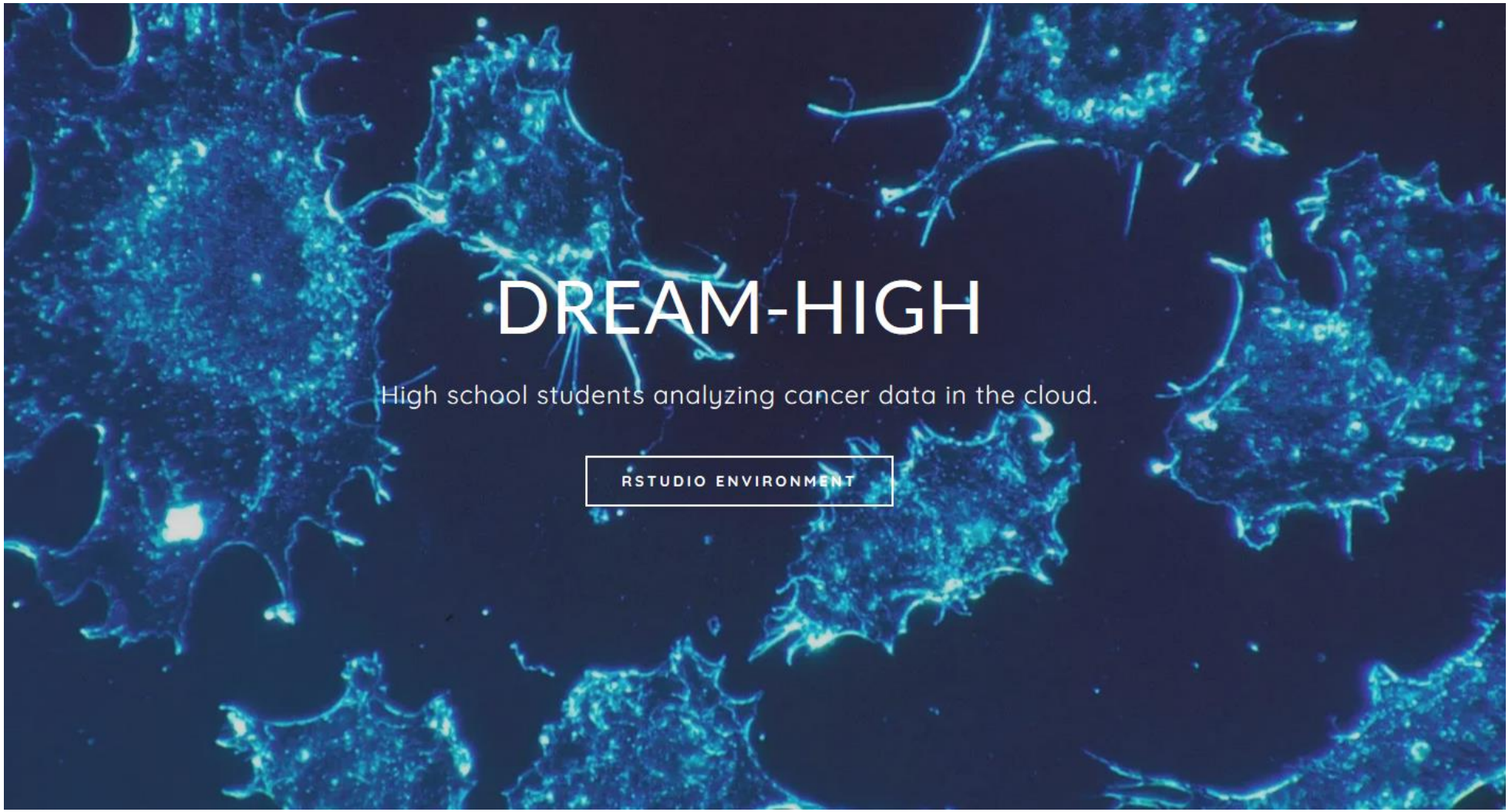


Week 1: July 7, 2020

Cancer Systems Biology

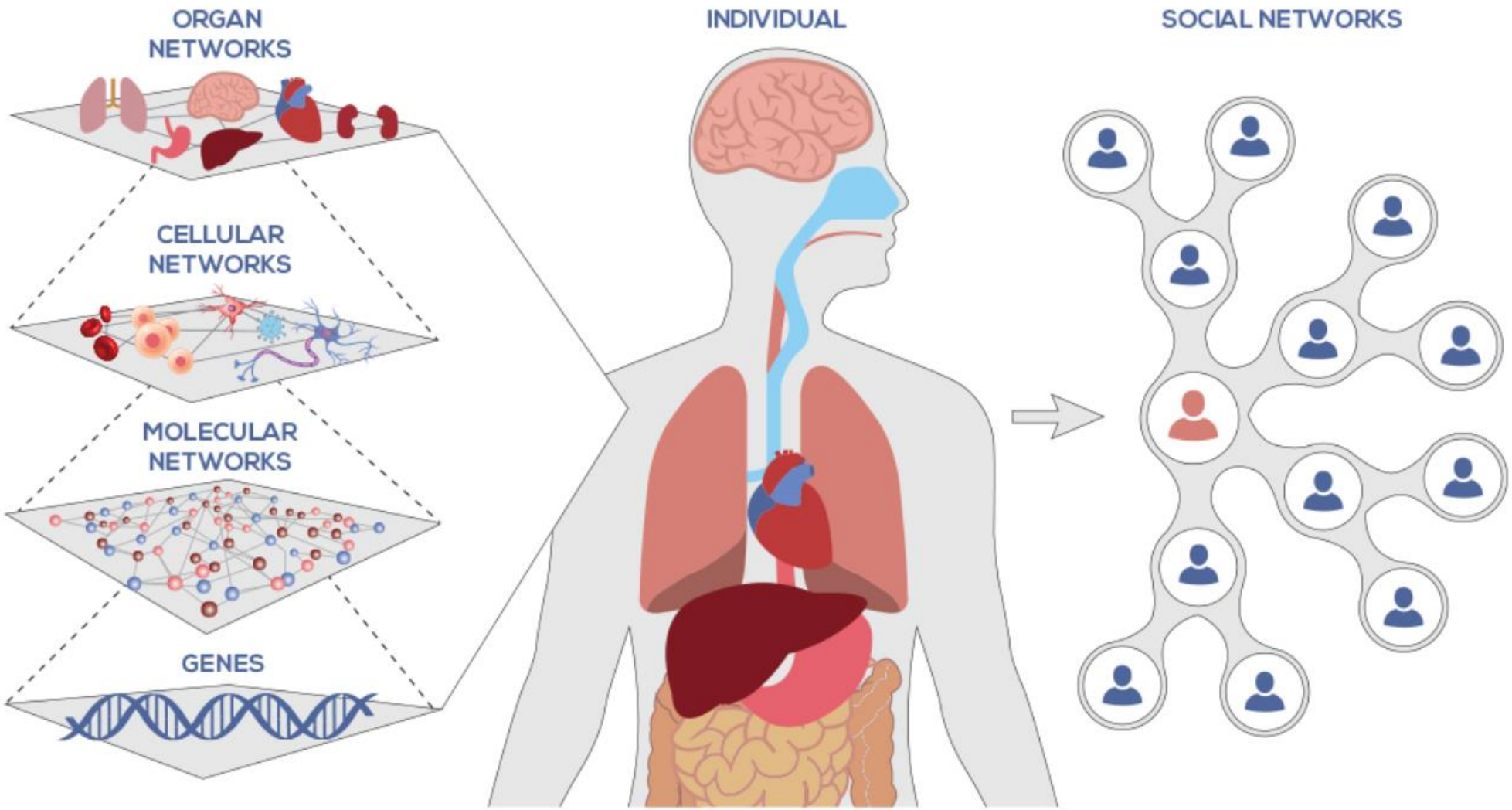
integrates experimental and computational approaches to study the complexities of cancer.

Cancer is a complex disease system involving multiple molecular, genetic, and cellular events.

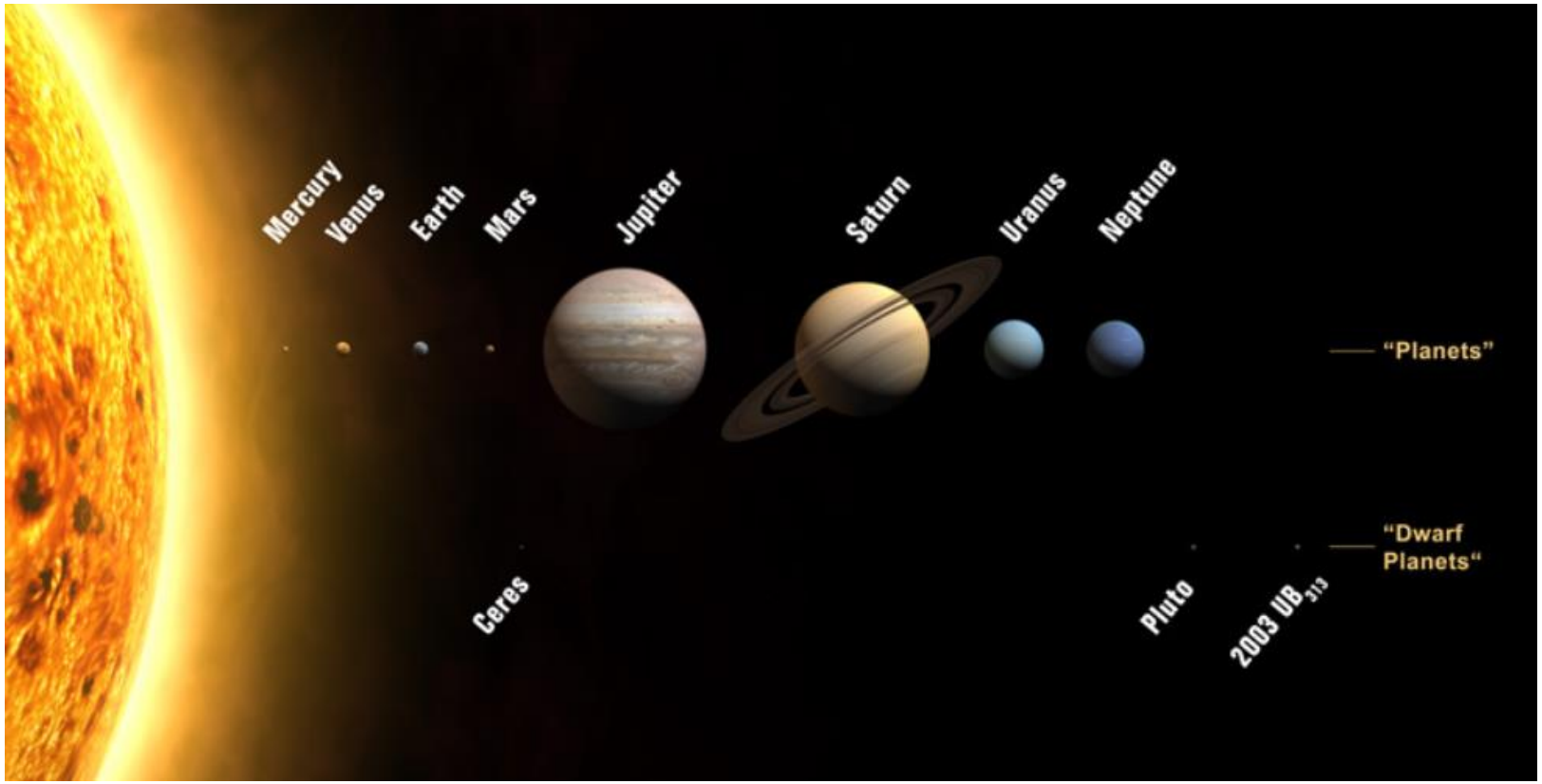
Systems biology is based on the understanding that the whole is greater than the sum of the parts.

Computers are essential components of modern biological research.

Systems biology is based on the understanding that the whole is greater than the sum of the parts.



Last week, we loosely defined a “system” as a set of things working together as parts of an interconnecting network, and we considered the human body as a system (molecules, cells, organs).

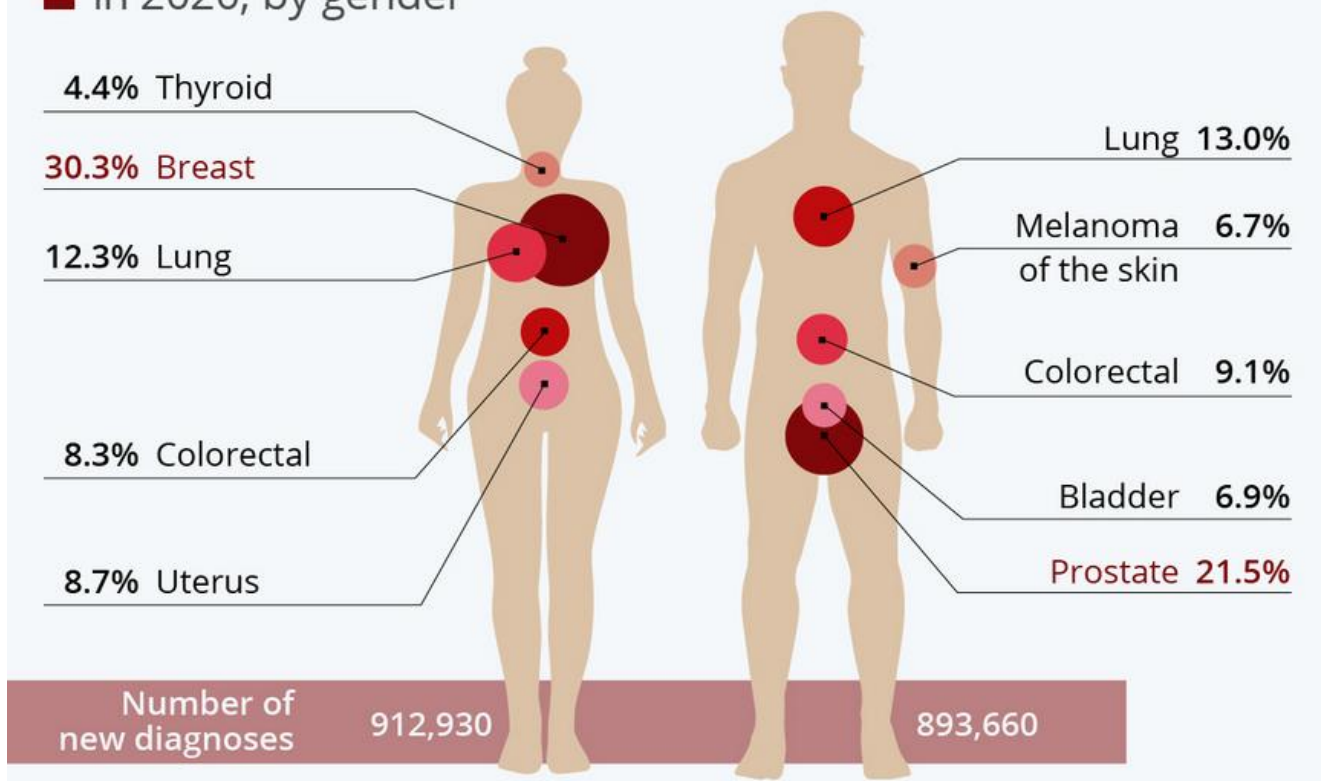


What are some systems you come across or know about?

- hospital system
- our government system
- deli system
- Mail system
- transporting food
- School system
- Train systems
- Your coworkers
- Ecosystems

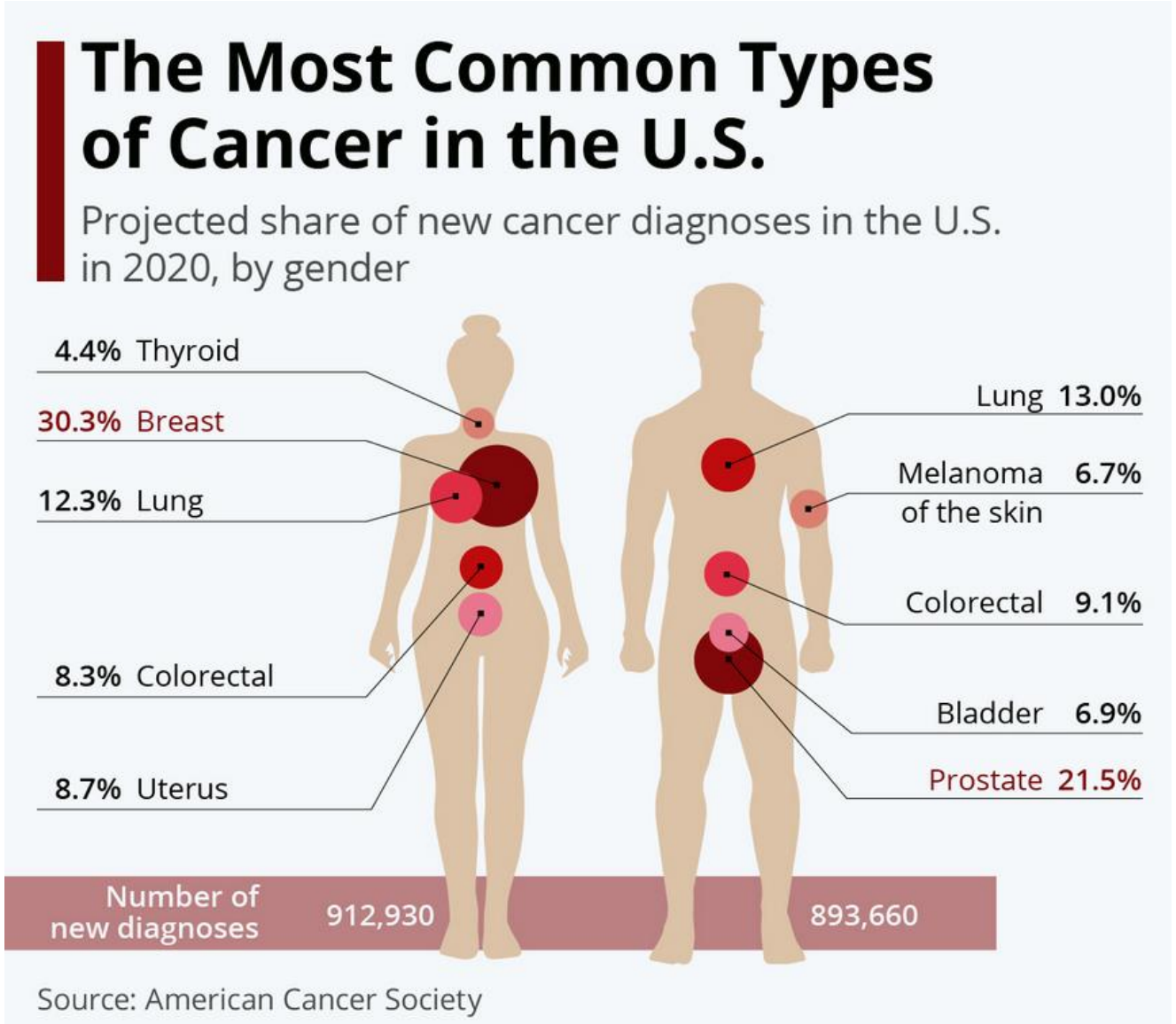
The Most Common Types of Cancer in the U.S.

Projected share of new cancer diagnoses in the U.S. in 2020, by gender



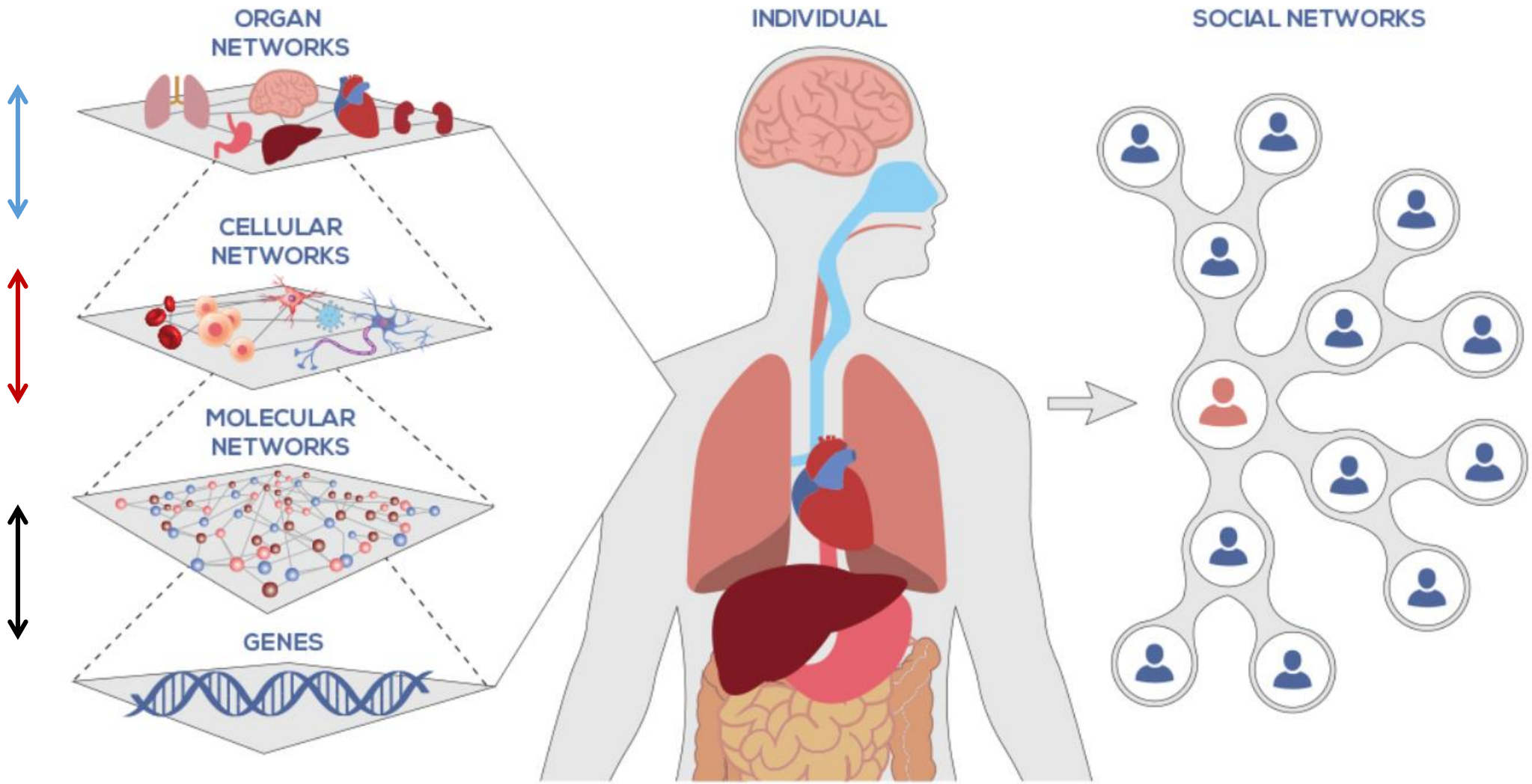
Source: American Cancer Society

64% of all cases

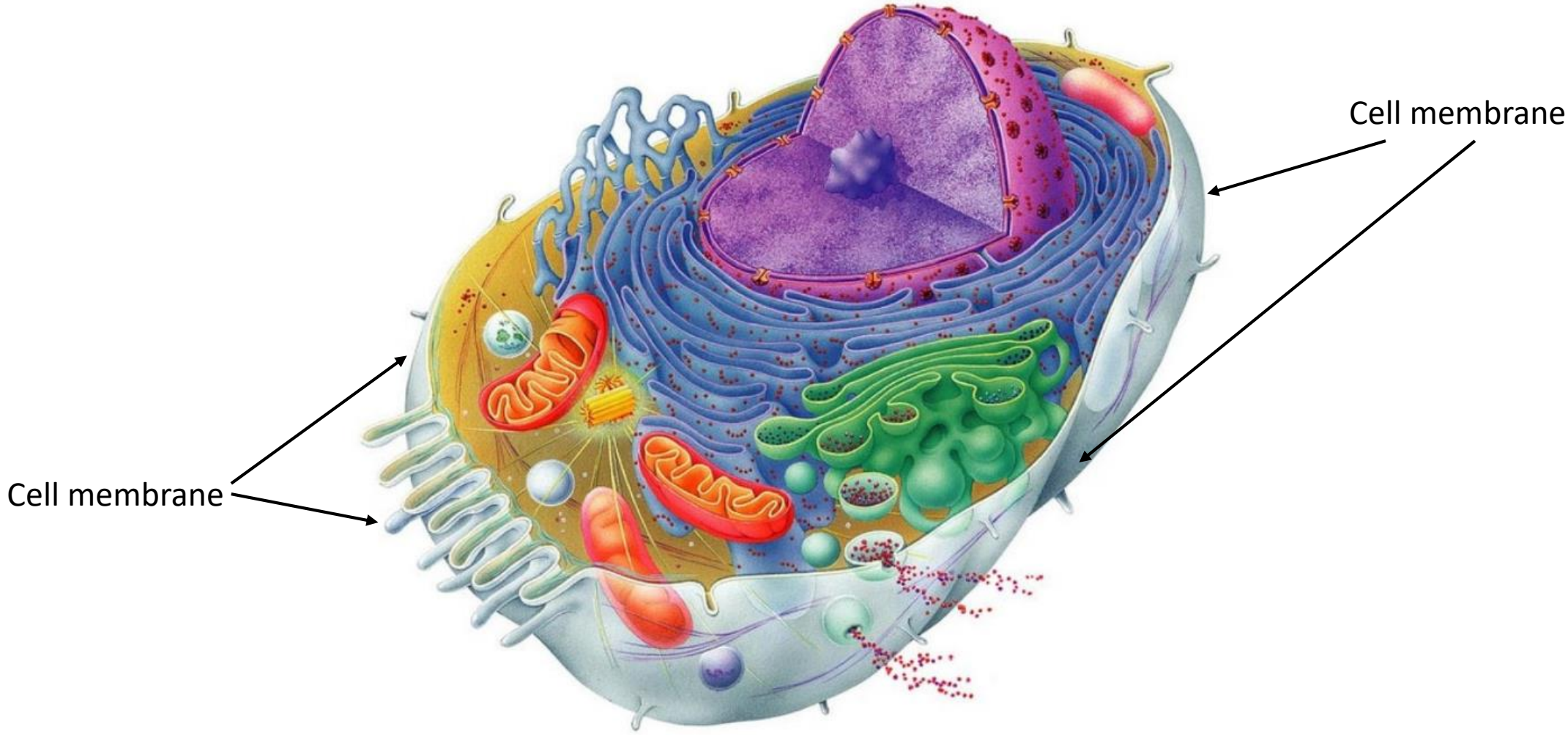


57% of all cases

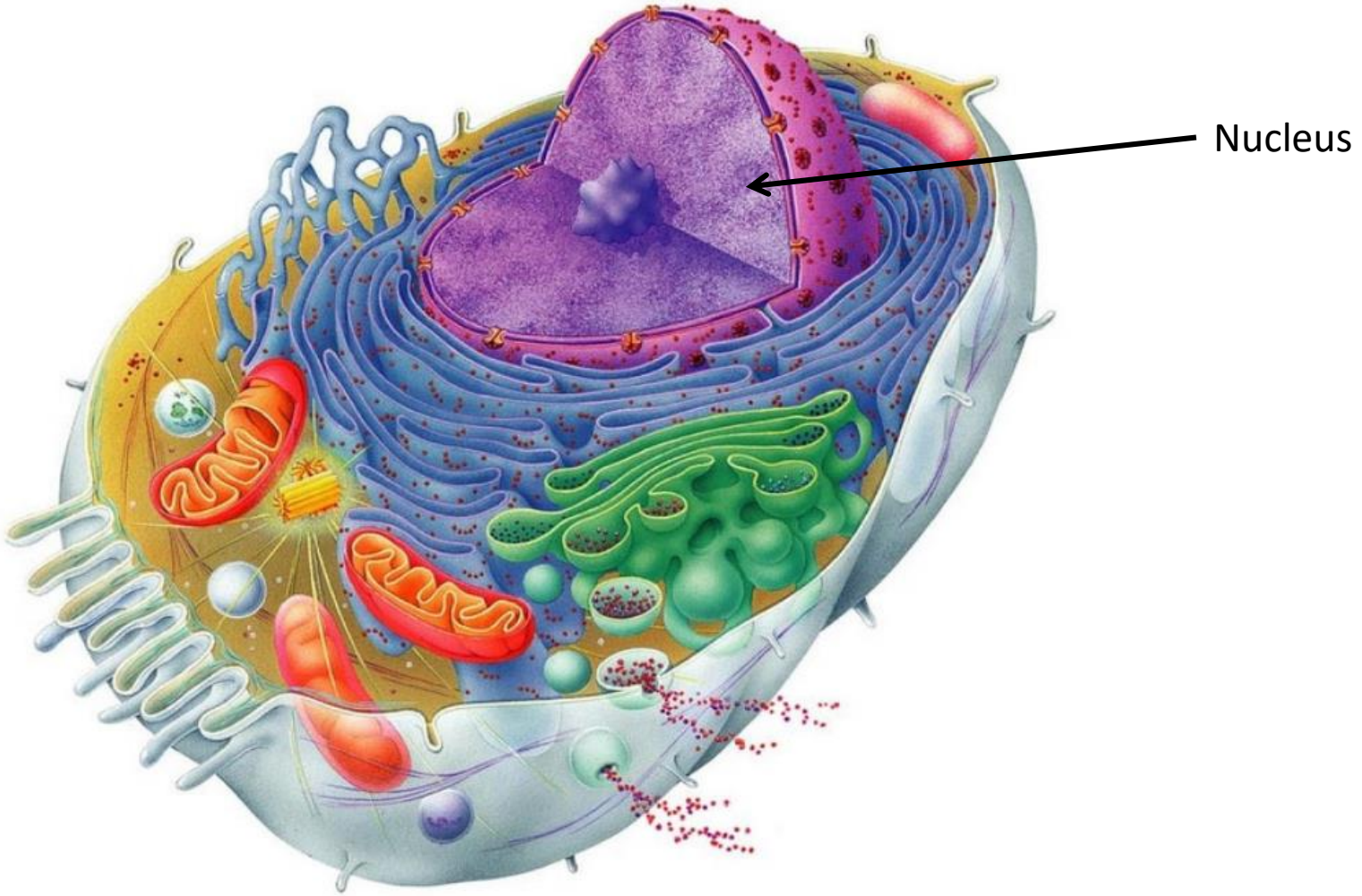
Systems biology is based on the understanding that the whole is greater than the sum of the parts.



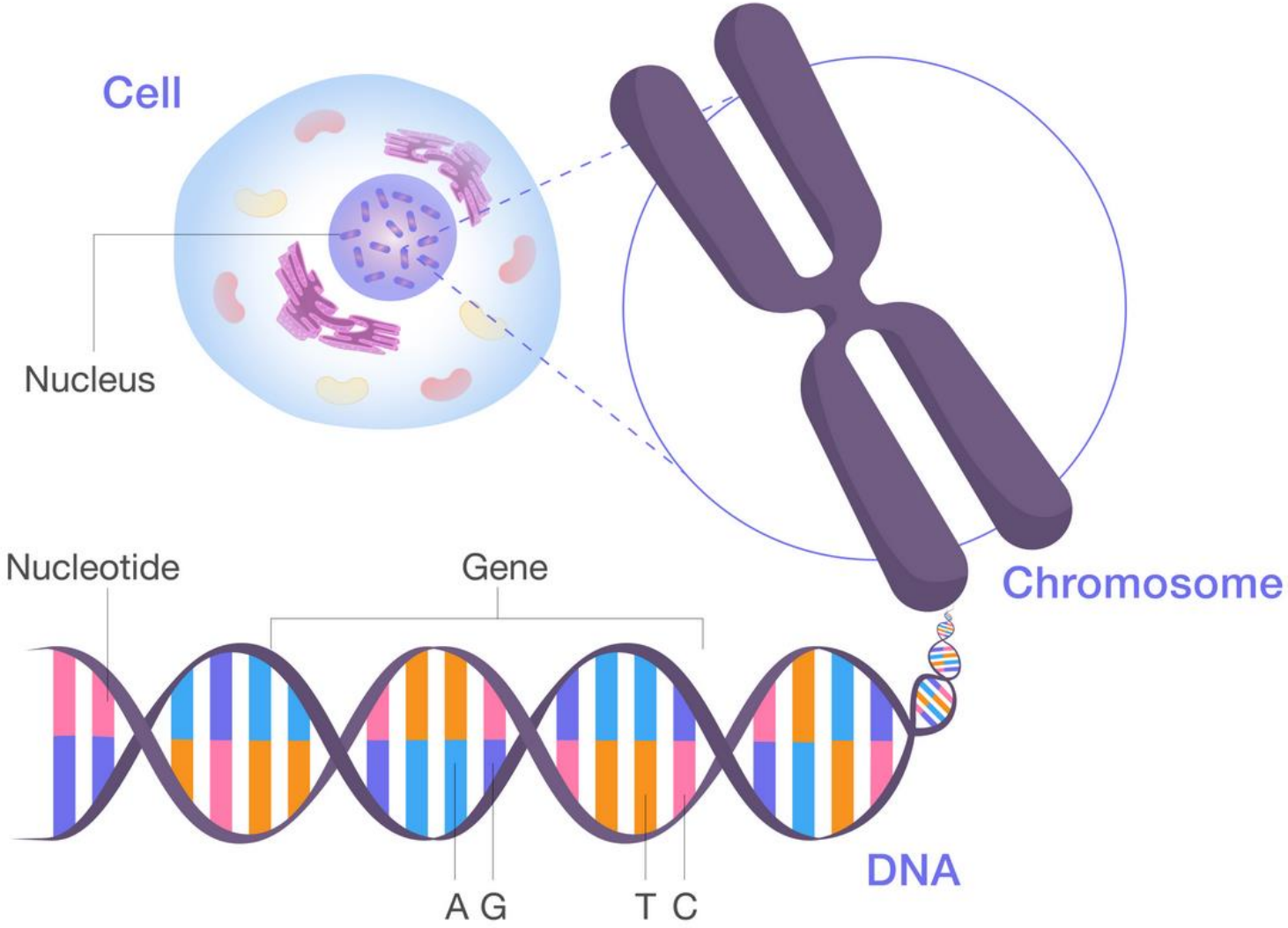
In the diagram of a human cell, click on the cell membrane.



In the diagram of a human cell, click on the nucleus.

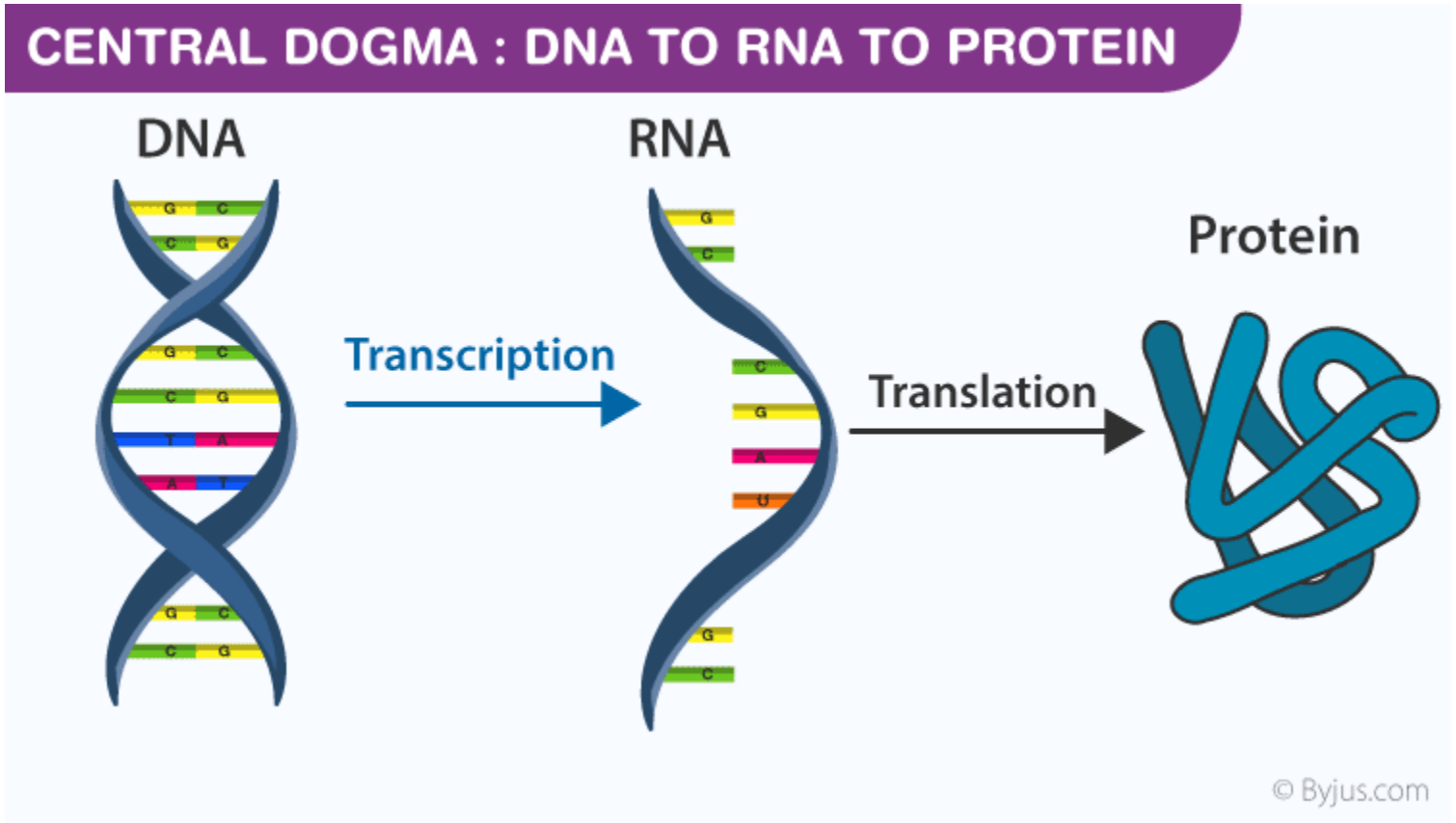


The nucleus of the cell contains our “genetic code.”



Central dogma of molecular biology

Our genes (DNA) contain instructions to make proteins, which do most of the work in our cells.



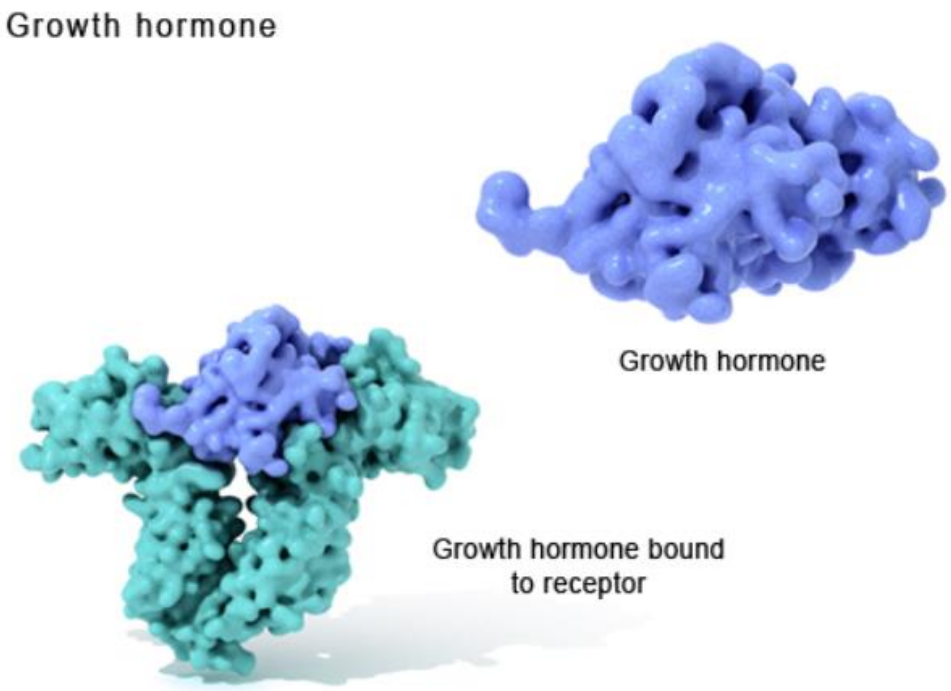
What are proteins and what do they do?

Proteins are large, complex molecules that play many critical roles in the body. They do most of the work in cells and are required for the structure, function, and regulation of the body's tissues and organs.

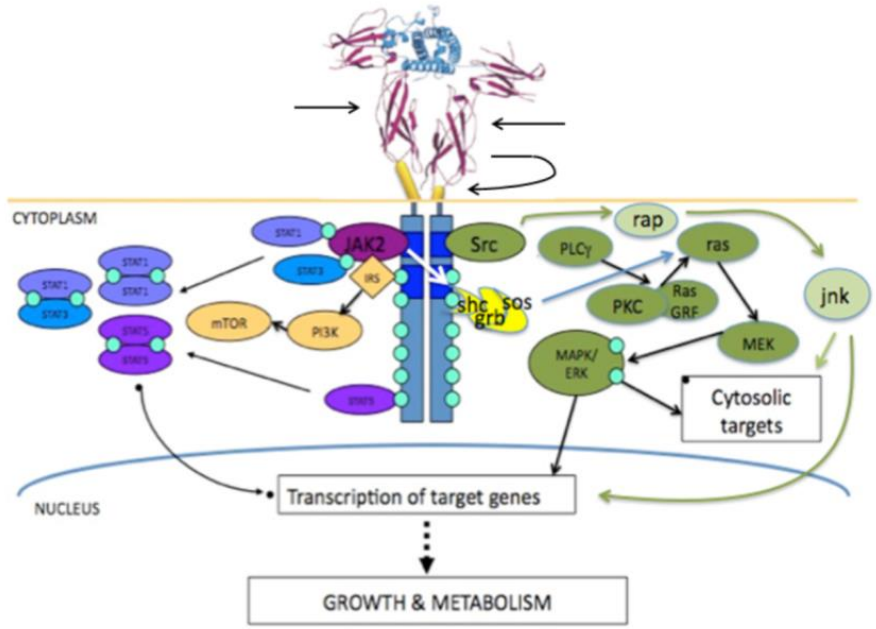
Examples of protein functions

Function	Description
Antibody	Antibodies bind to specific foreign particles, such as viruses and bacteria, to help protect the body.
Enzyme	Enzymes carry out almost all of the thousands of chemical reactions that take place in cells. They also assist with the formation of new molecules by reading the genetic information stored in DNA.
Messenger	Messenger proteins, such as some types of hormones, transmit signals to coordinate biological processes between different cells, tissues, and organs.
Structural component	These proteins provide structure and support for cells. On a larger scale, they also allow the body to move.
Transport/storage	These proteins bind and carry atoms and small molecules within cells and throughout the body.

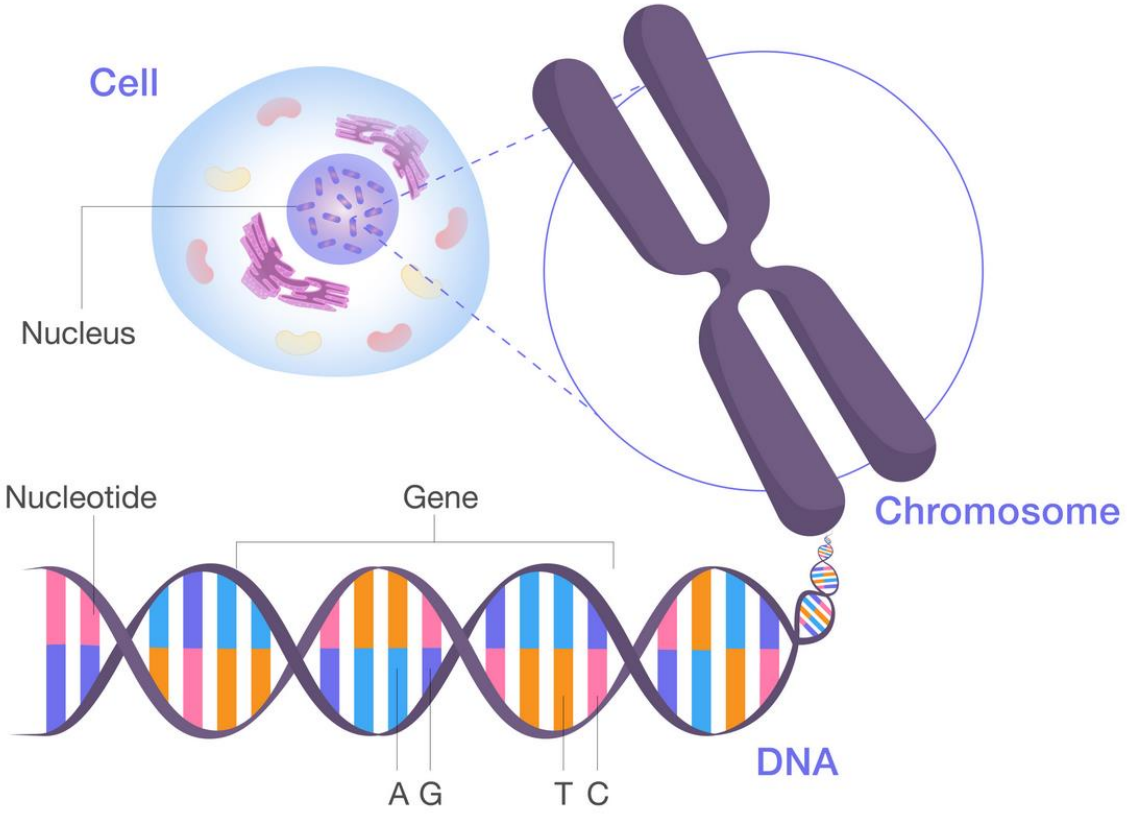
Messenger protein example: **Growth hormone**



Function of the growth hormone protein in a cell



Cancer is a group of more than 100 diseases caused by mutations in the genetic code.



Cancer is a group of more than 100 diseases caused by mutations in the genetic code.

Types of mutations

Wild type "Normal Gene"	**THE ONE BIG FLY HAD ONE RED EYE**
Missense	THQ ONE BIG FLY HAD ONE RED EYE
Nonsense	THE ONE BIG
Frameshift	THE ONE QBI GFL YHA DON ERE DEY
Deletion	THE ONE BIG HAD ONE RED EYE
Duplication	THE ONE BIG FLY FLY HAD ONE RED EYE
Insertion	THE ONE BIG WET FLY HAD ONE RED EYE

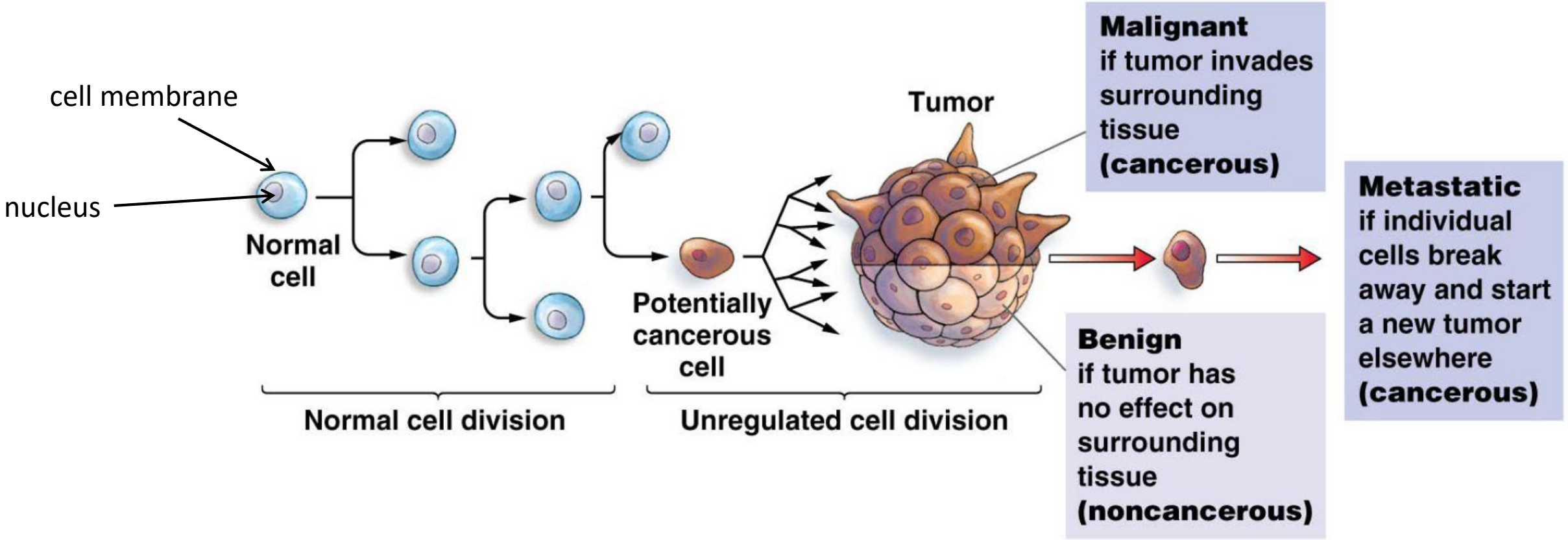
Different mutations affect protein functions in different ways.

Mutations lead to cell behavior that is not normal (abnormal).

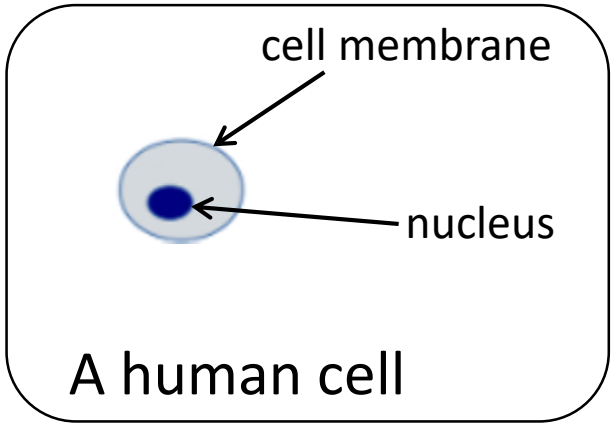
If genes are like words, and a mutation is like a misspelled word, how could we figure out what mutation might be causing cancer?

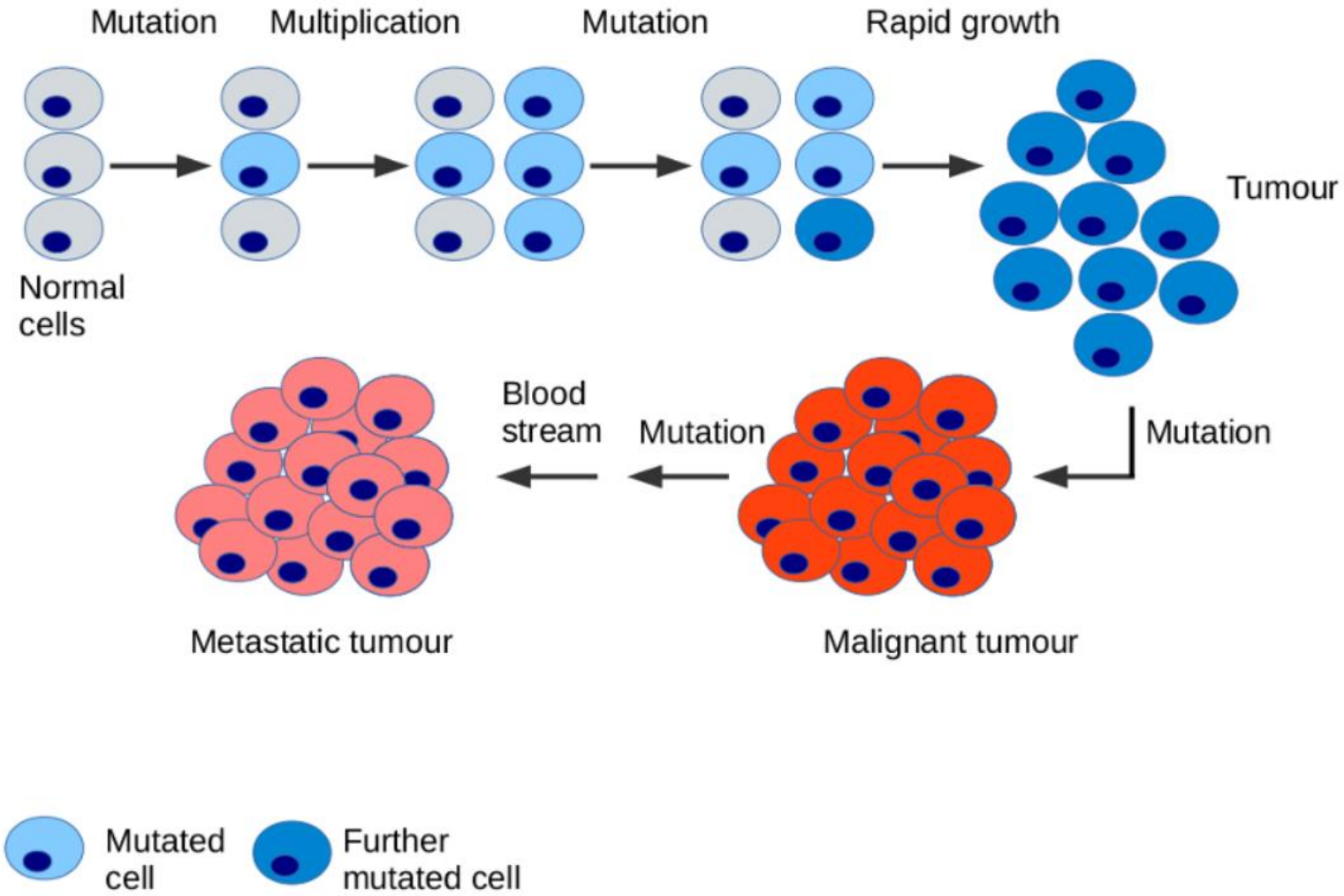
- Proof reading
- find the pattern, then find when it changes
- Contrast
- Separate the misspelled words from the words that aren't misspelled
- Look at the DNA of the cells
- Auto Correct

How cancer develops



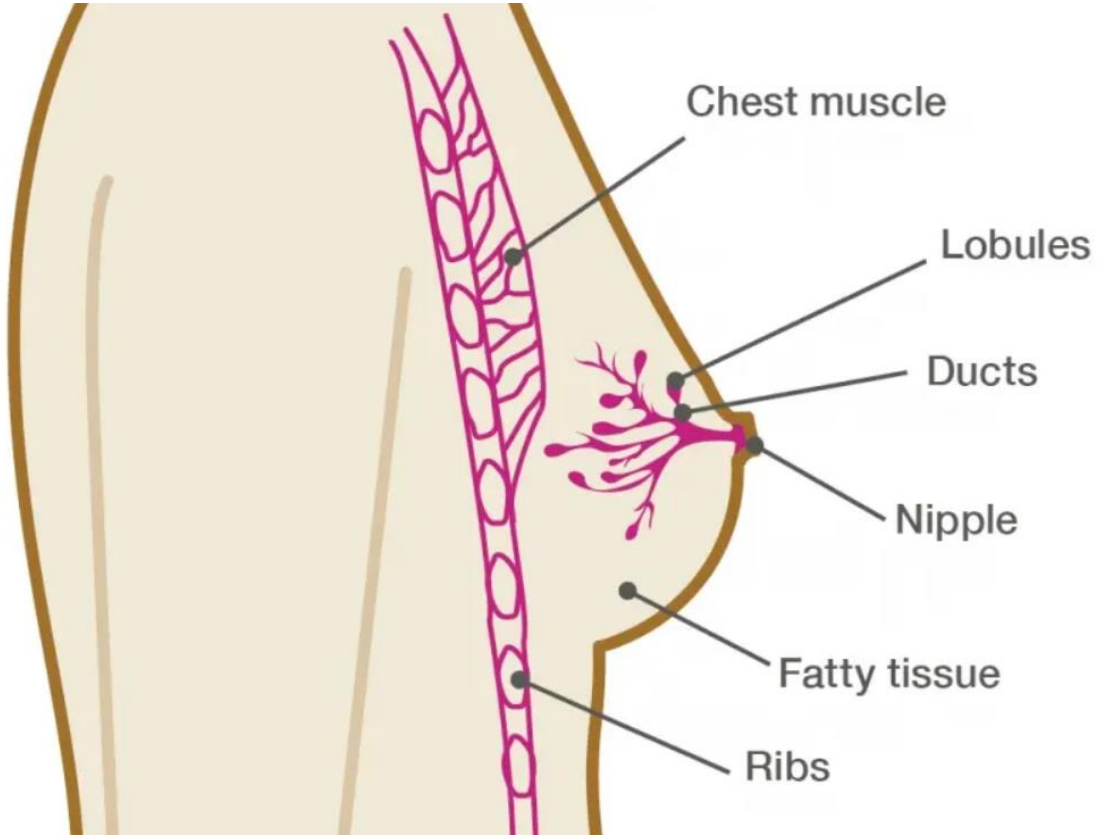
How cancer develops

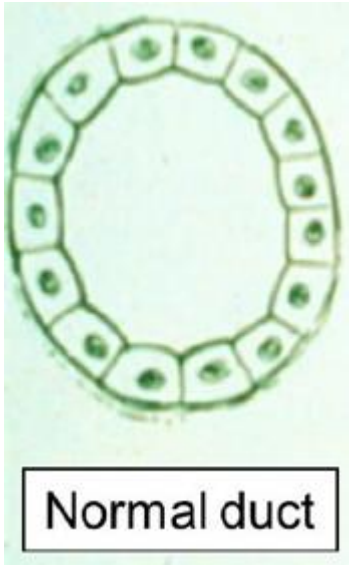




Breast cancer development

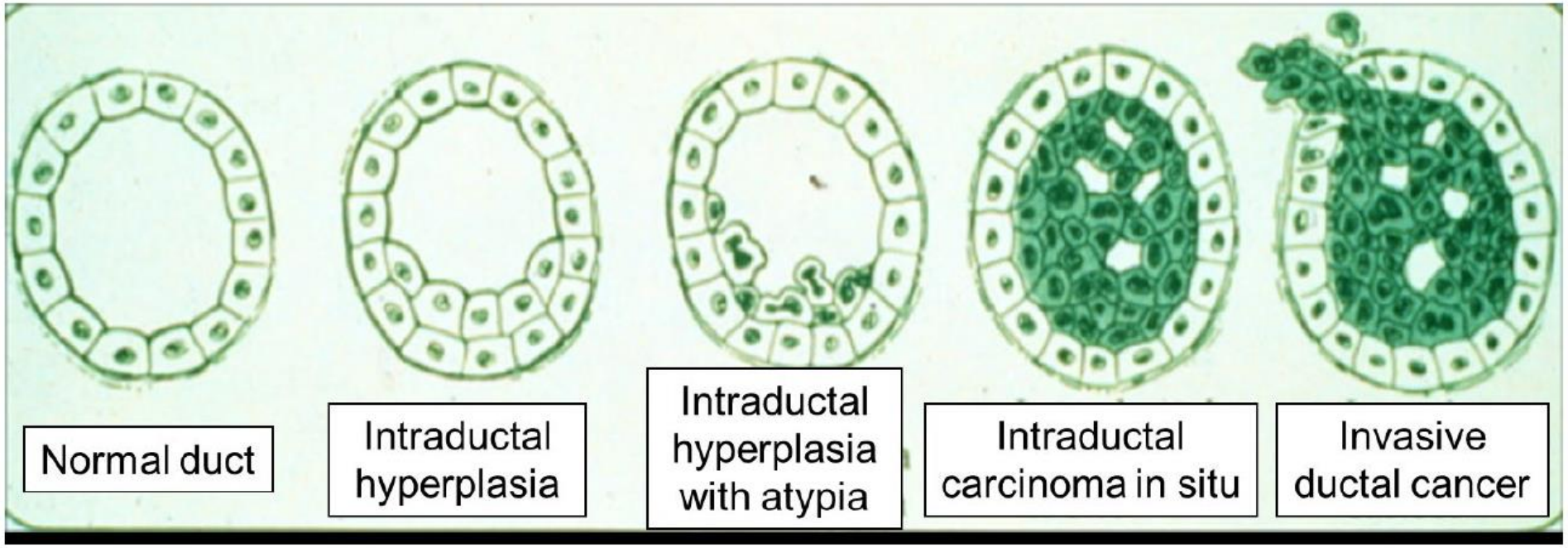
Breast duct or milk duct: A thin tube in the breast that carries milk from the breast lobules to the nipple.





Cross-section of a duct tube.

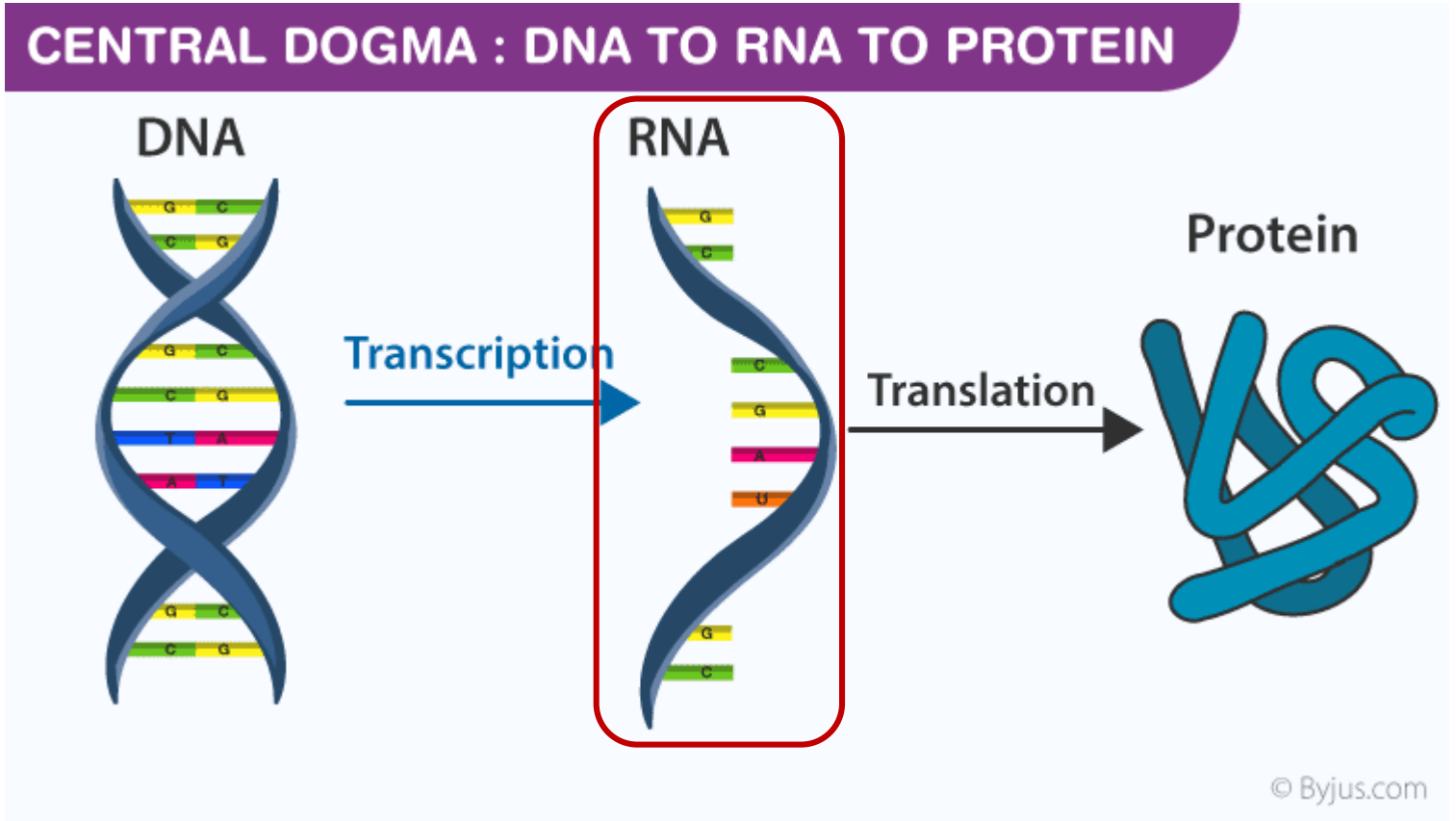
Breast cancer development



5 year survival:
Stage 1: 95-100%
Stage 2: 86%
Stage 3: 57%
Stage 4: 20%

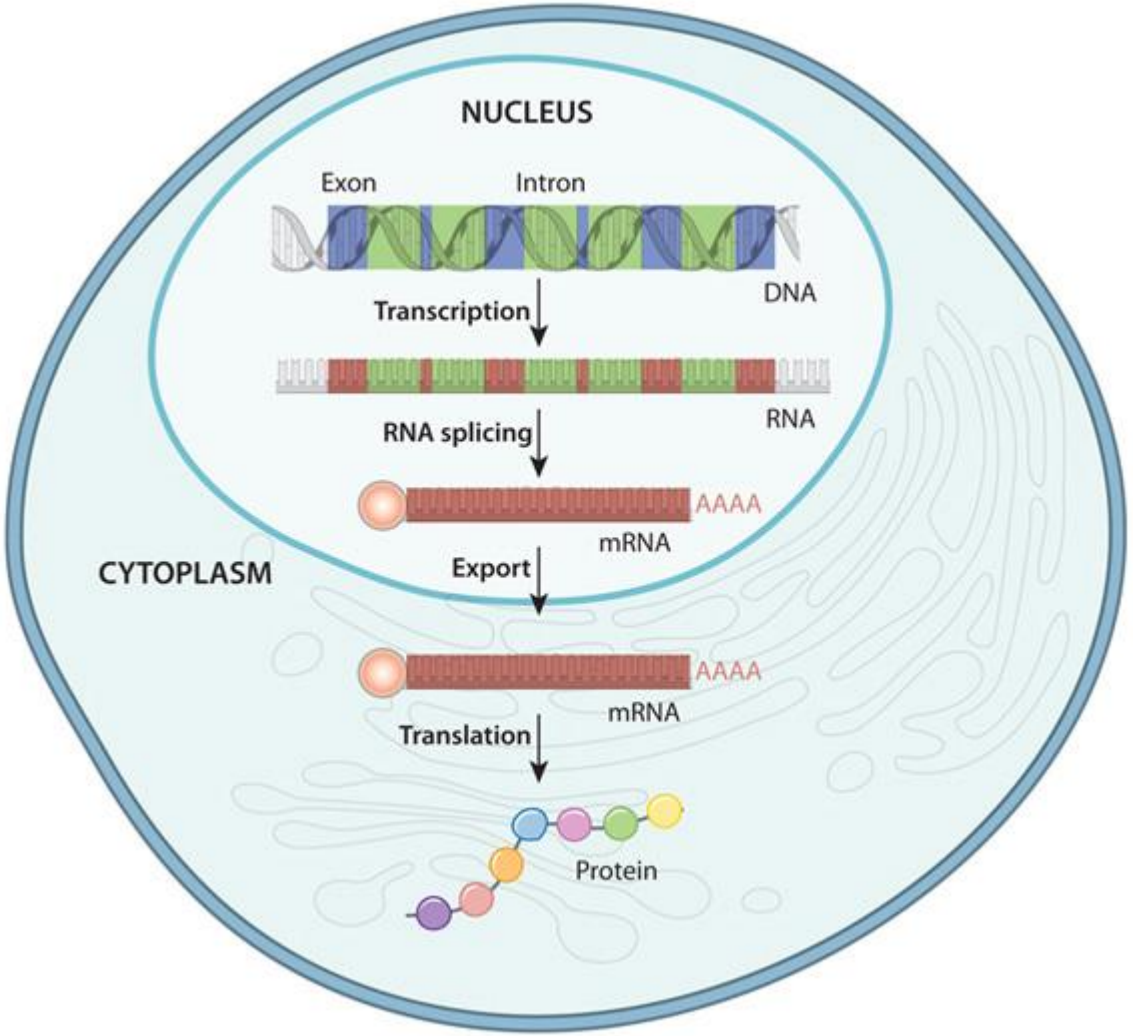
Central dogma of molecular biology

Our genes (DNA) contain instructions to make proteins, which do most of the work in our cells.



Measuring RNA tells us about the proteins in cells.

A more detailed version of the central dogma of molecular biology



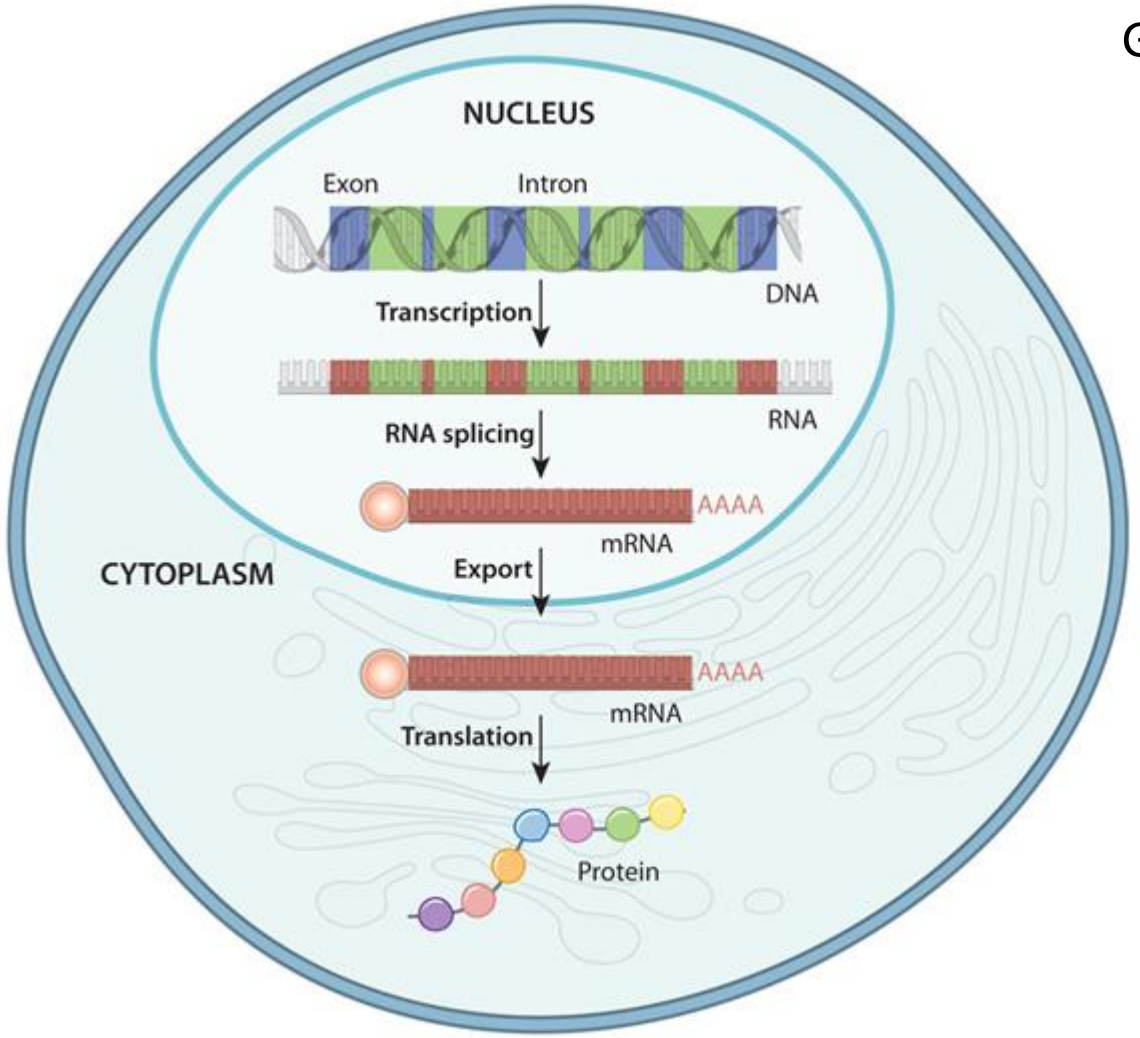
Genes in the nucleus carry our genetic information.
Genes are made up of DNA.

The DNA in genes are copied or transcribed to RNA.

The RNA is edited to create messenger RNA or mRNA.

mRNA transcripts serve as templates for building proteins.

DNA → RNA → protein



Humans have somewhere around 20,000 genes.

Genes are DNA molecules that code for mRNA molecules.

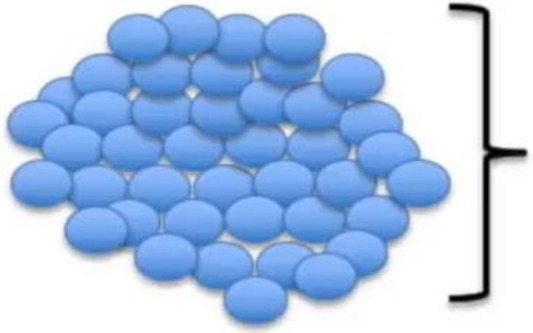
mRNA molecules are used in the formation of a protein.

High-throughput sequencing experiments measure the mRNA in a collection of cells.

Measuring mRNA tells us about the proteins in the cells.

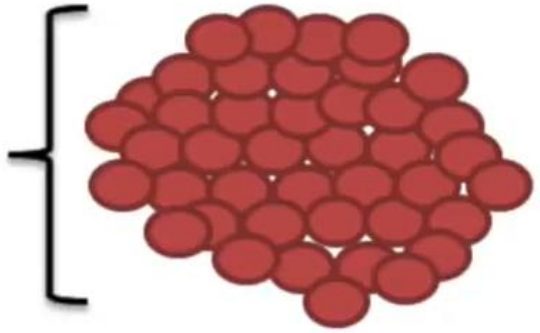
The proteins in a cell dictate how the cell behaves.

In this course, we will connect information on how cells behave with information from the genes (mRNA).



A bunch of
normal cells.

A bunch of
cancer cells.



The cancer cells behave differently than the normal cells.

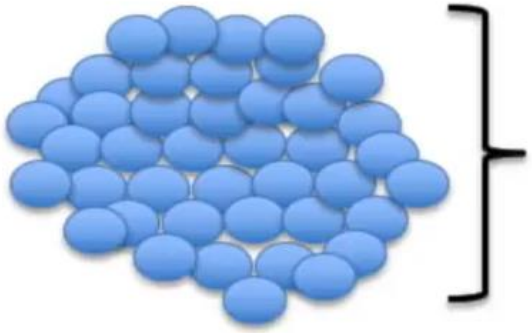
The cancer cells have mutated genes.

Mutated genes have changes in their DNA.

Mutated genes cause changes in protein function.

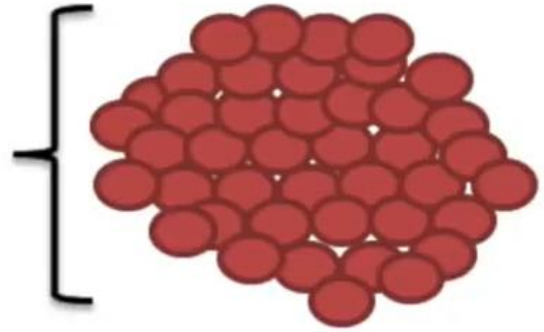
Changes in protein function can cause the cell to behave abnormally.

We want to understand how the genes are different in the two types of cells.



A bunch of
normal cells.

A bunch of
cancer cells.

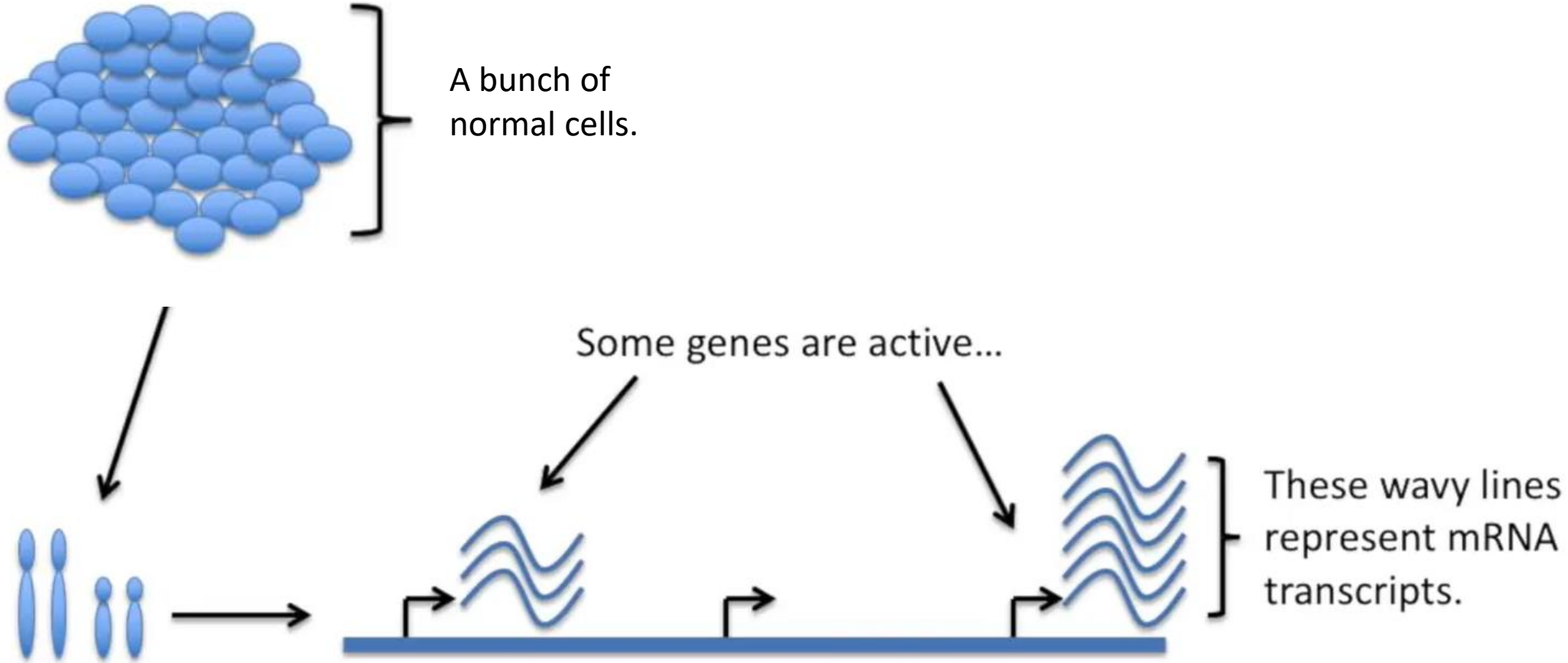


The mutated cells behave differently than the normal cells.

Mutated means there is a change in the DNA of a gene.

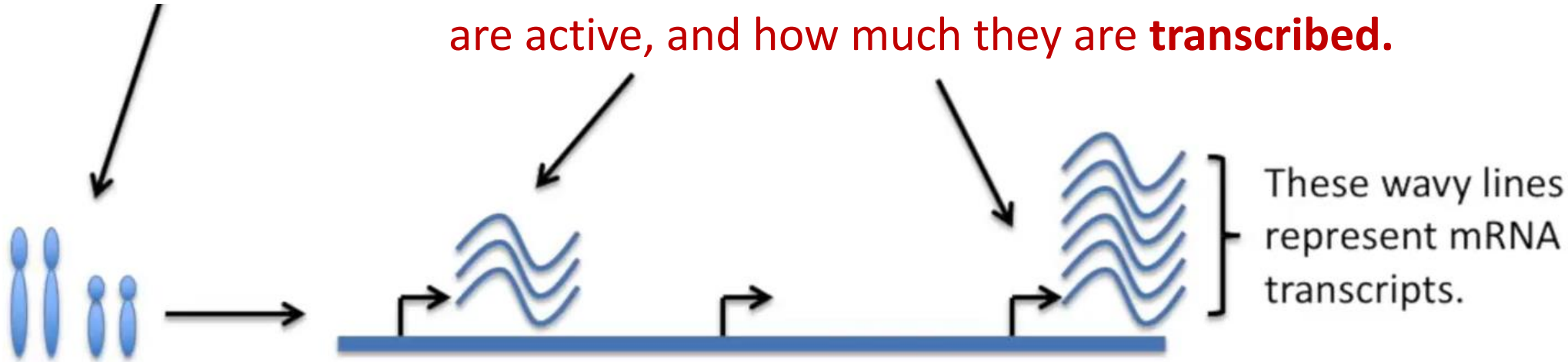
We want to understand how the genes are different in the two types of cells.

This can be done by looking at the expression of genes in the two cells.


A bunch of
normal cells.
Some genes are active…
These wavy lines
represent mRNA
transcripts.

A bunch of
normal cells.

High-throughput sequencing tells us which genes are active, and how much they are **transcribed.**

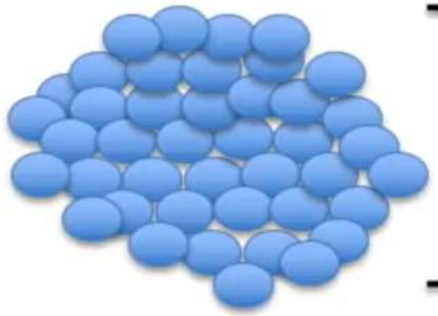


These wavy lines represent mRNA transcripts.

High throughput sequencing tells us which genes are active, and how much they are transcribed.

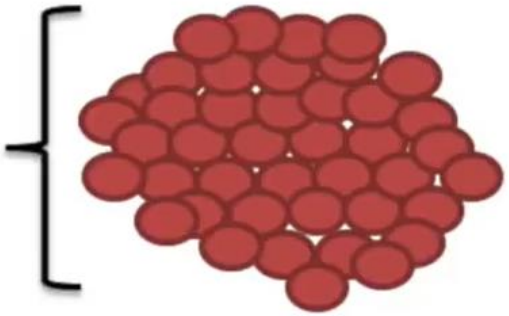
= a normal cell

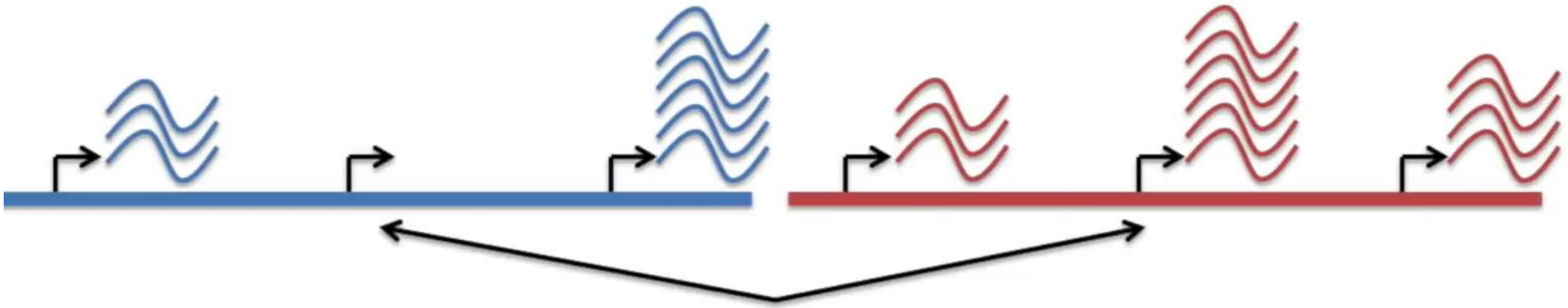
= a cancer cell



A bunch of normal cells.

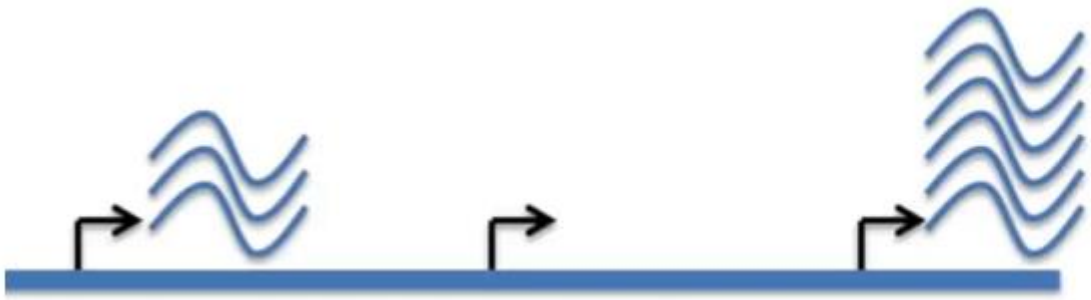
A bunch of cancer cells.





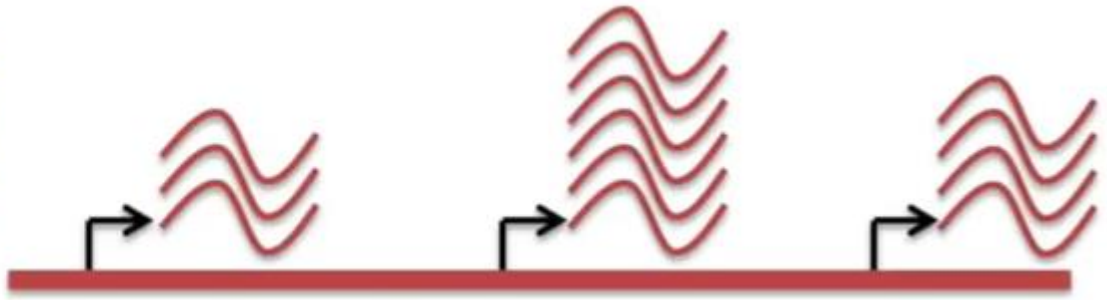
Then we can compare the two cell types and figure out what's different in the mutated cells.

Transcripts from normal cells



Gene 1 Gene 2 Gene 3

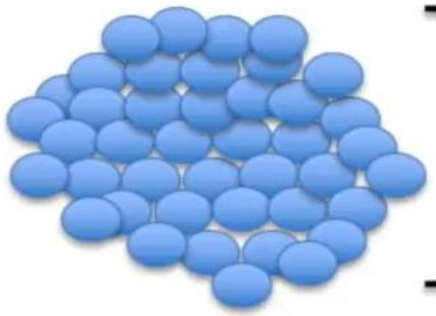
Transcripts from cancer cells



Gene 1 Gene 2 Gene 3

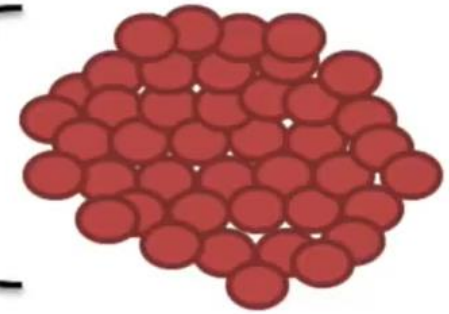
= a normal cell

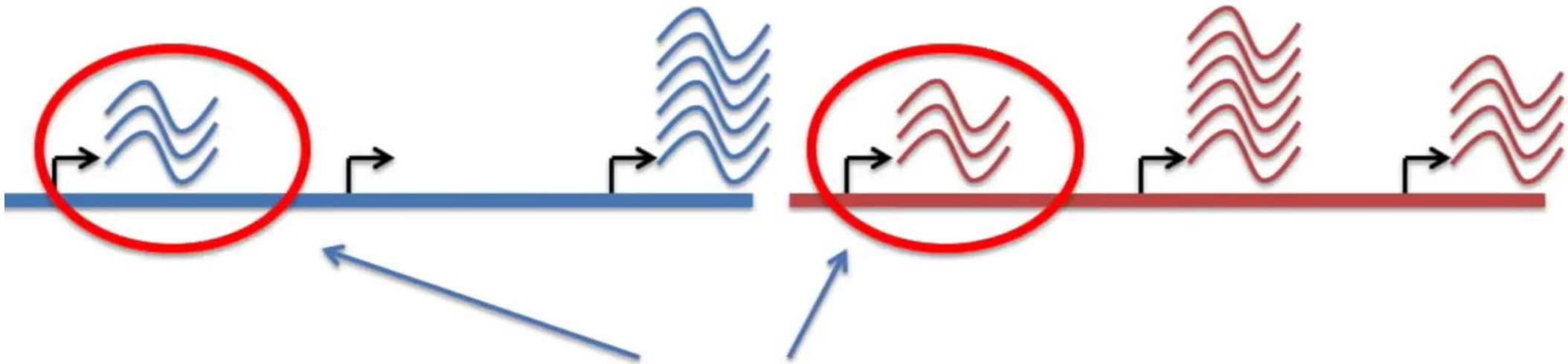
= a cancer cell



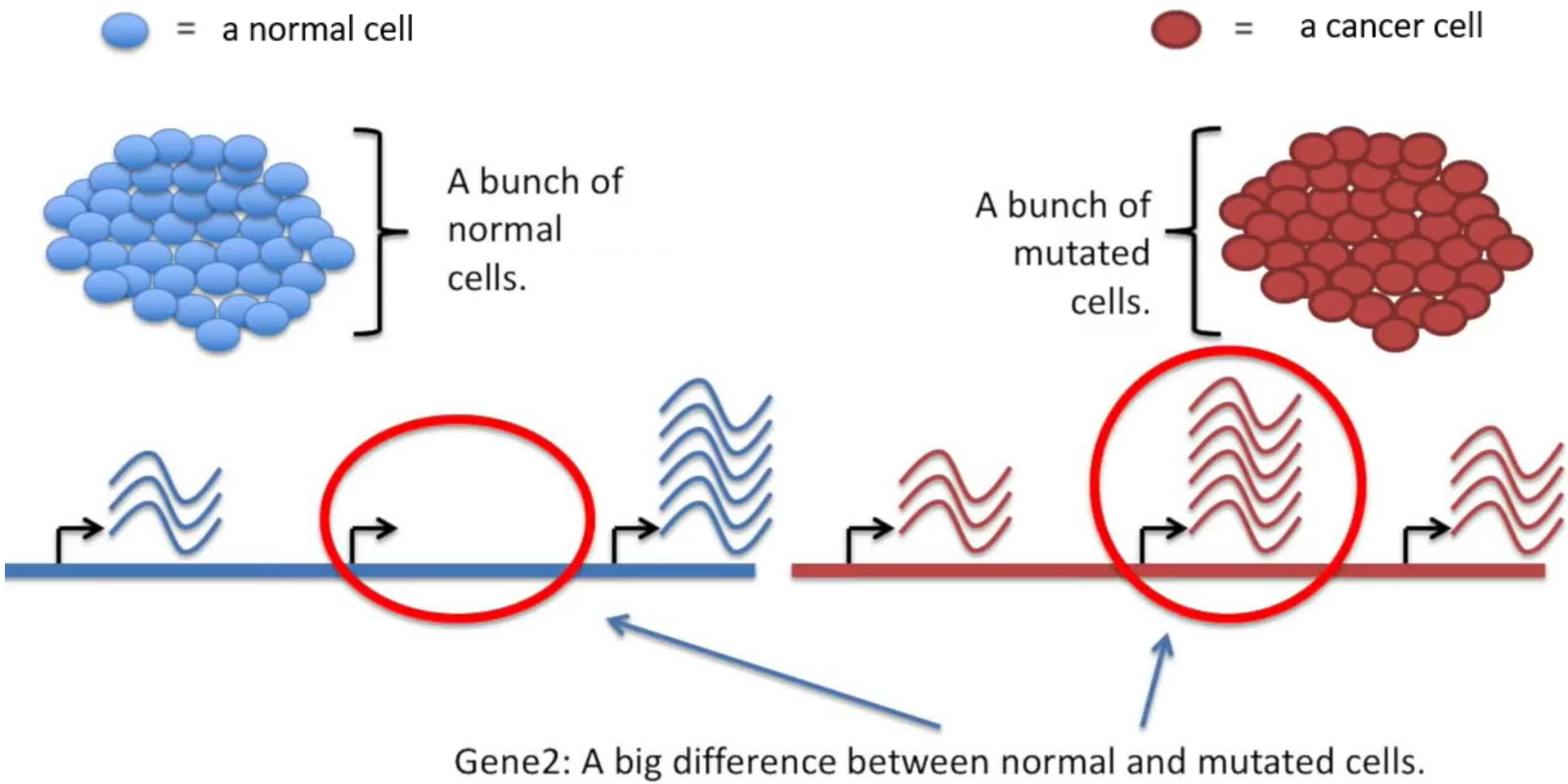
A bunch of normal cells.

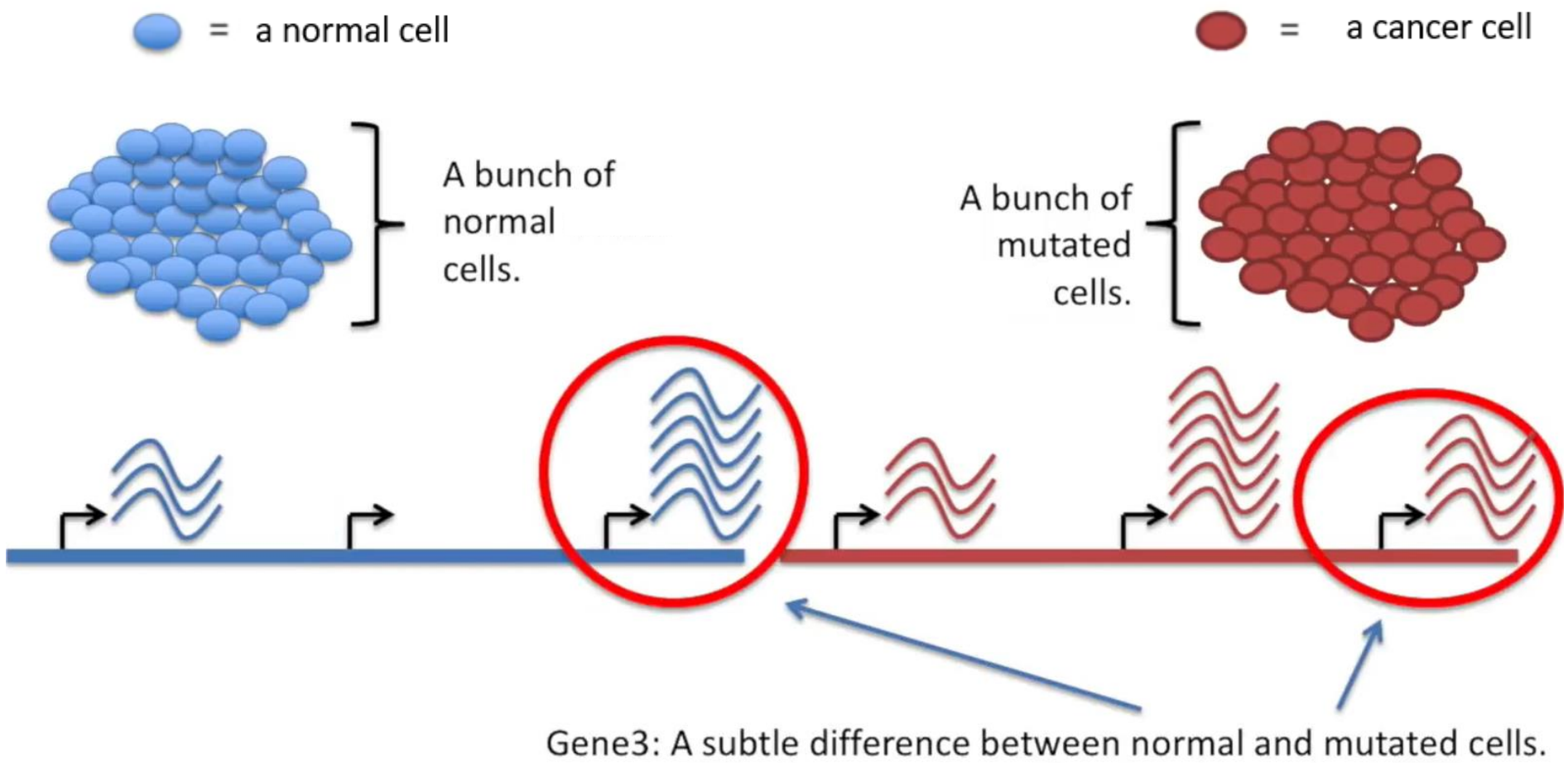
A bunch of mutated cells.





Gene1: No difference between normal and mutated cells.


= a normal cell
= a cancer cell
A bunch of normal cells.
A bunch of mutated cells.
Gene2: A big difference between normal and mutated cells.


= a normal cell
= a cancer cell
A bunch of normal cells.
A bunch of mutated cells.
Gene3: A subtle difference between normal and mutated cells.