Week 1:
July 9, 2020
DREAM-HIGH
High school students analyzing cancer data in the cloud.
RSTUDIO ENVIRONMENT

Cancer Systems Biology

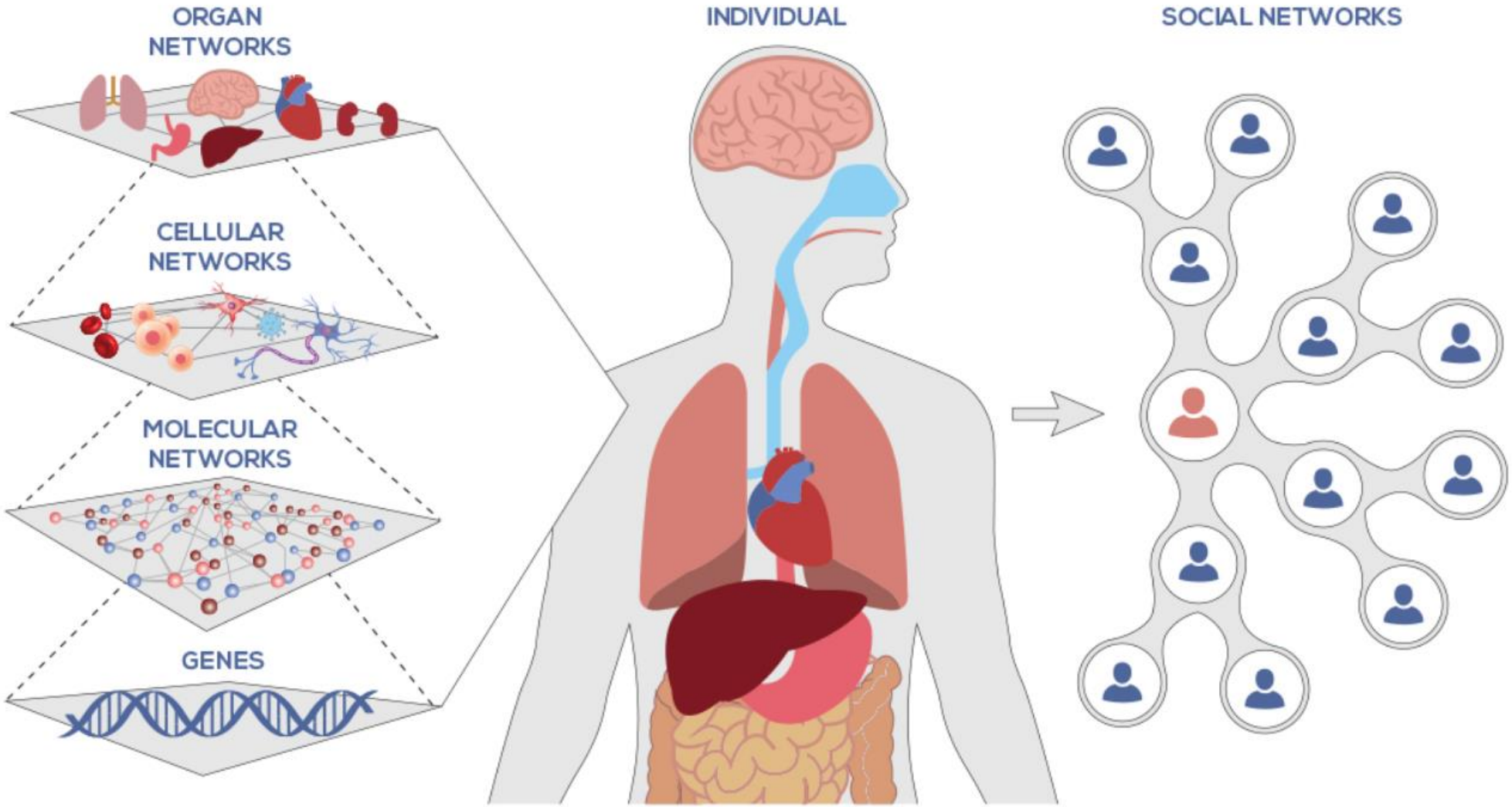
integrates experimental and computational approaches to study the complexities of cancer.

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.



List some things that may contribute to lung cancer.

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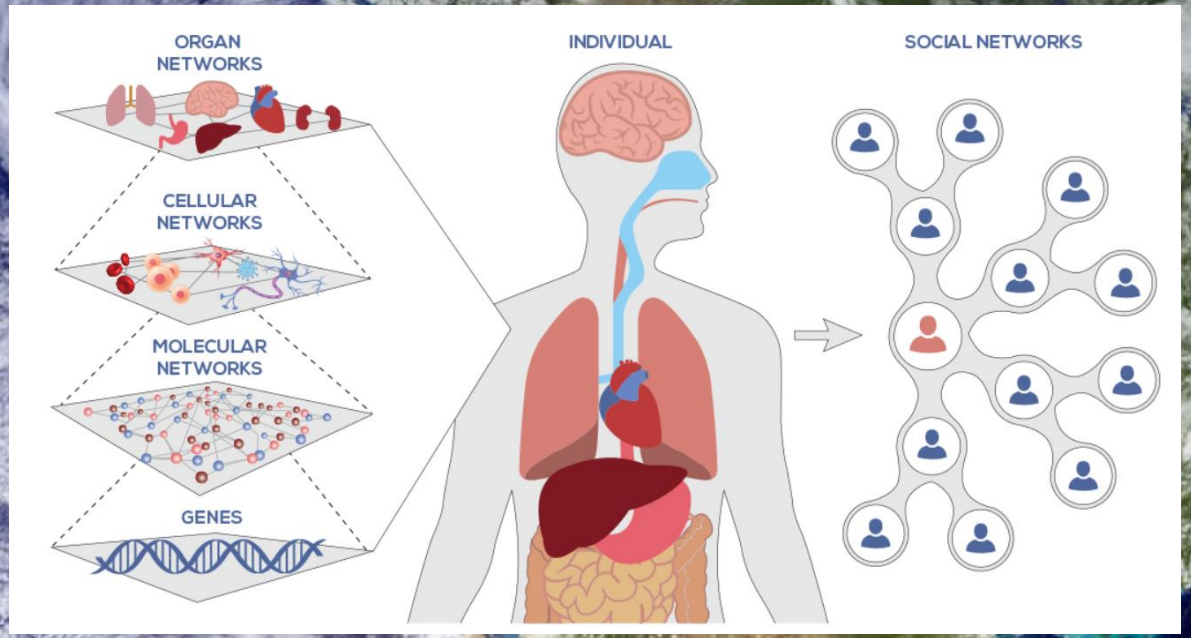
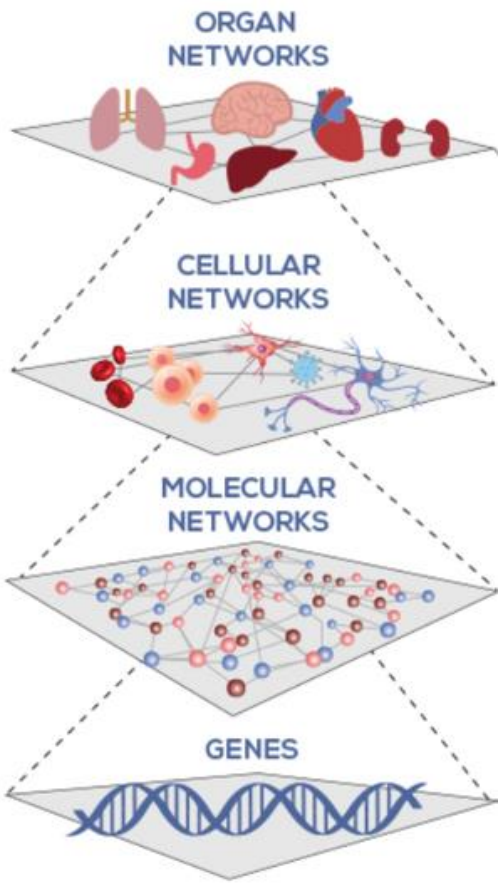
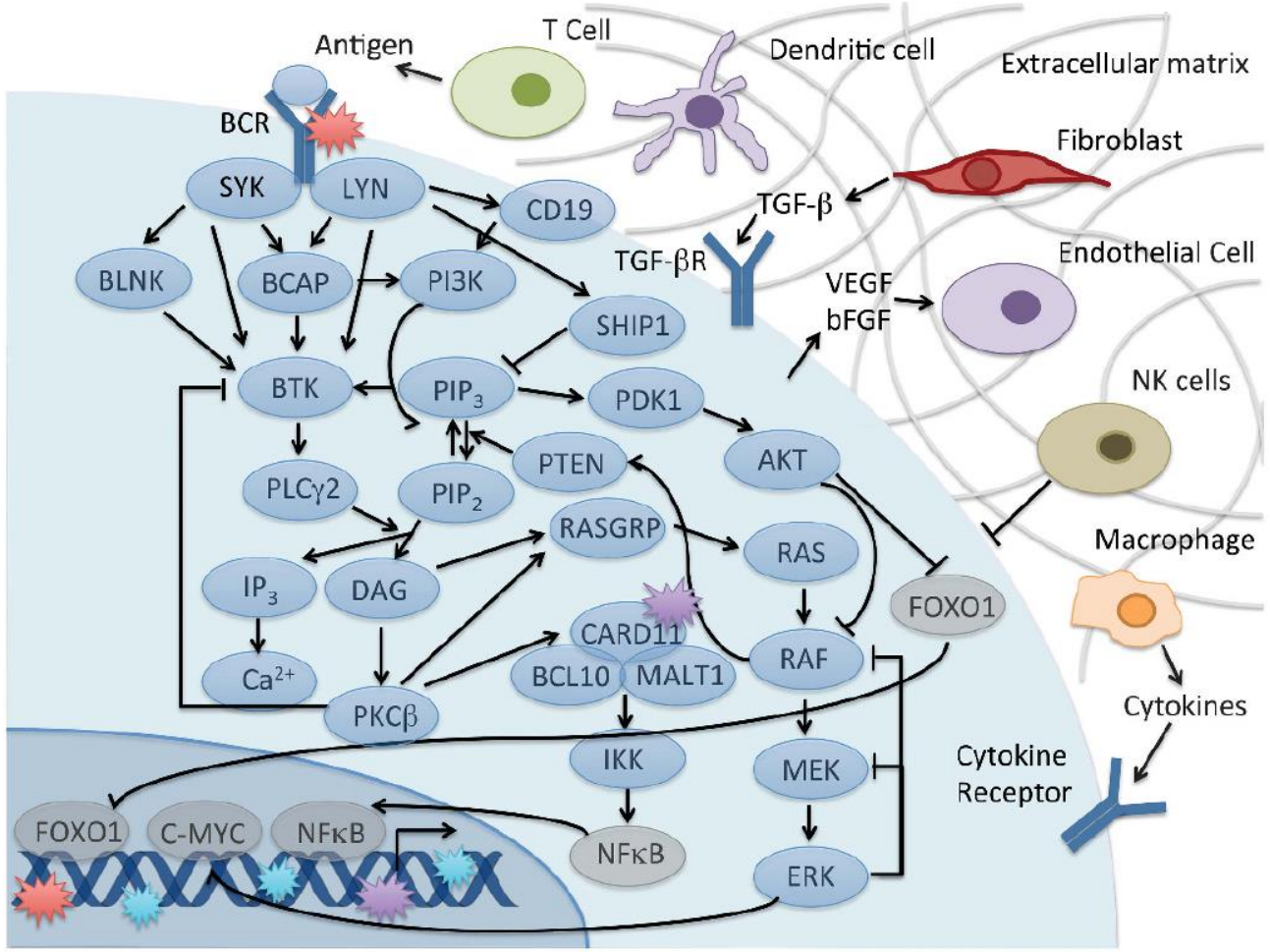
What contributes to lung cancer?


ORGAN NETWORKS
CELLULAR NETWORKS
MOLECULAR NETWORKS
GENES
INDIVIDUAL
SOCIAL NETWORKS

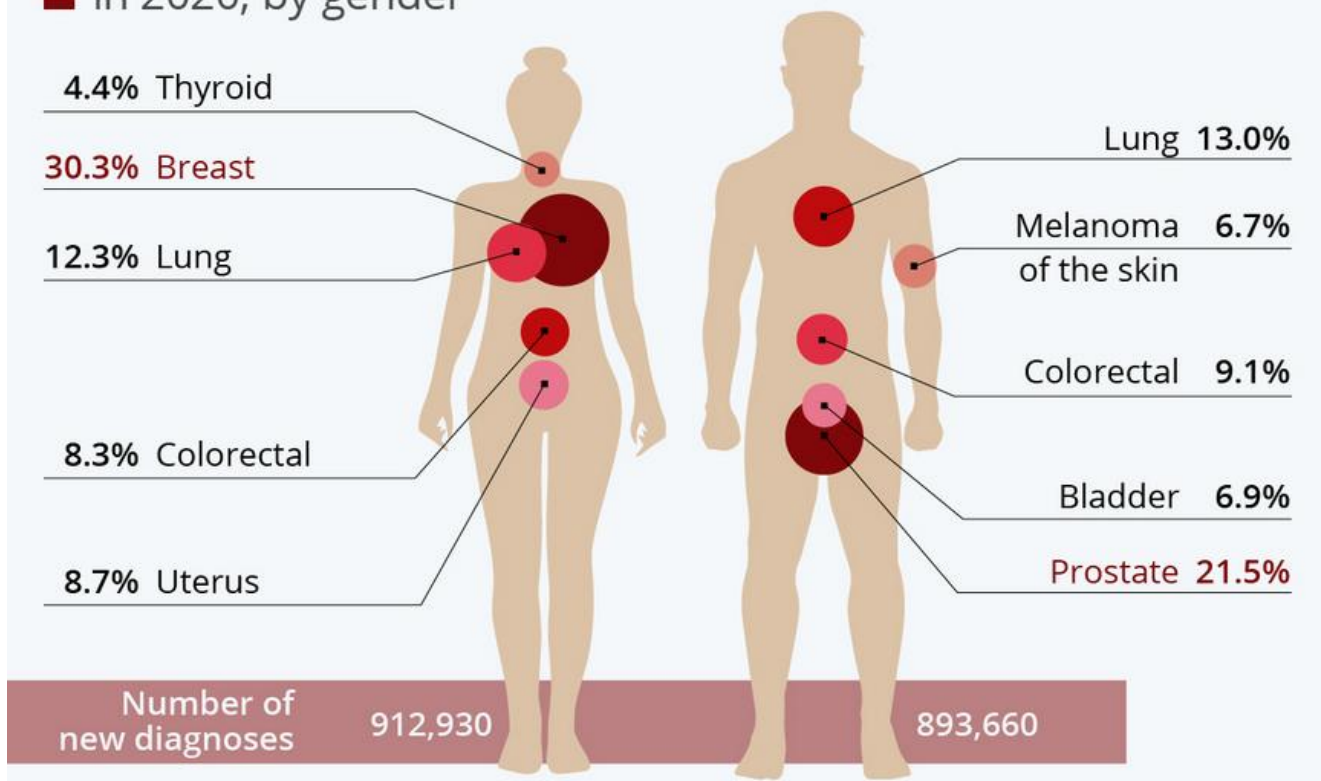
A challenge in understanding cancer: Highly complex patterns of interactions are observed





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

Breast Cancer Stats and Facts

When it comes to breast cancer, what you don't know can hurt you. These figures reveal the scary truth.

This year, 232,670 **new cases of breast cancer will be diagnosed in women.**

1 in 8 women who live to be age 70 will develop breast cancer in her lifetime.

Breast cancer accounts for about **30%** of cancers in women.

It's the most common cancer diagnosis for women in Utah.

About 85% of diagnoses occur in women with no family history of breast cancer.

But there's good news.

Breast cancer's **mortality rate has been declining since 1989**, due to early detection and improved treatment.

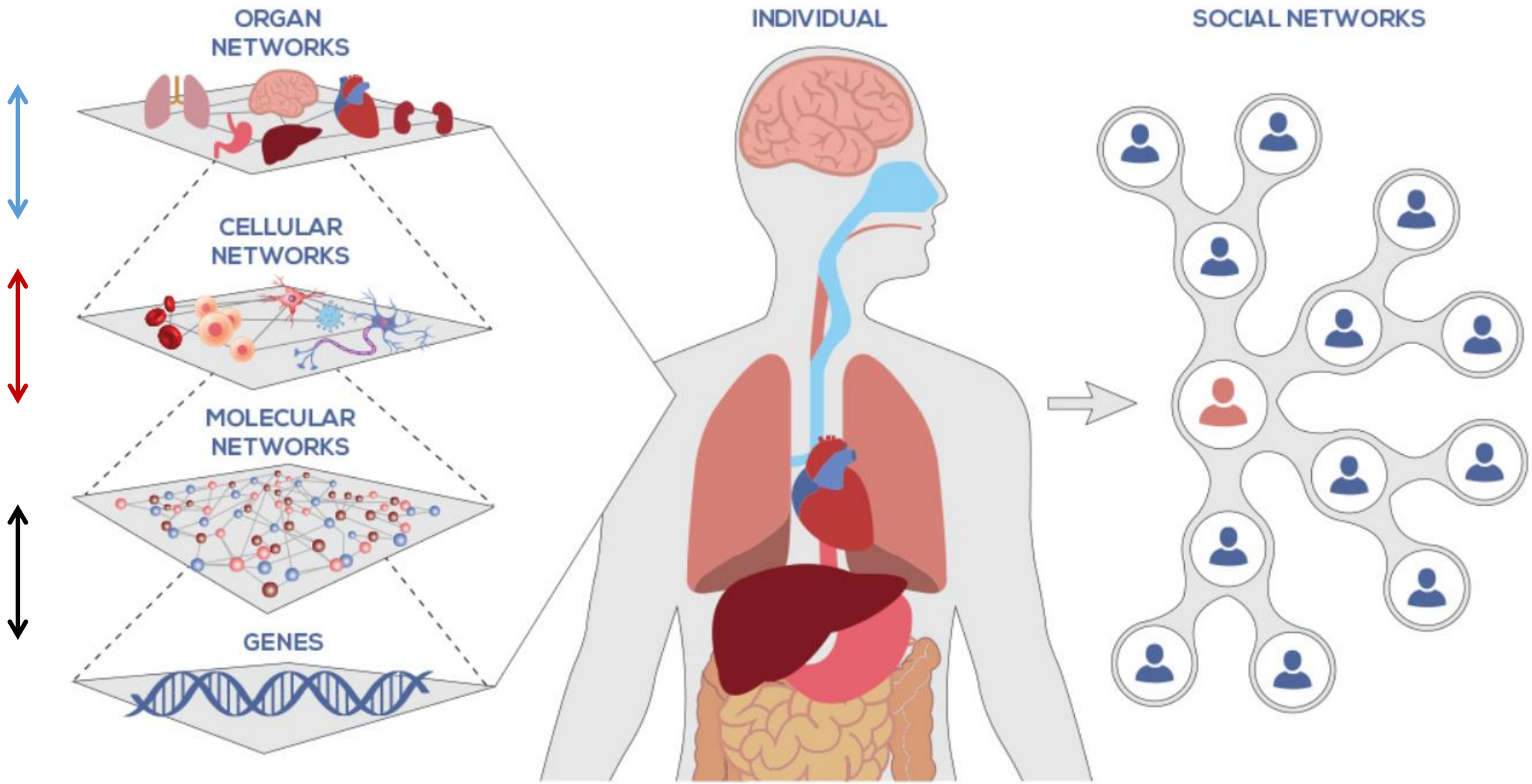
Physically active women are 25% less likely to develop breast cancer than those who are inactive.

More than 2.8 million

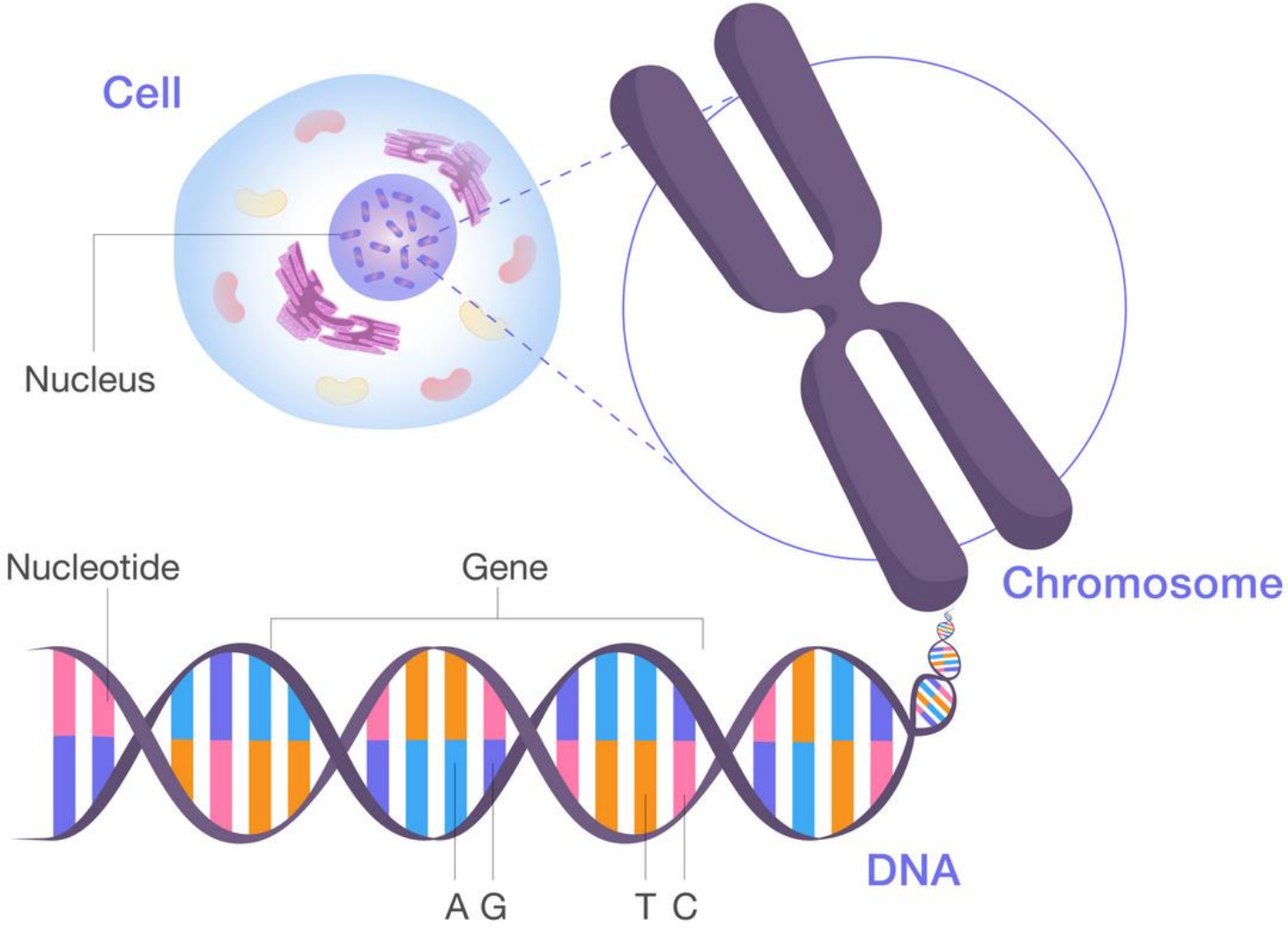
people living in the U.S. are breast cancer survivors.

ACT NOW Breast cancer education and screenings can save up to 37 lives every day in the U.S., according to the World Health Organization. Share this infographic and discuss a screening plan with your doctor.

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

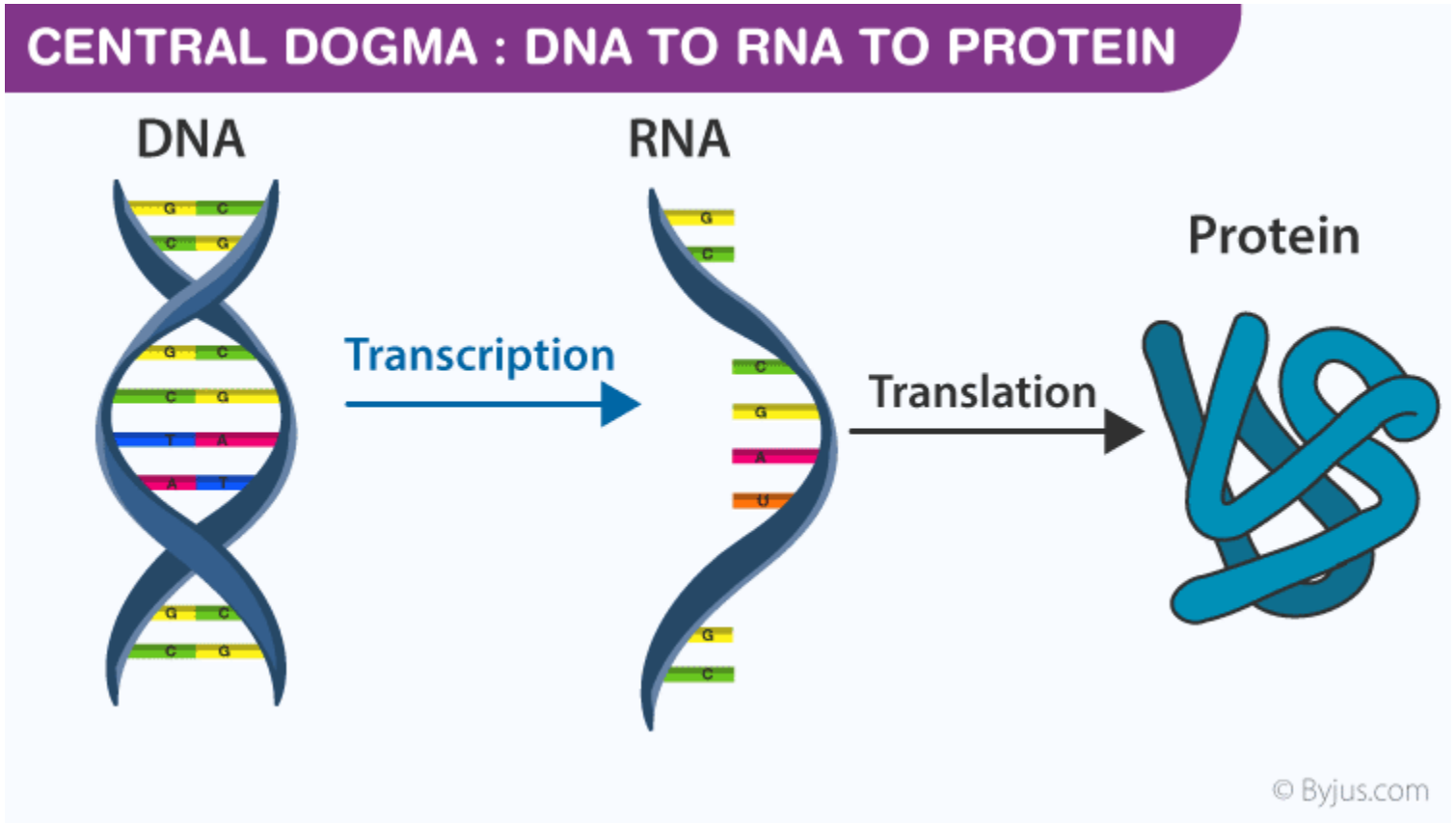


The nucleus of the cell contains our “genetic code.”



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.

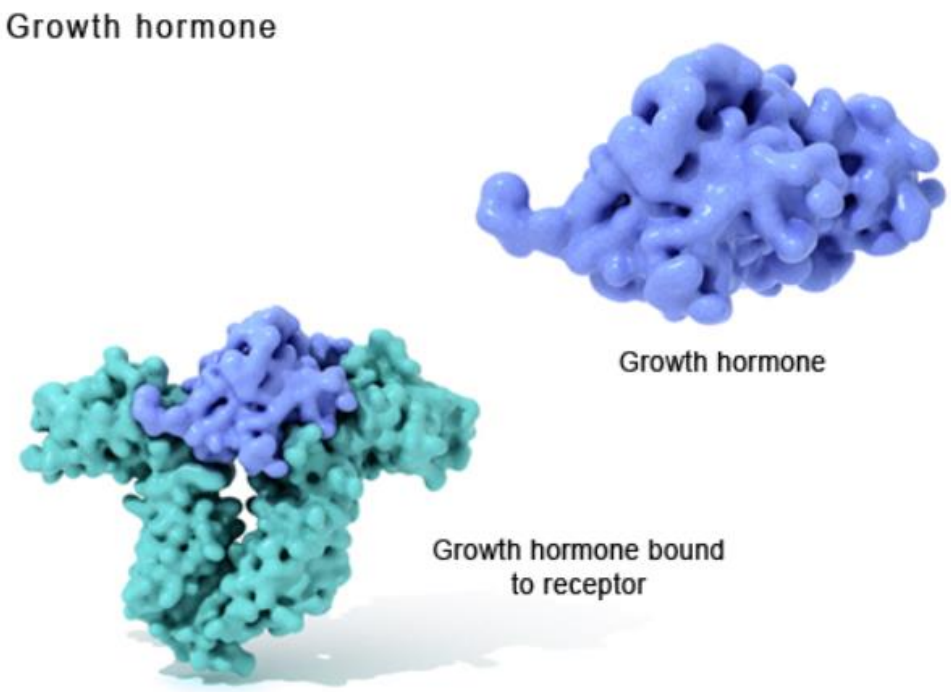
Examples of protein functions

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.

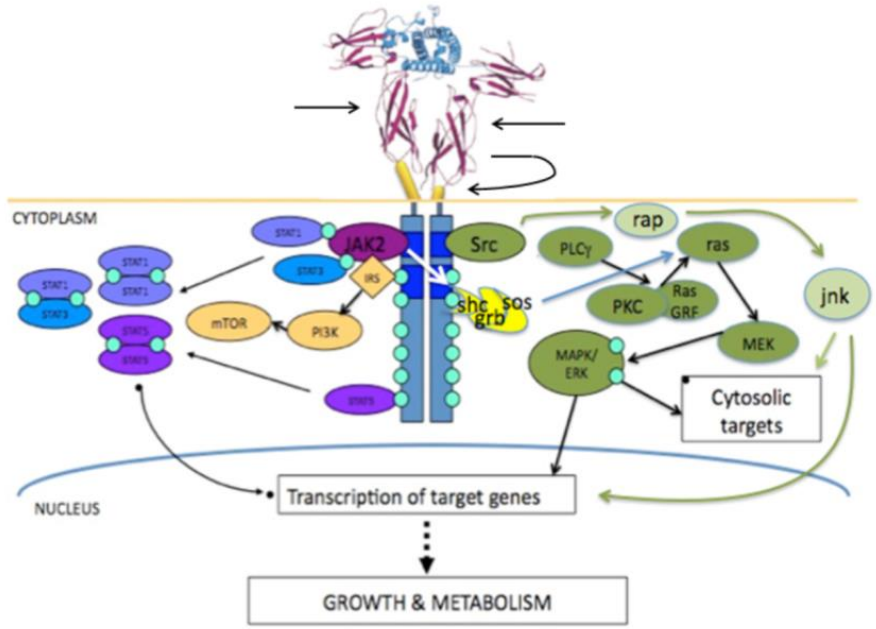
Helicases are a class of enzymes vital to all organisms. Their main function is to unpack an organism's genes. They are motor proteins that move along a gene and separate double-stranded DNA.

Keratin is one of a family of fibrous structural proteins. α-Keratin is the key structural material making up hair, nails, feathers, horns, claws, hooves, calluses, and the outer layer of skin in vertebrates.

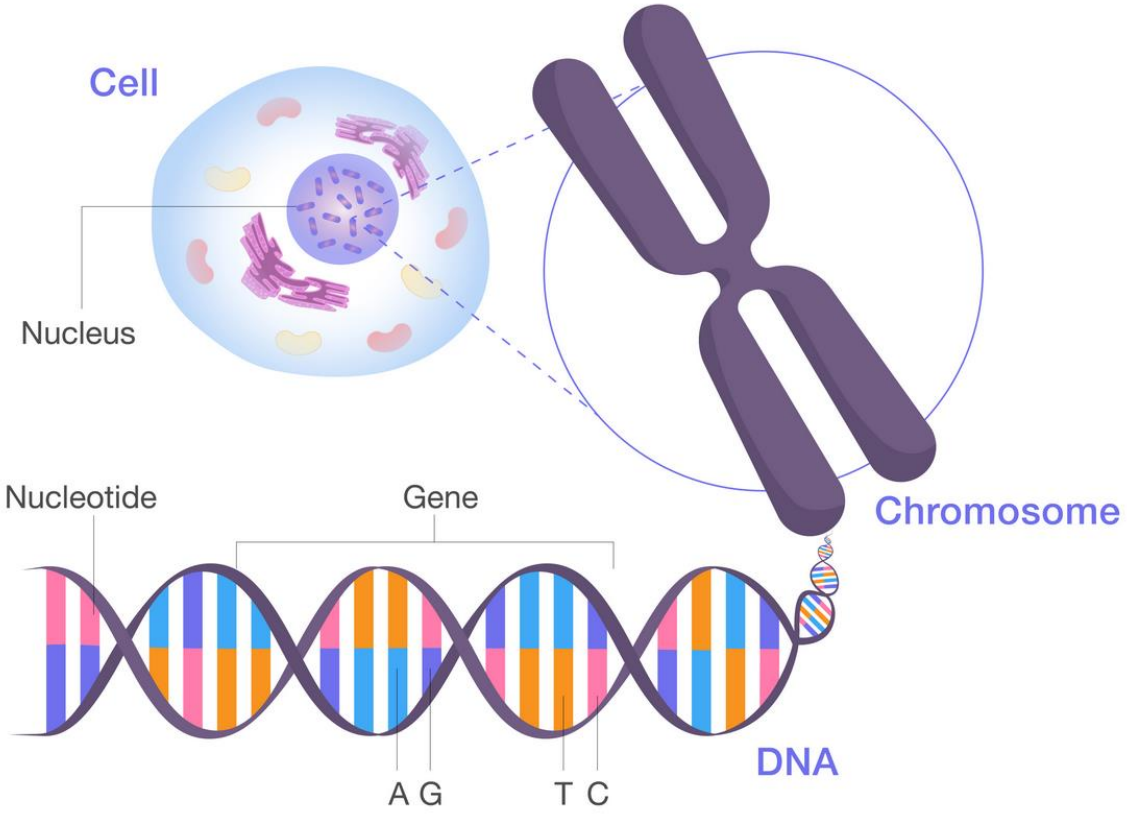
Messenger protein example: **Growth hormone**



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

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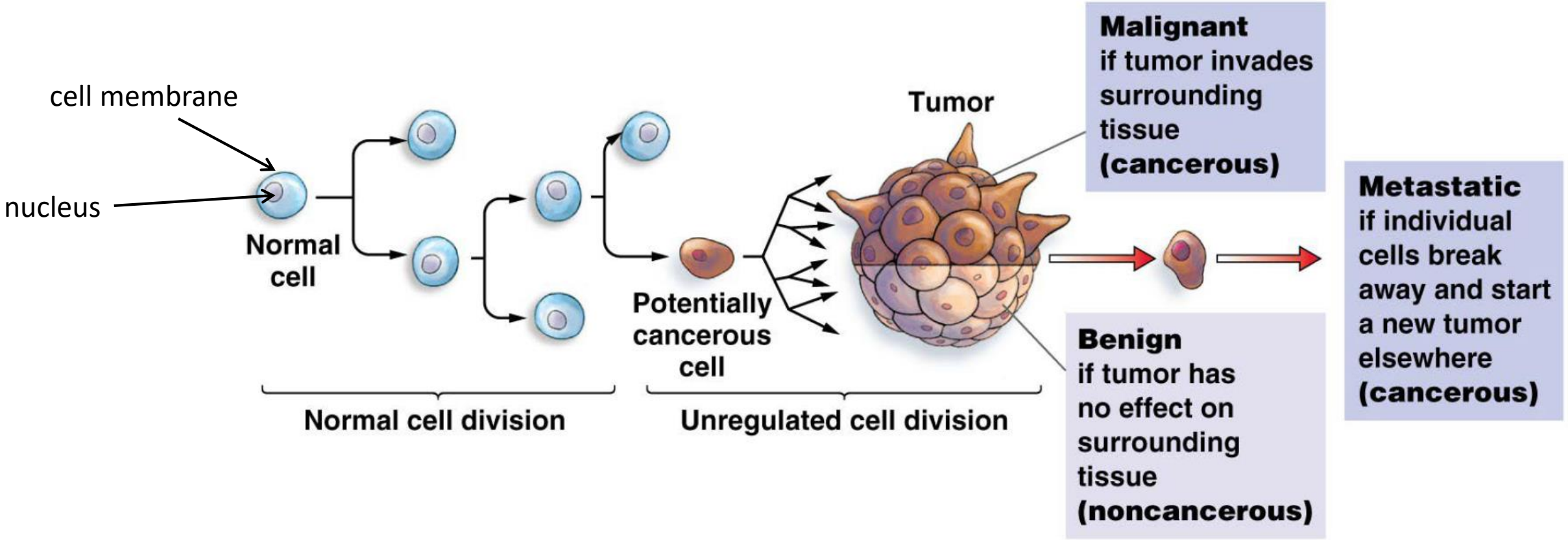
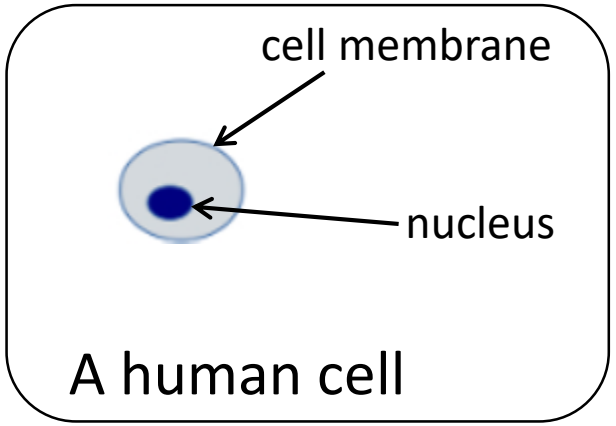
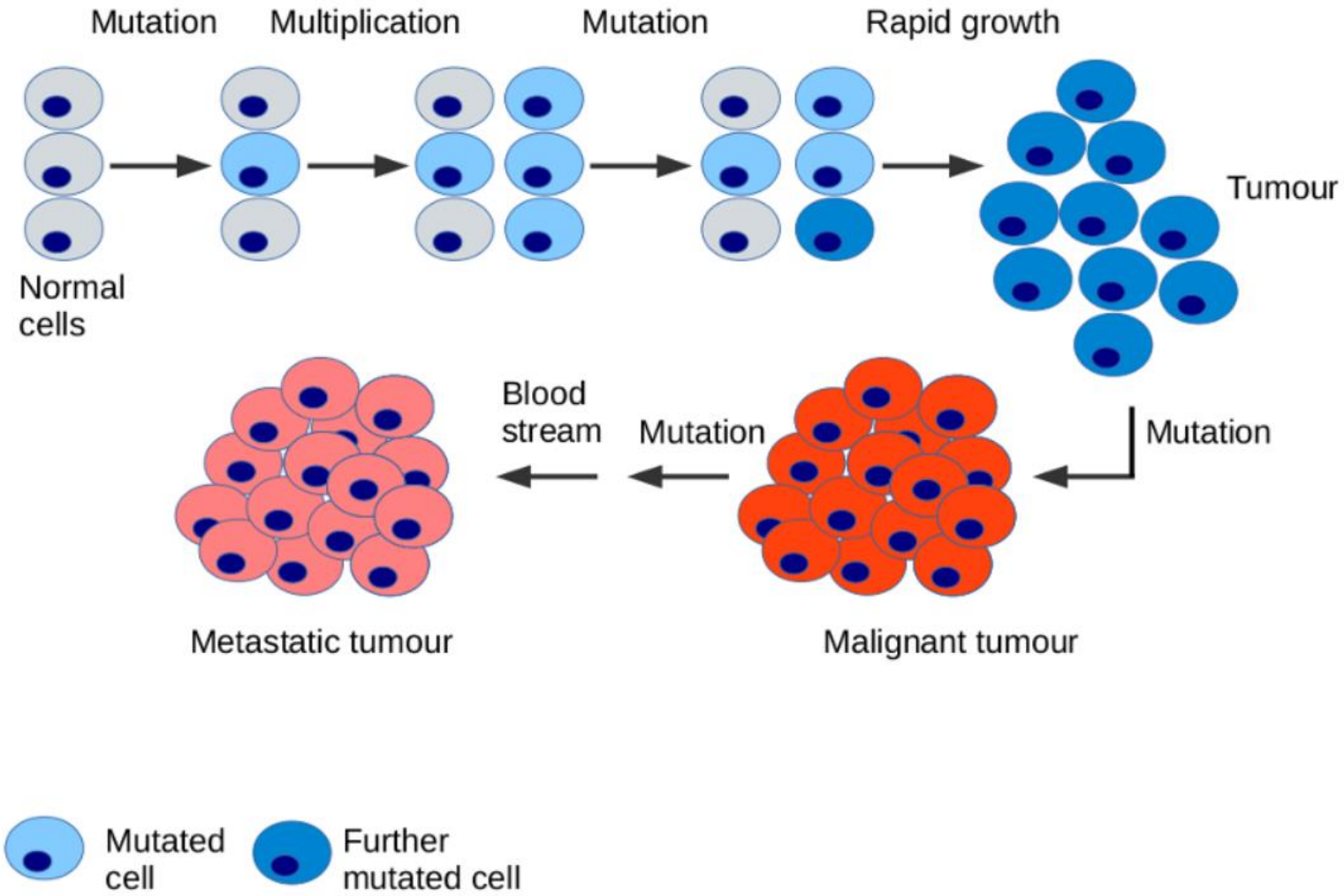
How cancer develops



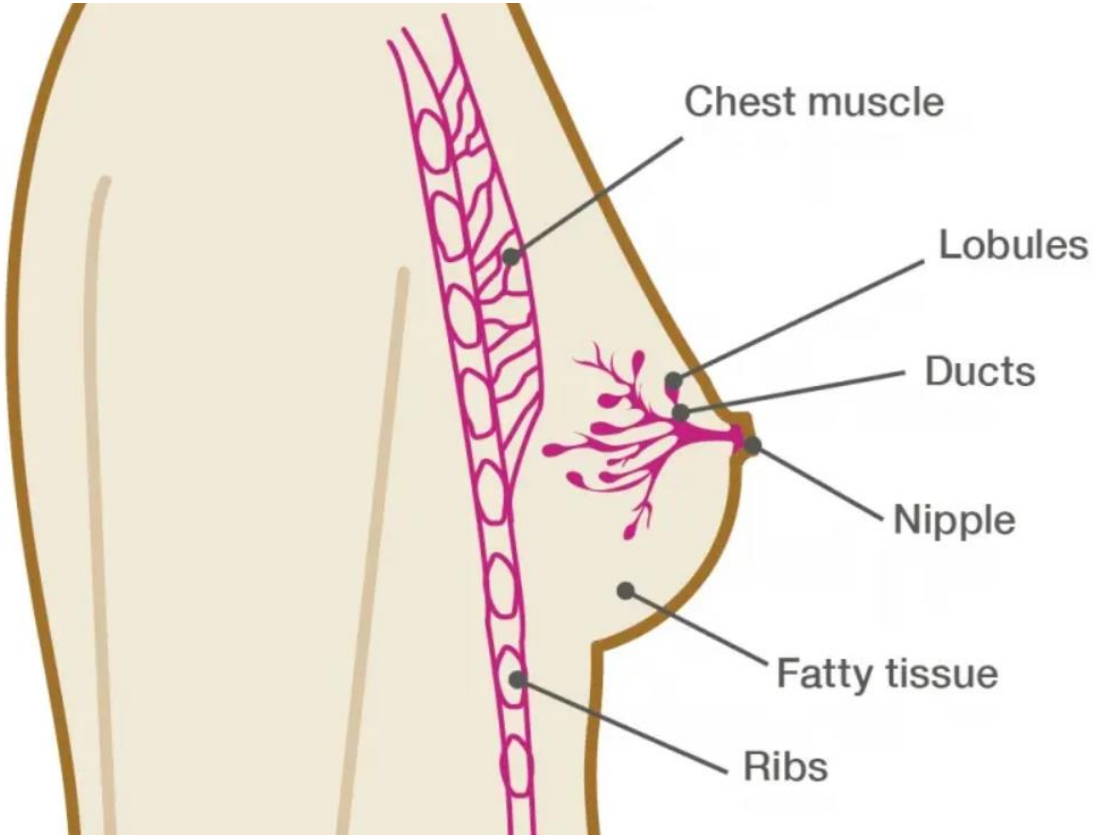
How cancer develops

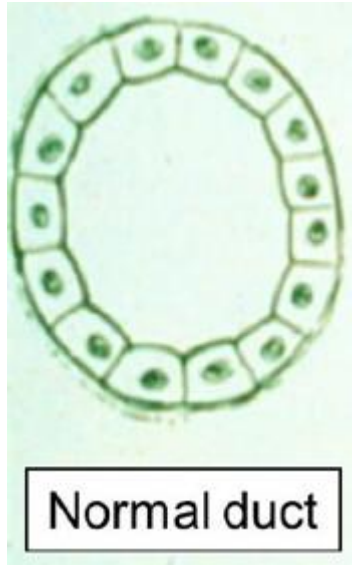




Breast cancer development

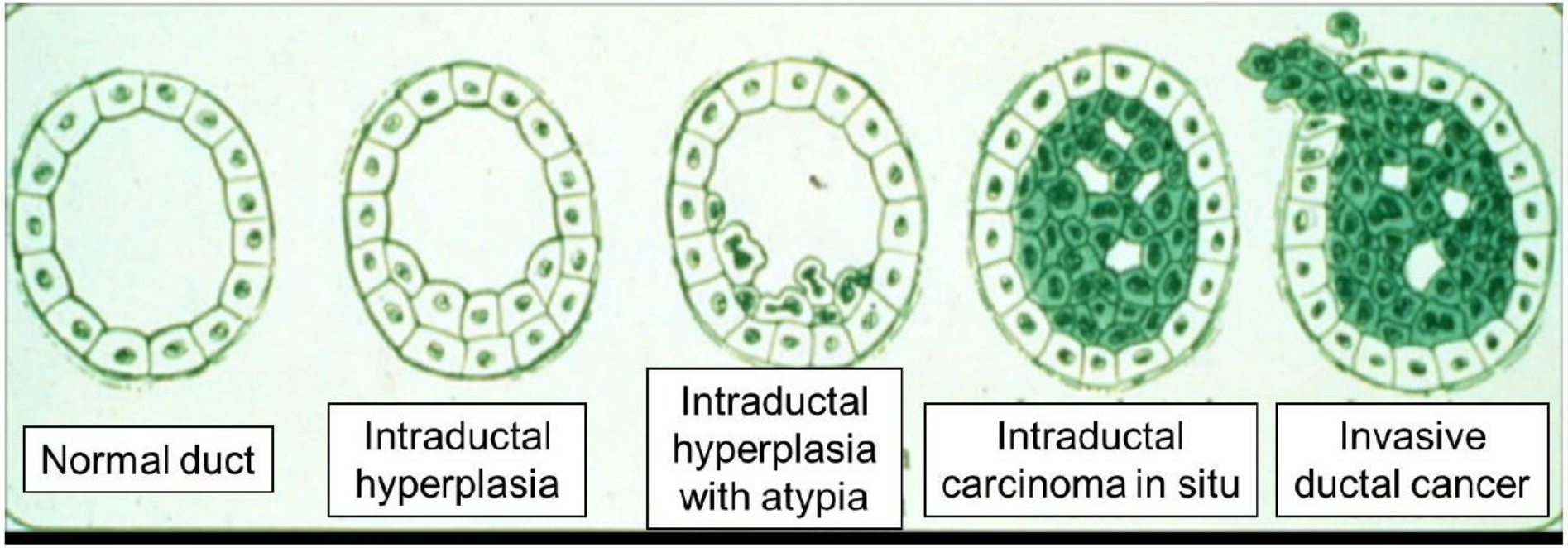
Breast duct or milk duct: A thin tube in the breast that carries milk from the breast lobules to the nipple.





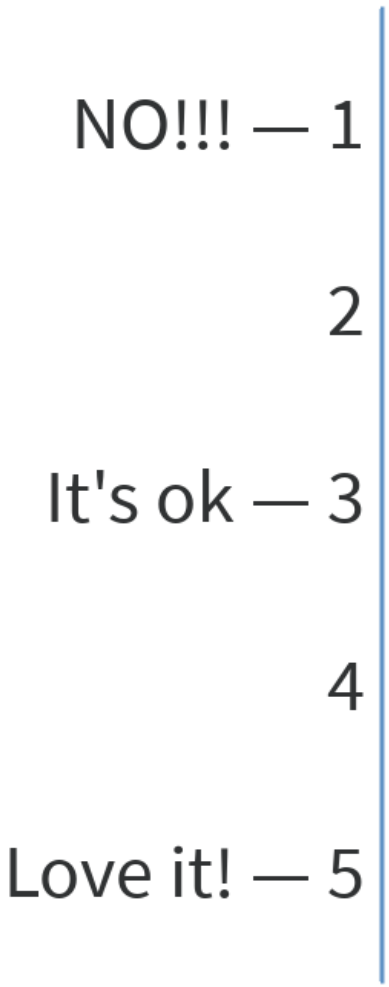
Cross-section of a duct tube.

Breast cancer development



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

I enjoy learning about the origins of words.



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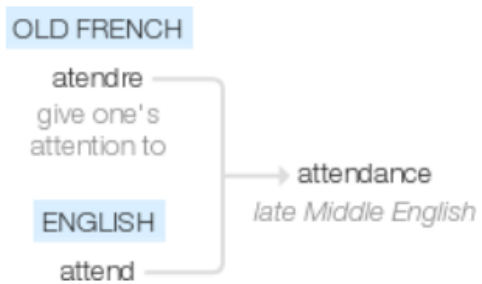
at·tend·ance

/əˈtendəns/

Origin

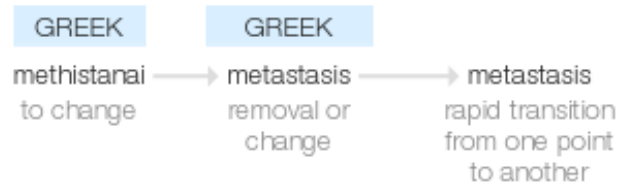


late Middle English: from Old French, from ***atendre*** ‘give one's attention to’

me·tas·ta·sis

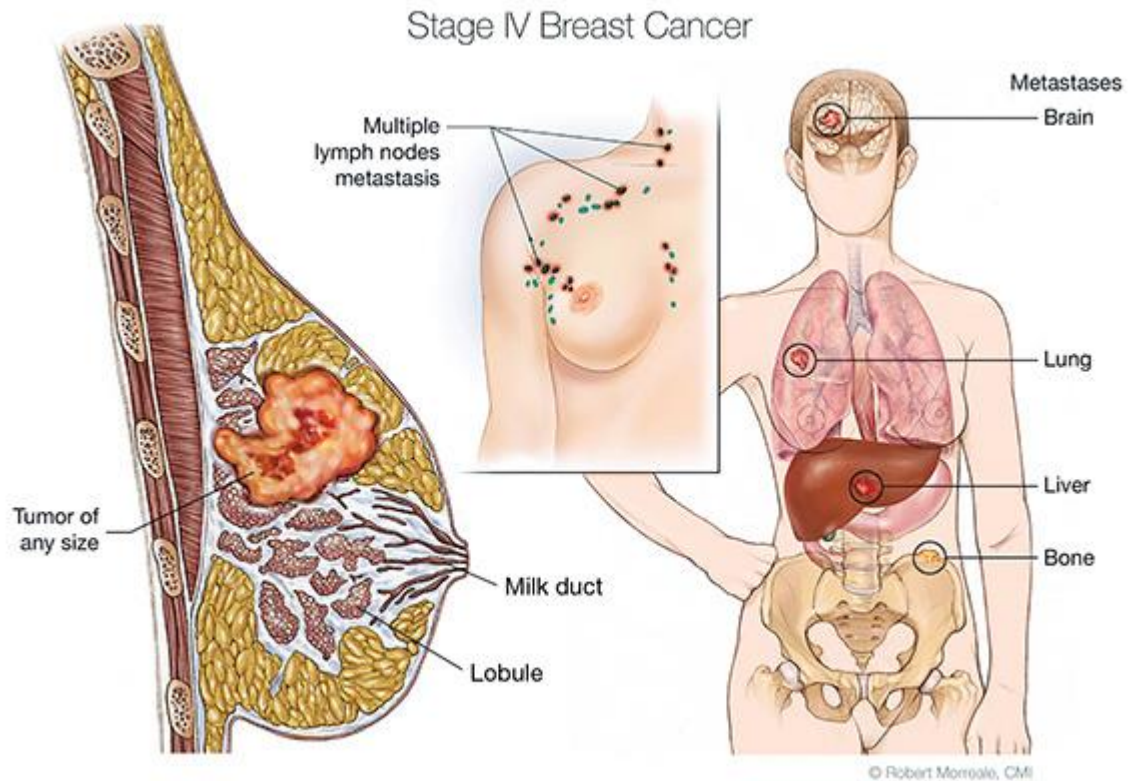
/məˈtastəsəs/

Origin



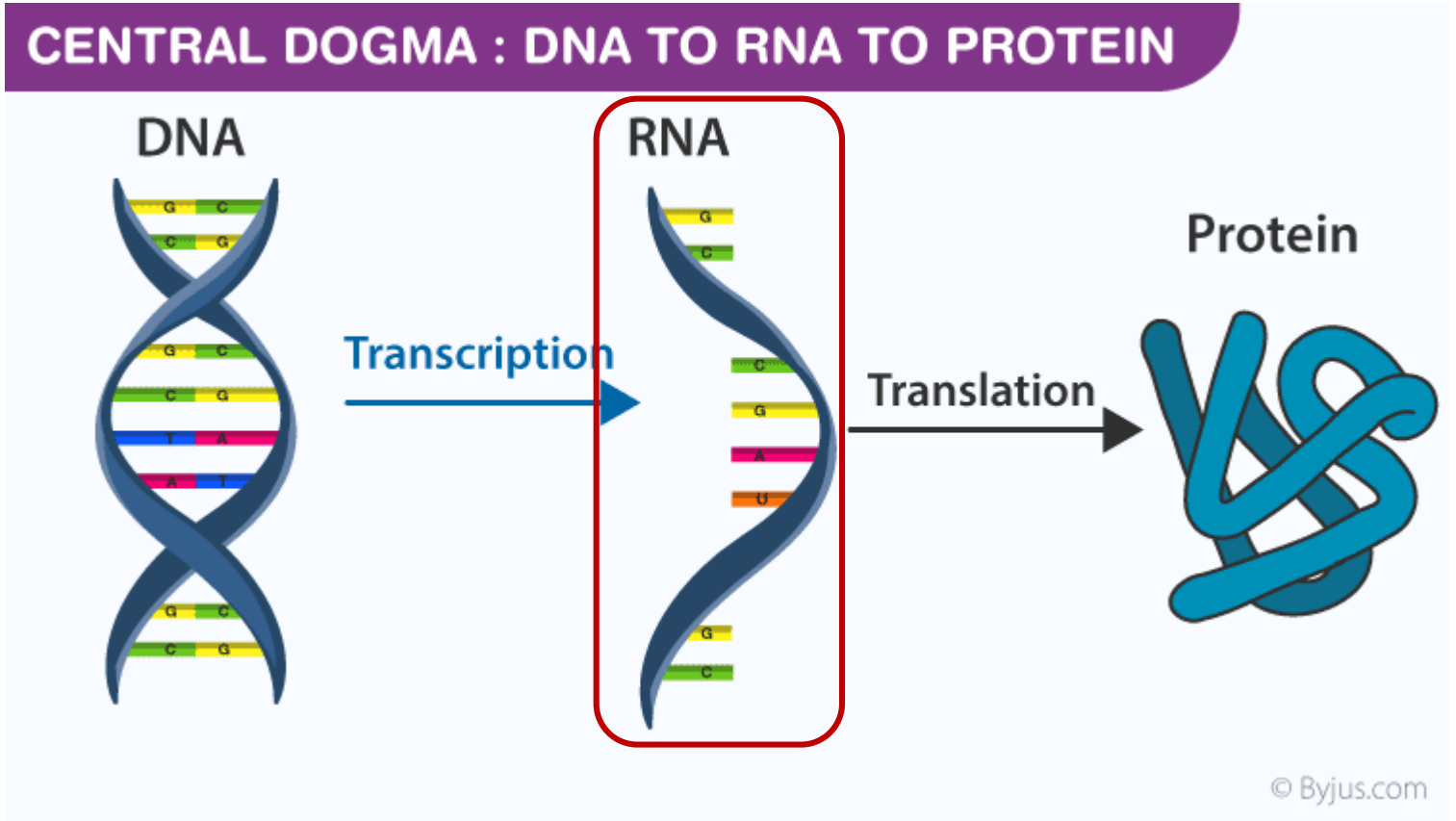
late 16th century (as a rhetorical term, meaning ‘rapid transition from one point to another’): from Greek, literally ‘removal or change’, from *methistanai* ‘to change’.

Metastasis: the development of secondary malignant growths at a distance from a primary site of cancer.



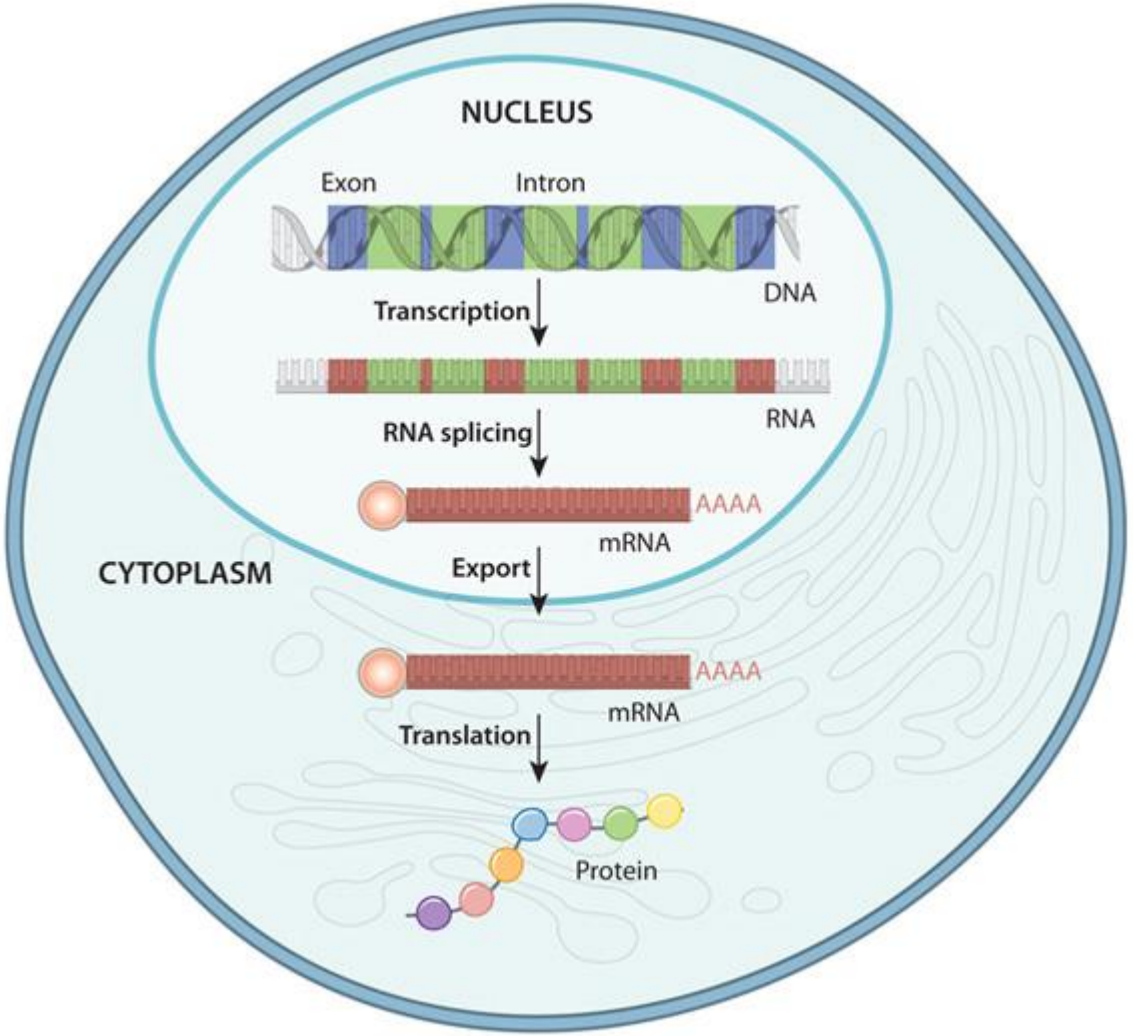
Central dogma of molecular biology

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



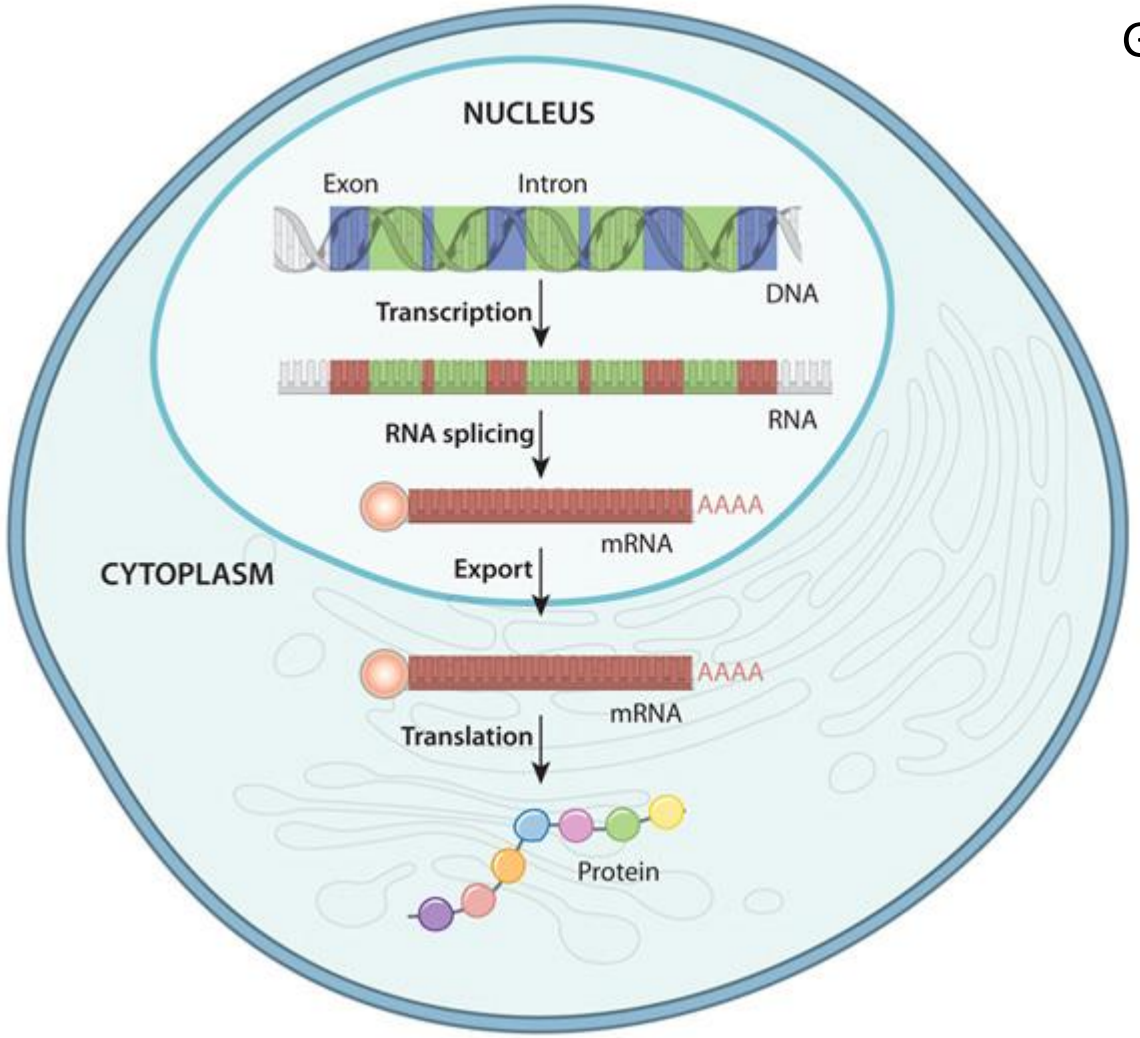
Genes in the nucleus carry our genetic information.
Genes are made up of DNA.

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.

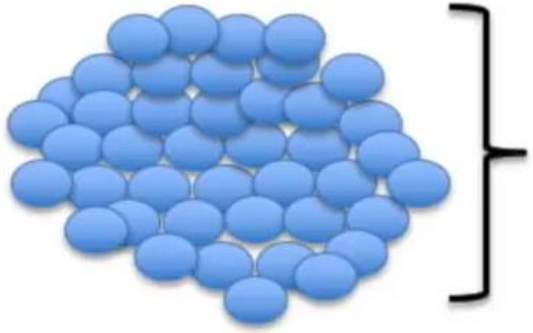
mRNA molecules are used in the formation of a protein.

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

Measuring mRNA tells us about the proteins in the cells.

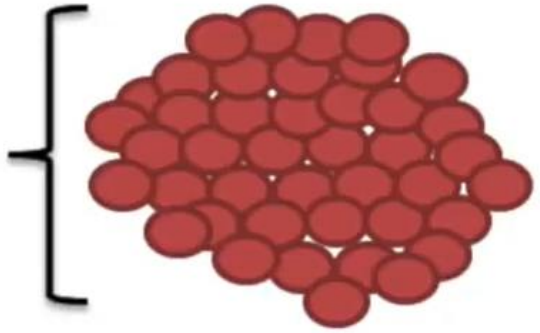
The proteins in a cell dictate how the cell behaves.

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.

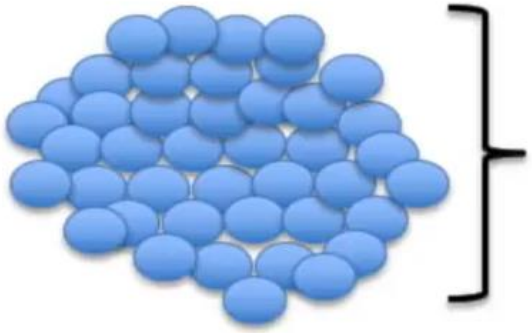
The cancer cells have mutated genes.

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
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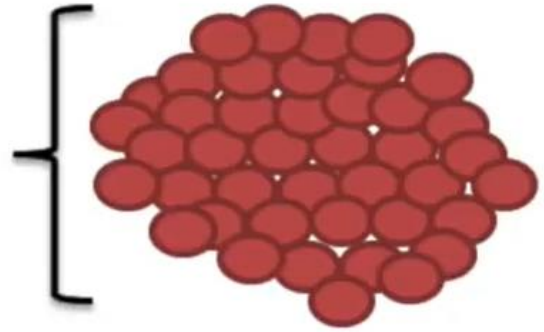
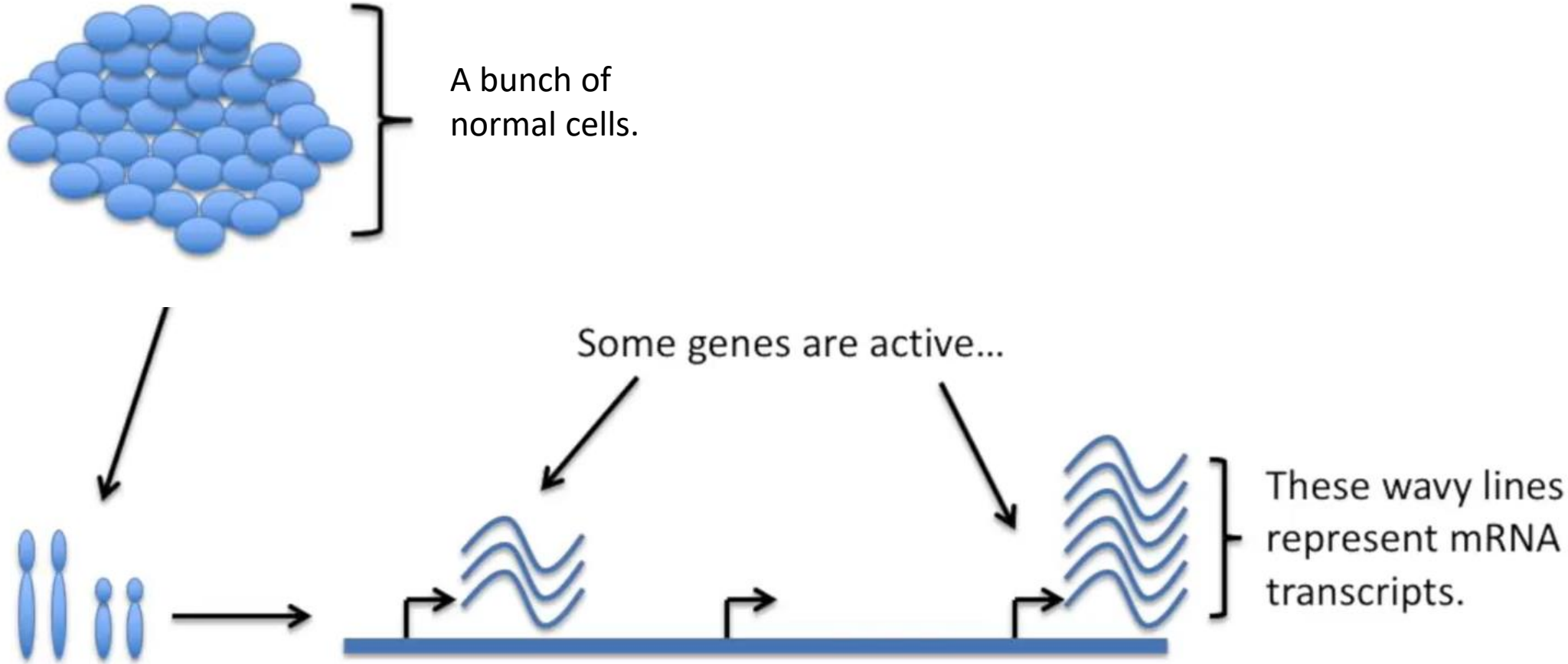


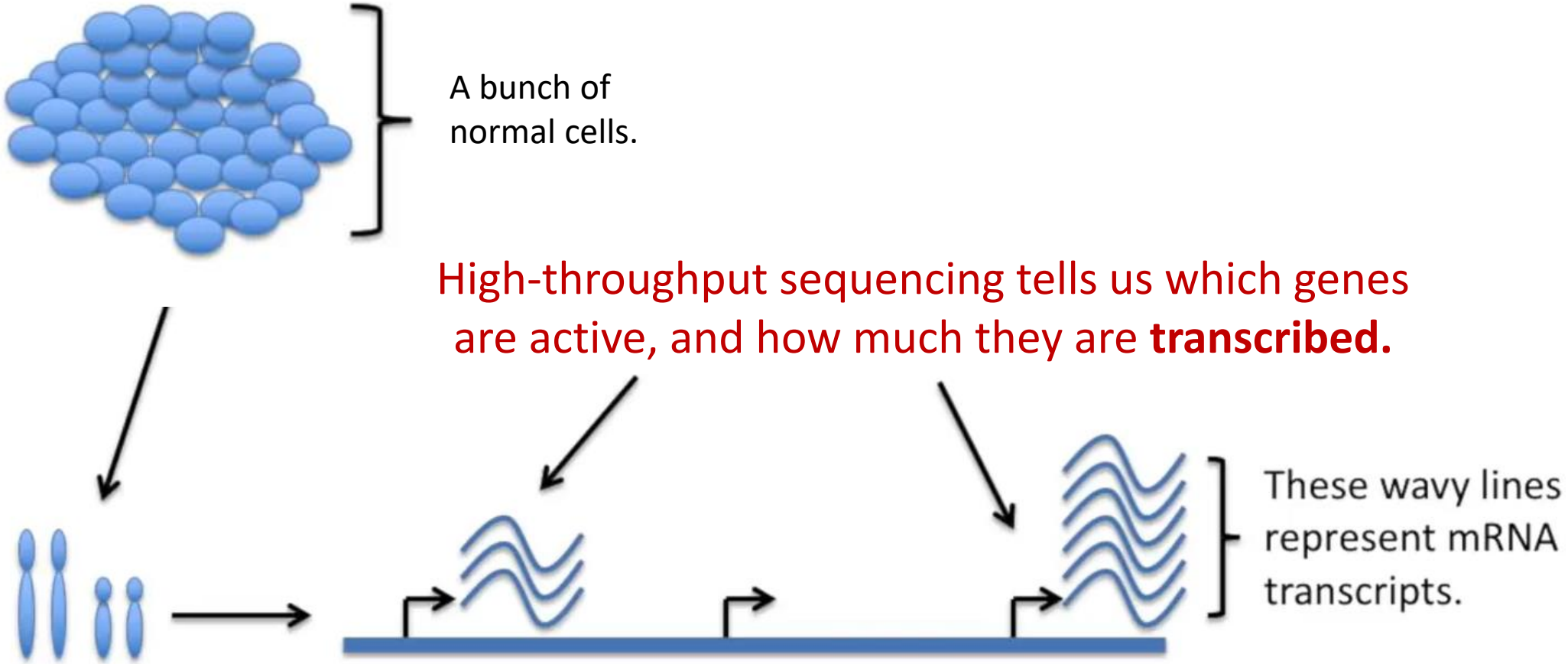
The mutated cells behave differently than the normal cells.

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.

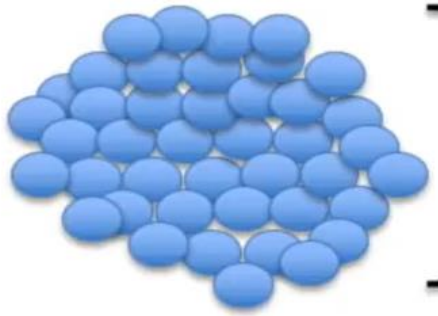

A bunch of
normal cells.
Some genes are active…
These wavy lines
represent mRNA
transcripts.


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.

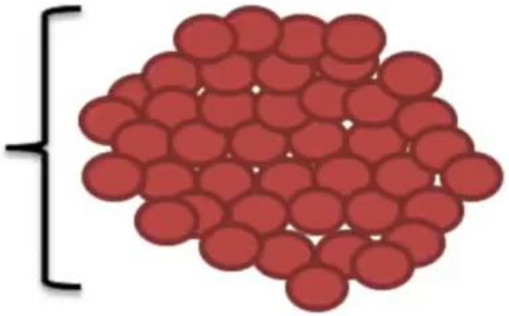
= a normal cell

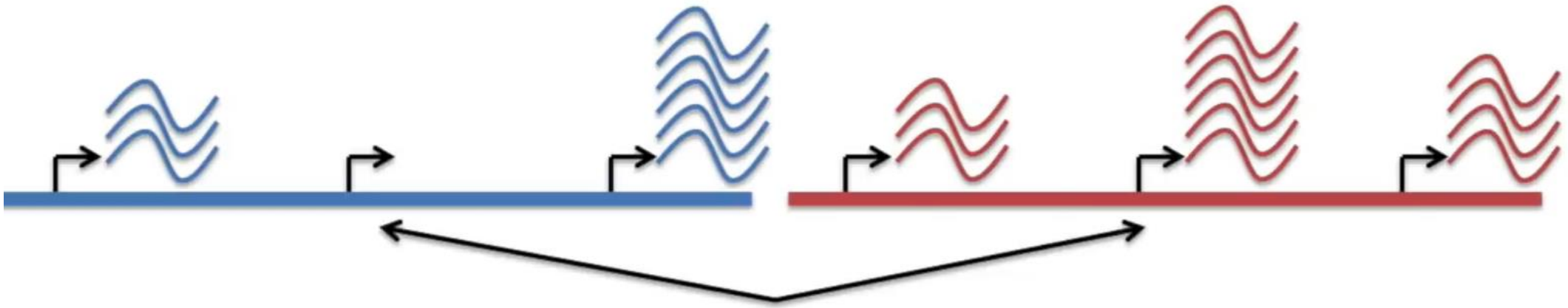
= a cancer cell



A bunch of normal cells.

A bunch of cancer cells.



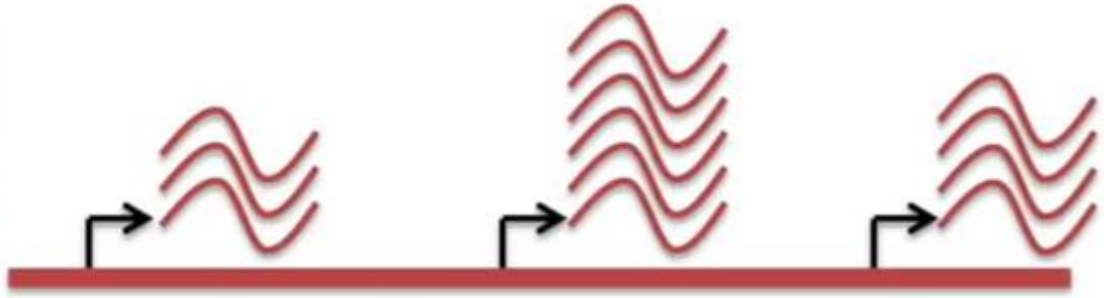


Then we can compare the two cell types and figure out what's different in the mutated cells.

Transcripts from normal cells

Gene 1 Gene 2 Gene 3

Transcripts from cancer cells



Gene 1 Gene 2 Gene 3

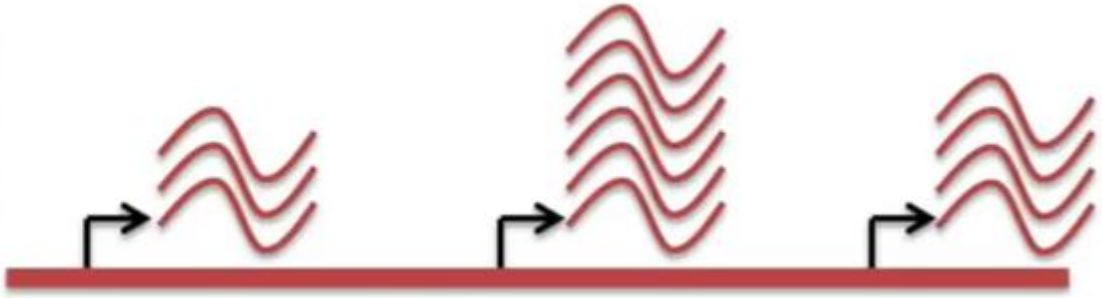
Transcripts from cancer cells

Patient 1

Gene 1 Gene 2 Gene 3

Transcripts from cancer cells

Patient 2



Gene 1 Gene 2 Gene 3

1,000 breast cancer patients each with 20,000 genes

Count the number of transcripts for each gene in each patient

1,000 samples * 20,000 transcript values per patient = 20,000,000 transcript values

I have used Microsoft Excel.

Yes

No

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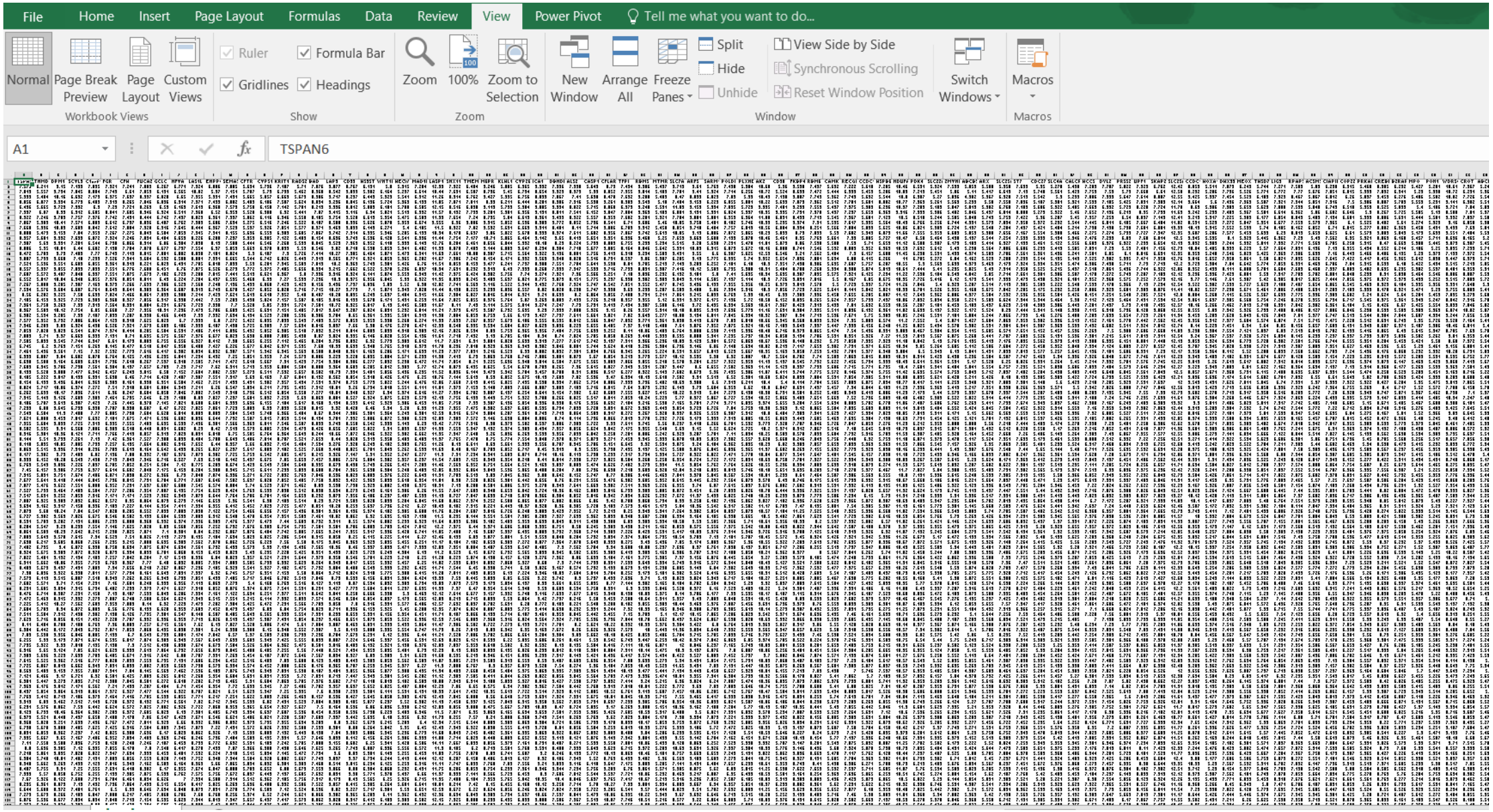
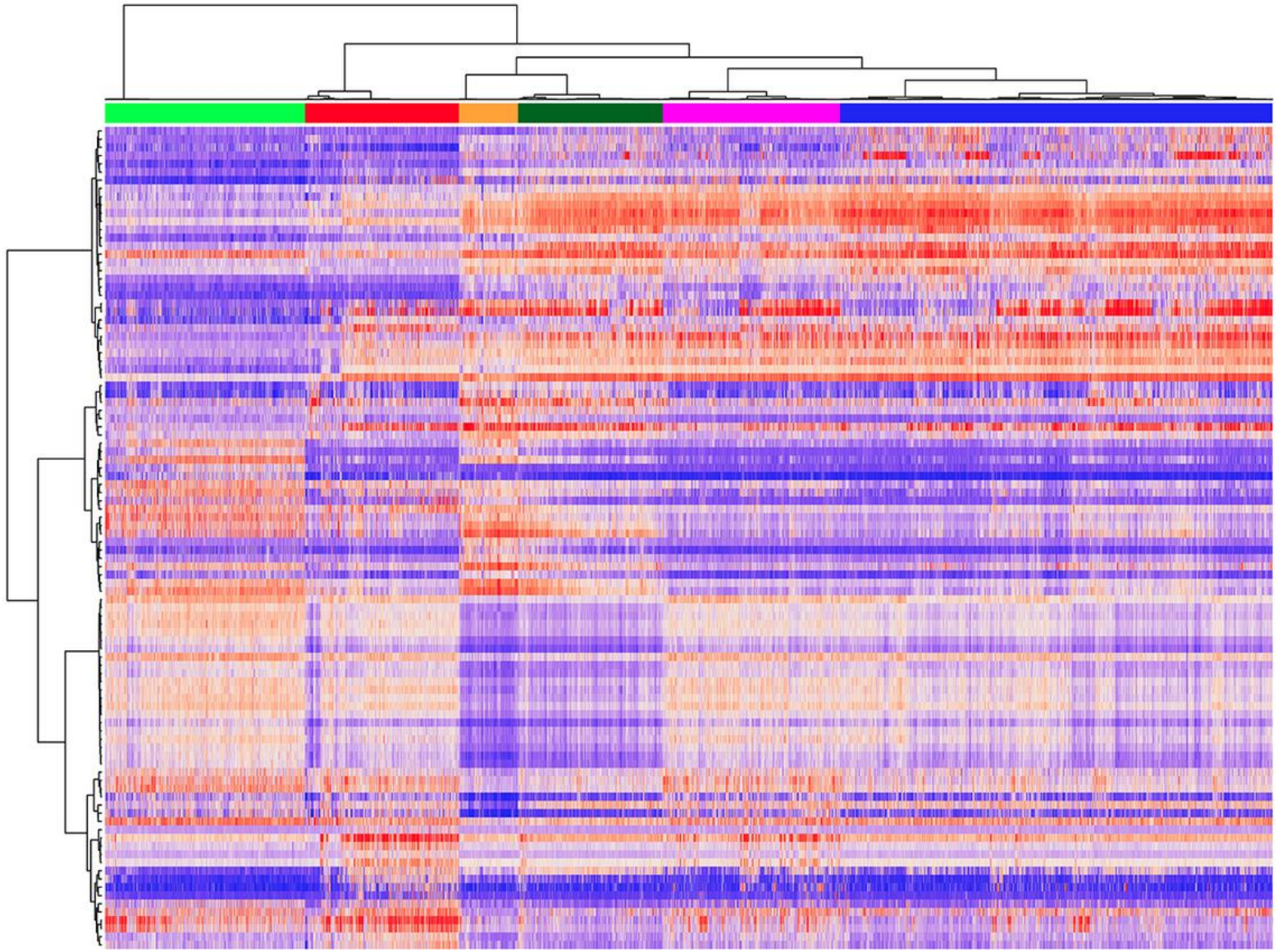

File
Home
Insert
Page Layout
Formulas
Data
Review
View
Power Pivot
Tell me what you want to do...
Normal
Page Break Preview
Page Layout
Custom Views
Workbook Views
Ruler
Formula Bar
Gridlines
Headings
Show
Zoom
100%
Zoom to Selection
Zoom
New Window
Arrange All
Freeze Panes
Split
Hide
Unhide
View Side by Side
Synchronous Scrolling
Reset Window Position
Switch Windows
Window
Macros
Macros
A1
TSPAN6

Patient samples

High

Low

relative number of transcripts

Genes