

Week 1: July 7, 2020

Week 6: August 13, 2020

Cancer Systems Biology

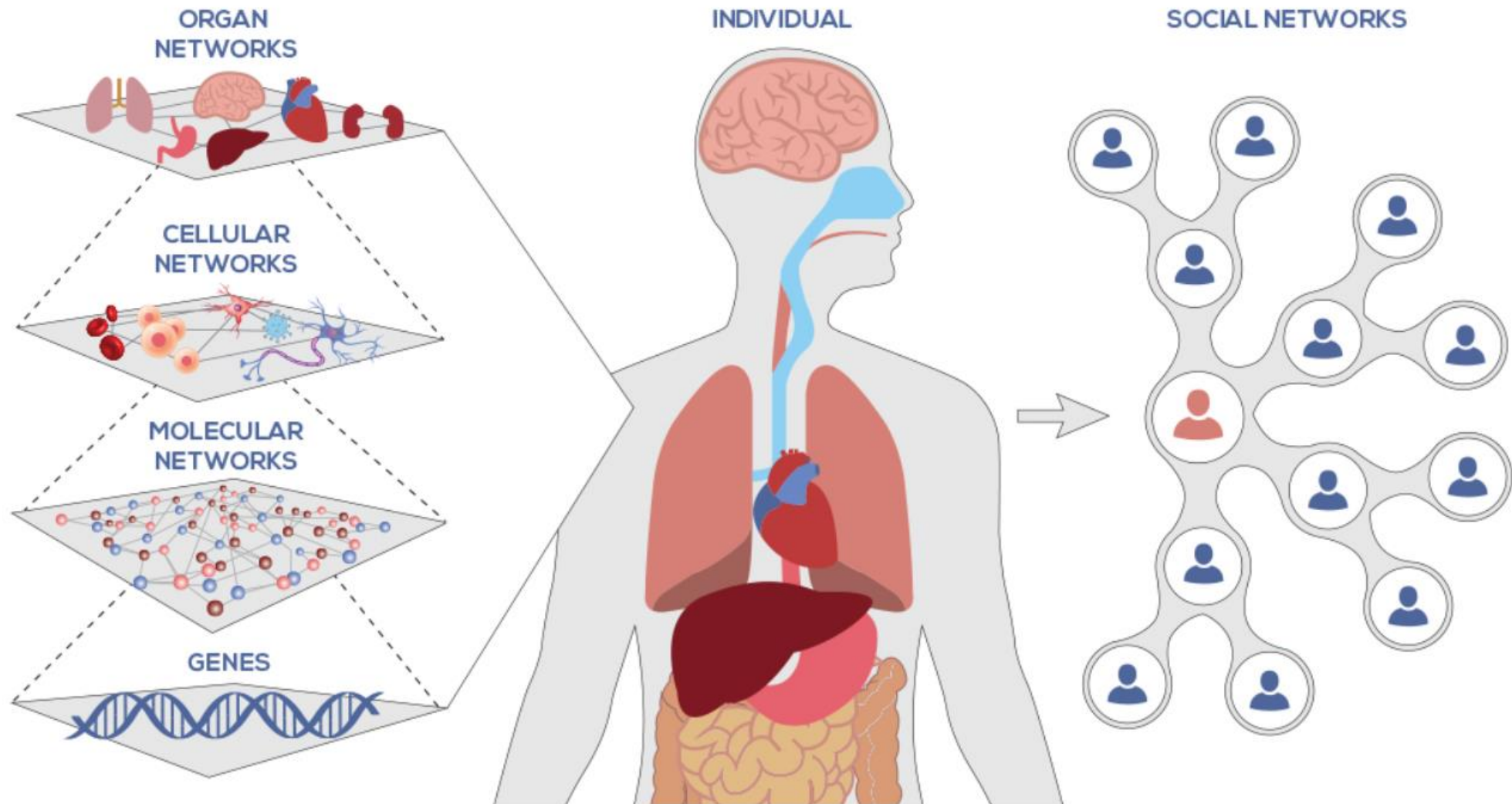
integrates experimental and computational approaches to study the complexities of cancer.

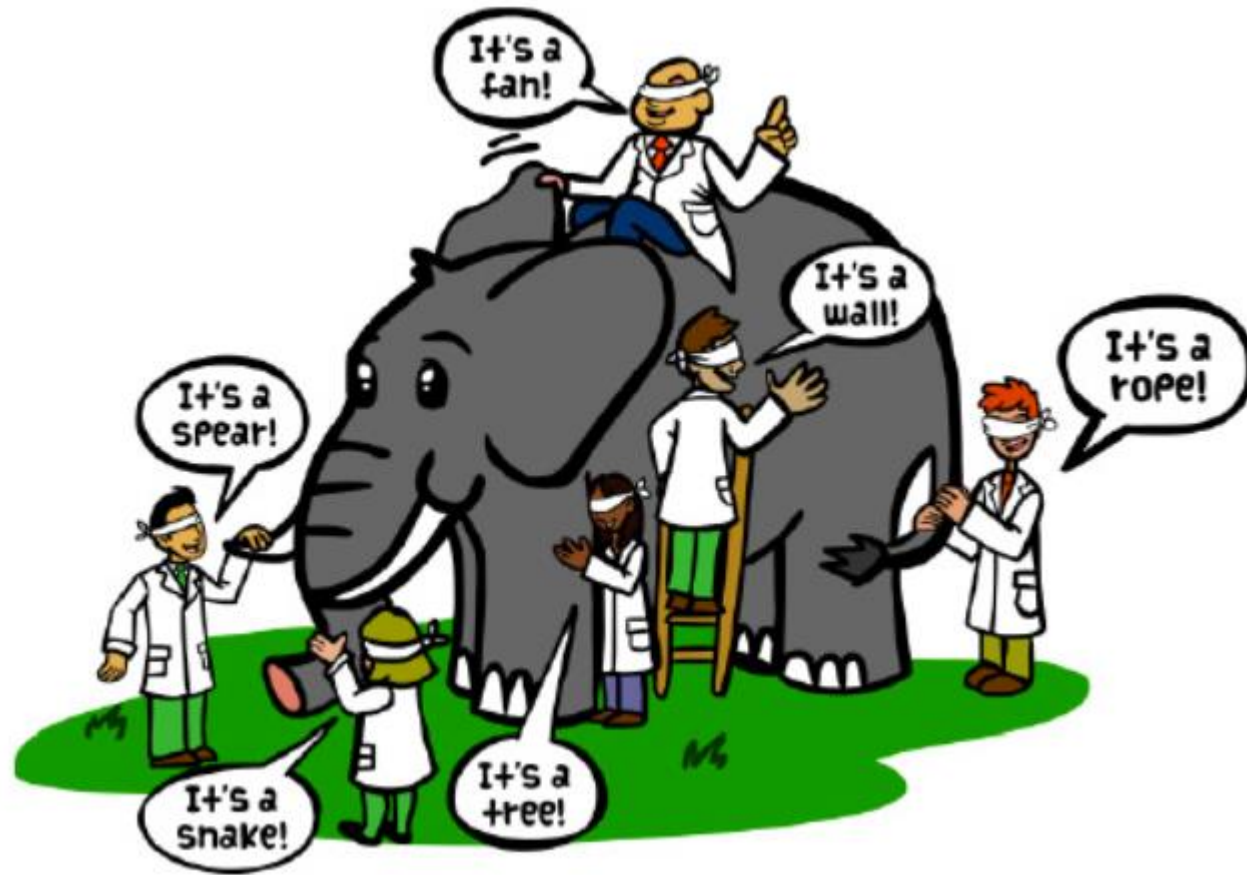
Cancer is a complex disease system involving multiple molecular, genetic, and cellular events.

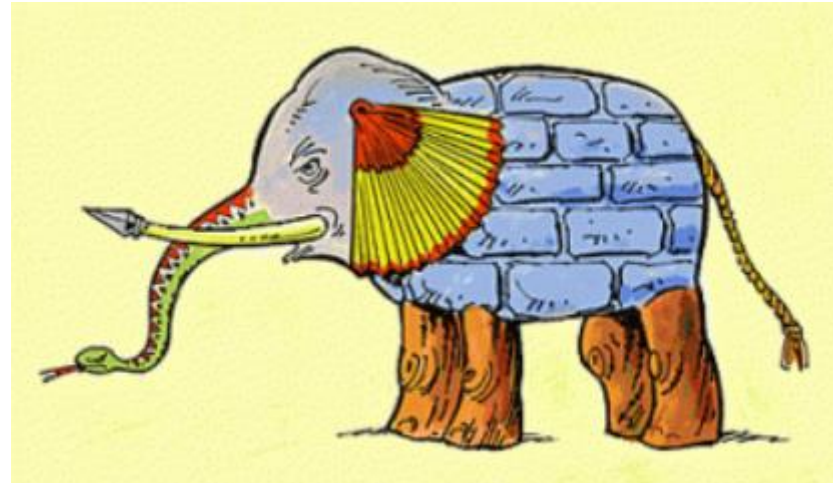
Systems biology is based on the understanding that the whole is greater than the sum of the parts.

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.

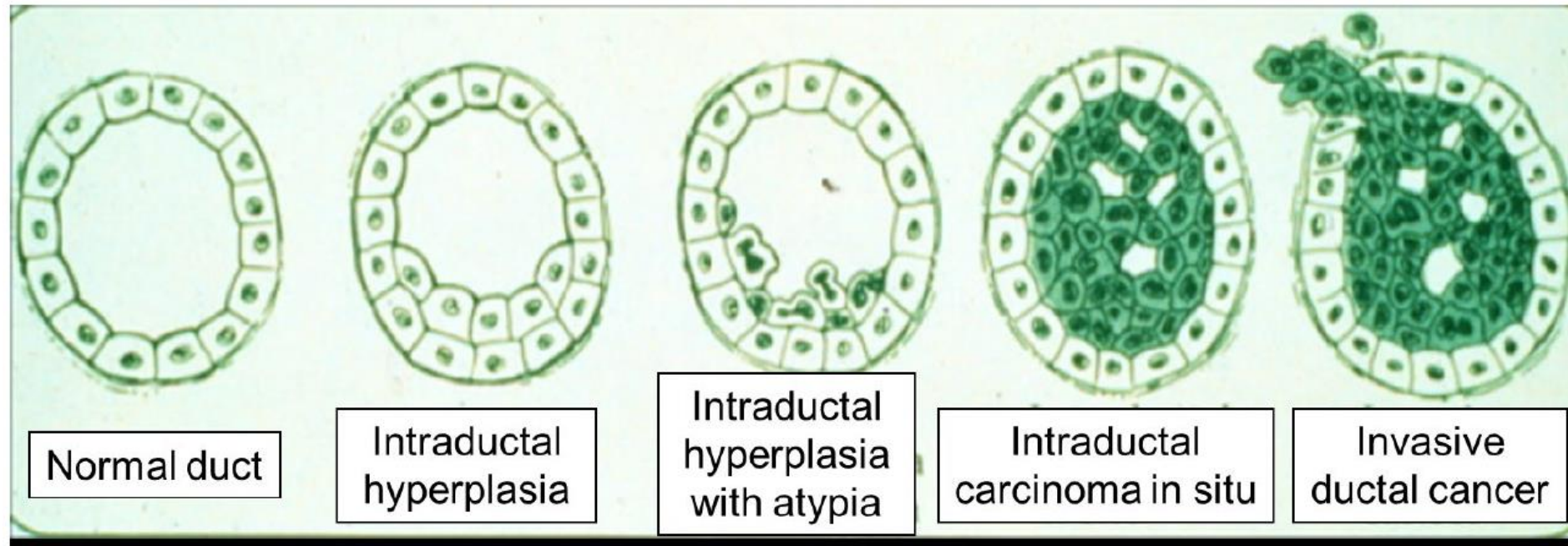






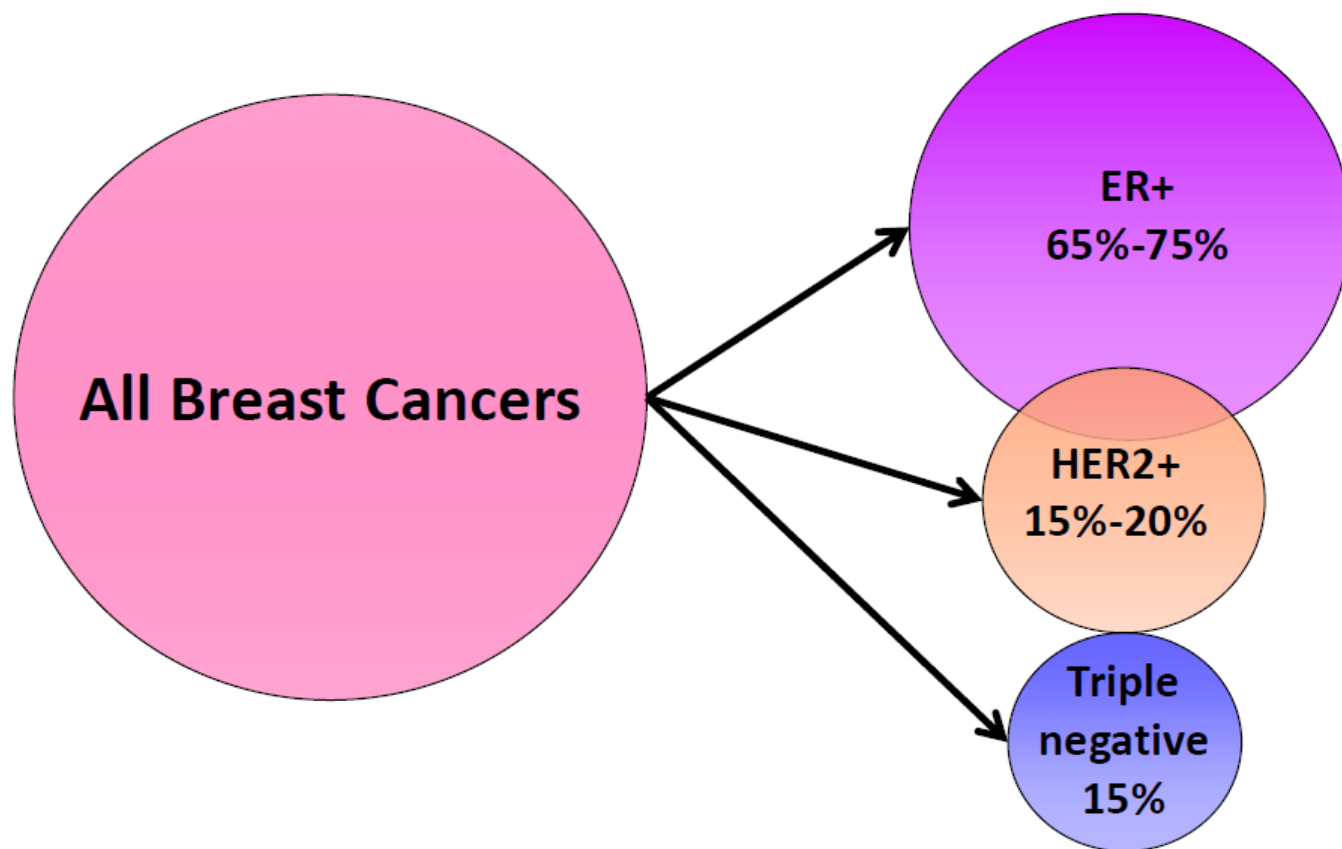
Breast cancer development

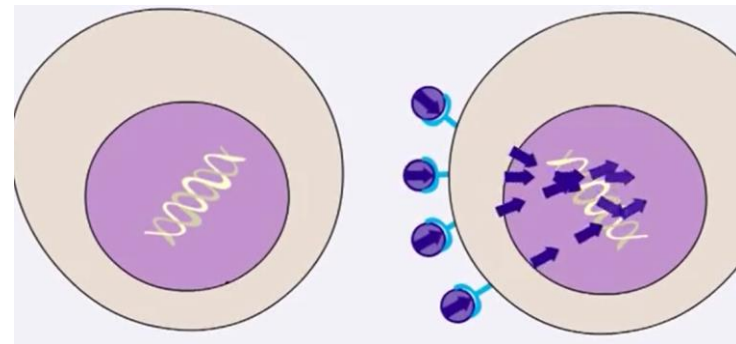
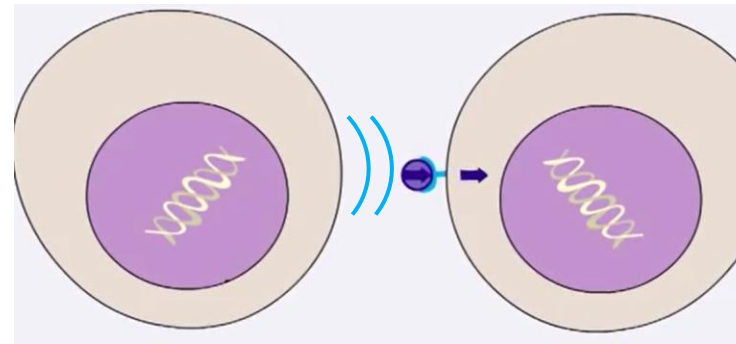
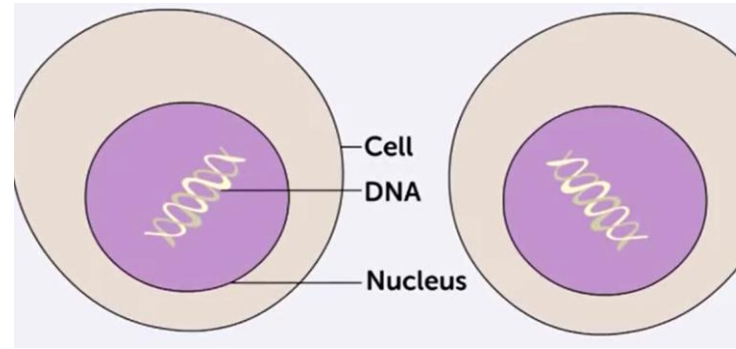
Cancer is a complex disease system involving multiple **molecular, genetic, and cellular events**.



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

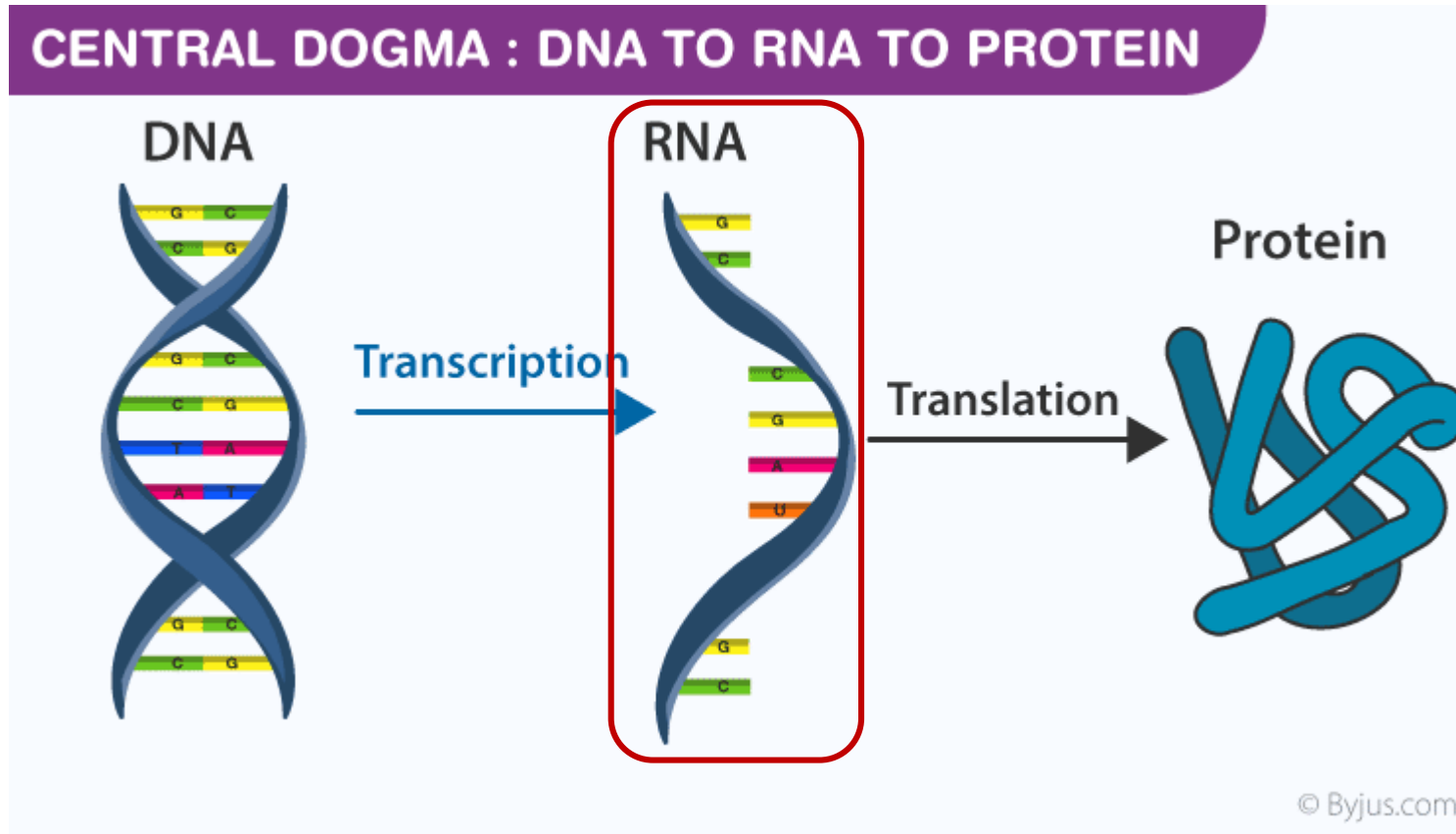
Invasive Breast Cancer Subsets Defined by IHC



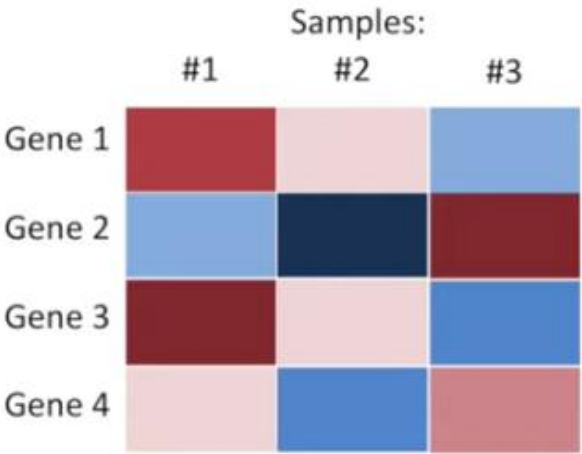


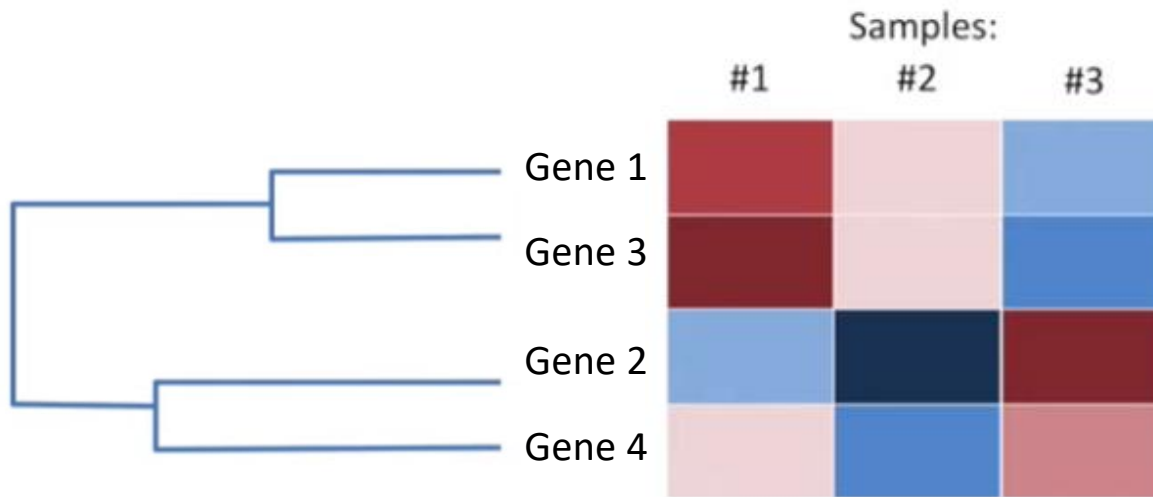
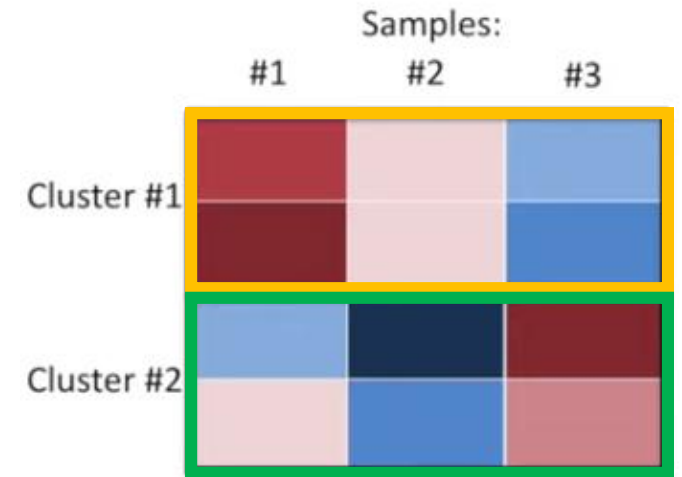
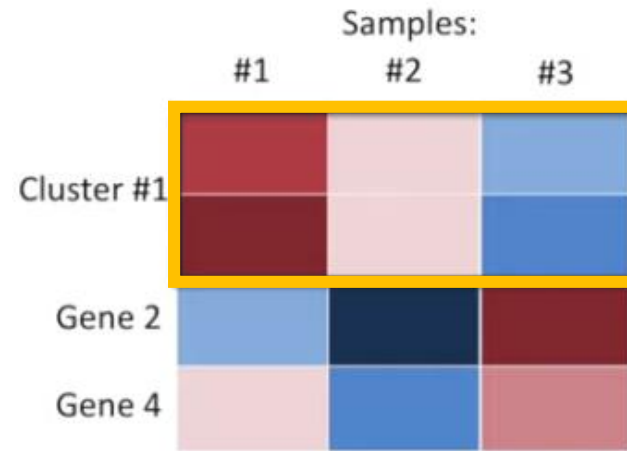
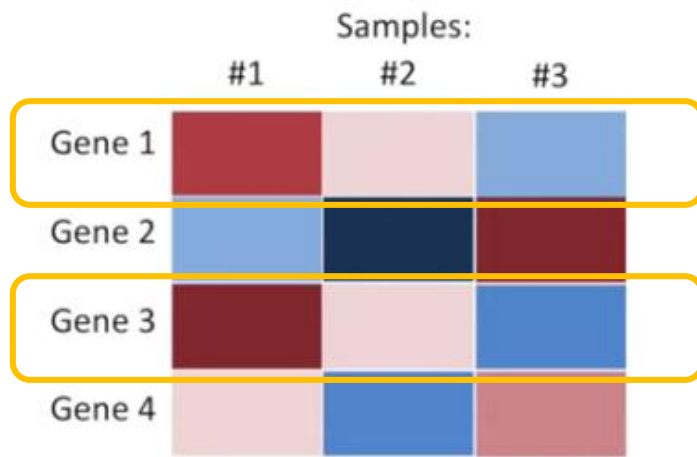
Central dogma of molecular biology

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.





The dendrogram tree shows how the close the genes and clusters are to each other.

Experiments

	#1	#2
Gene 1	8	5
Gene 2	0	15
Gene 3	8	3
Gene 4	3	12

	#1	#2	#2 - #1
Gene 1	8	5	3
Gene 2	0	15	-15
Gene 3	8	3	5
Gene 4	3	12	-9

Differential gene
expression

	#1	#2	#2 - #1
Gene 1	8	5	3
Gene 2	0	15	-15
Gene 3	8	3	5
Gene 4	3	12	-9

	Differential gene expression		
	#1	#2	#2 - #1
Gene 1	8	5	3
Gene 2	0	15	-15
Gene 3	8	2	6
Gene 4	3	12	-9

GENE	DGE
Gene 3	6
Gene 1	3
Gene 4	-9
Gene 2	-15

Differential gene
expression

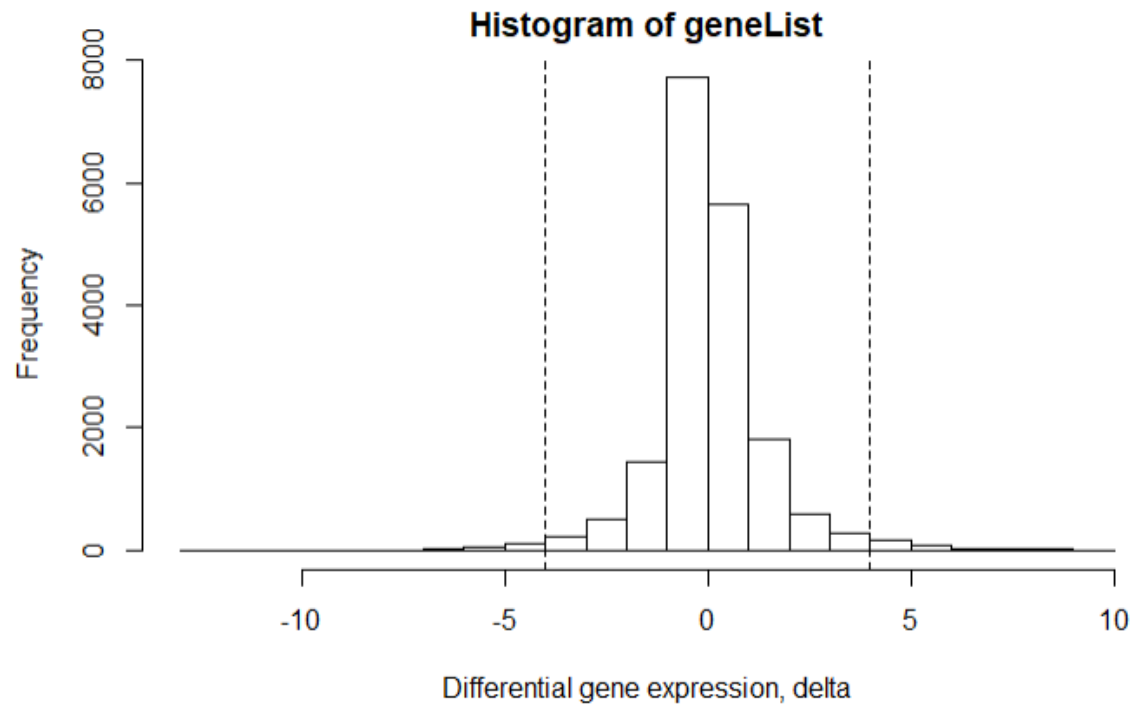
	#1	#2	#2 - #1
Gene 1	8	5	3
Gene 2	0	15	-15
Gene 3	8	2	6
Gene 4	3	12	-9

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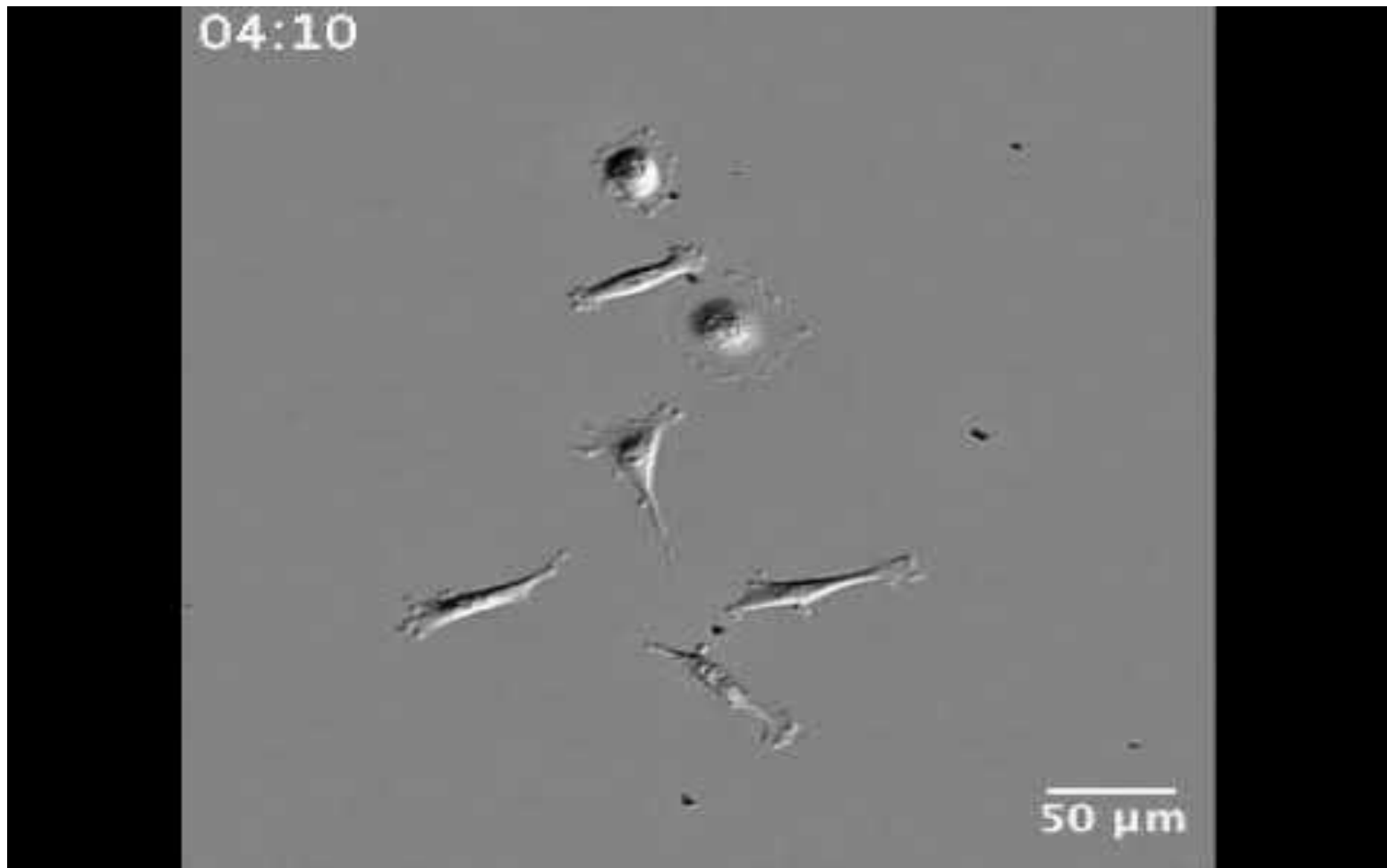


Breast cancer cell lines: Differential expression

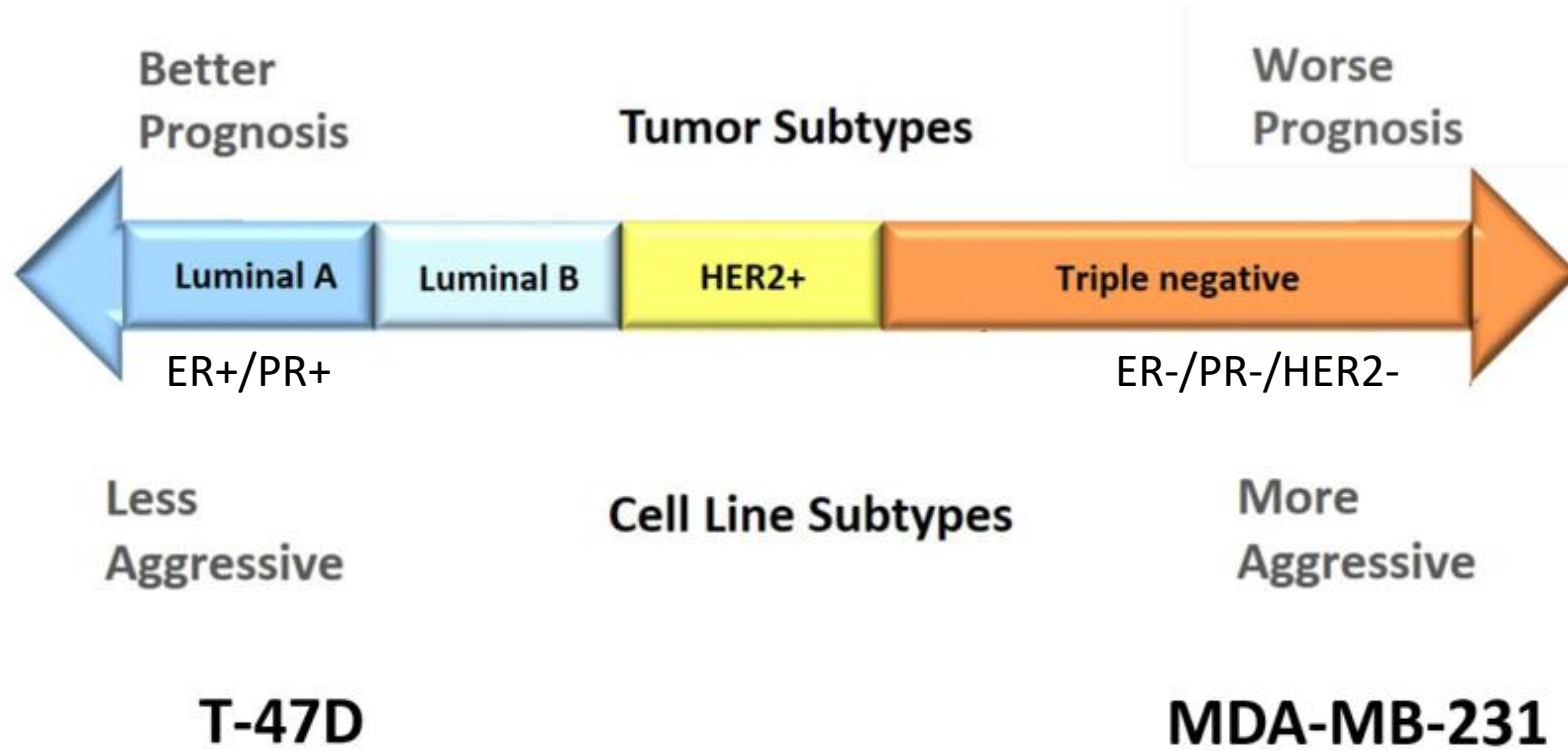
Differential expression in “fast” (MB-MDA-231)
versus “slow” (T-47D) breast cancer cell lines




Mesenchymal mode of MDA-MB-231 cell migration



Breast cancer patient samples and cell lines



<http://www.geneontology.org>

 Gene Ontology Consortium

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Enrichment analysis

Your gene IDs here...

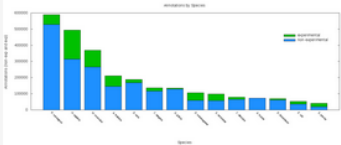
biological process ▾

Homo sapiens ▾

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Gene Ontology Consortium

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Ontology

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Gene Ontology: the framework for the model of biology. The GO defines concepts/classes used to describe gene function, and relationships between these concepts. It classifies functions along three aspects:

- molecular function**
molecular activities of gene products
- cellular component**
where gene products are active
- biological process**
pathways and larger processes made up of the activities of multiple gene products.

[more](#)

Annotations


[Download annotations](#) (standard files)

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GO annotations: the model of biology. Annotations are statements describing the functions of specific genes, using concepts in the Gene Ontology. The simplest and most common annotation links one gene to one function, e.g. FZD4 + Wnt signaling pathway. Each statement is based on a specified piece of evidence. [more](#)

The mission of the GO Consortium is to develop an up-to-date, comprehensive, **computational model of biological systems**, from the molecular level to larger pathways, cellular and organism-level systems. [more](#)

Search documentation

Search 

What is the Gene Ontology?

- [An introduction to the Gene Ontology](#)
- [What are annotations?](#)
- [Enrichment analysis](#)
- [Downloads](#)



on·tol·o·gy

/än'täləjē/

noun

1. the branch of metaphysics dealing with the nature of being.
2. a set of concepts and categories in a subject area or domain that shows their properties and the relations between them.

"what's new about our ontology is that it is created automatically from large datasets"



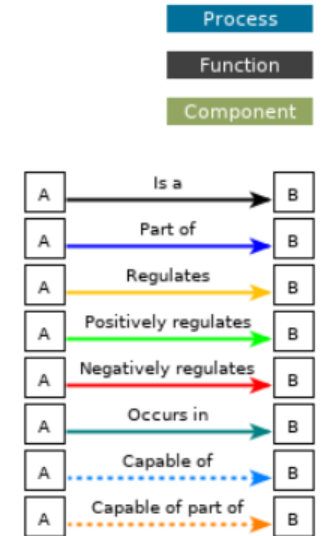
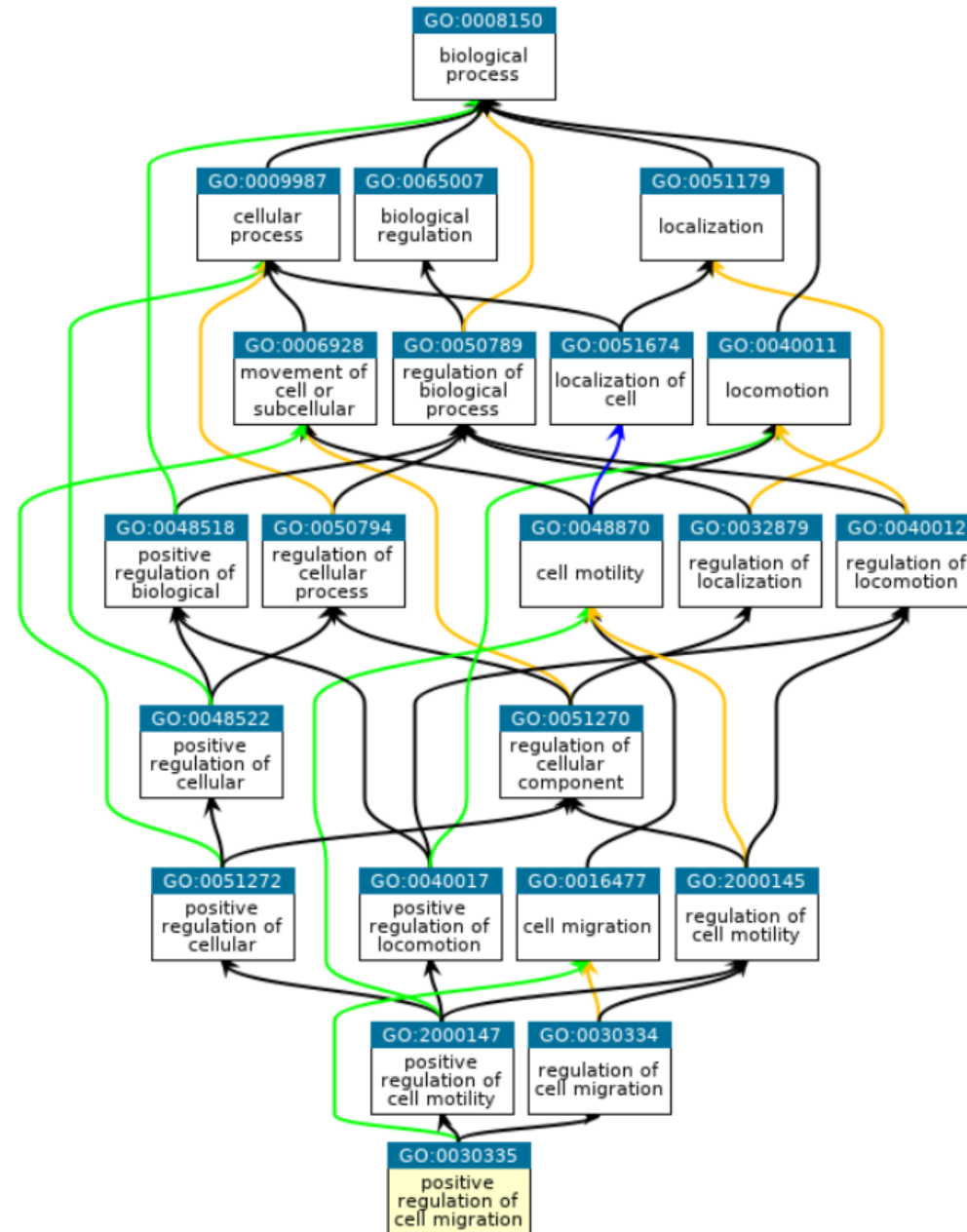
GENEONTOLOGY
Unifying Biology

THE GENE ONTOLOGY RESOURCE

The mission of the GO Consortium is to develop a comprehensive, **computational model of biological systems**, ranging from the molecular to the organism level, across the multiplicity of species in the tree of life.





























The Gene Ontology (GO) knowledgebase is the world's largest source of information on the functions of genes. This knowledge is both human-readable and machine-readable, and is a foundation for computational analysis of large-scale molecular biology and genetics experiments in biomedical research.

Terms for biological processes such as *positive regulation of cell migration* are carefully organized into an ontology that describes biology.



Each gene has Gene Ontology (GO) annotations associated with it.

MIEN1: Migration and invasion enhancer 1

Symbol	GO Term	Evidence	Reference
MIEN1	GO:0010269    response to selenium ion	ECO:0000318  IBA	PMID:21873635
MIEN1	GO:0043066    negative regulation of apoptotic process	ECO:0000318  IBA	PMID:21873635
MIEN1	GO:0051491    positive regulation of filopodium assembly	ECO:0000318  IBA	PMID:21873635
MIEN1	GO:0006915    apoptotic process	ECO:0000322  IEA	GO_REF:0000043
MIEN1	GO:0051491    positive regulation of filopodium assembly	ECO:0000314  IDA	PMID:21628459
MIEN1	GO:0043066    negative regulation of apoptotic process	ECO:0000314  IDA	PMID:21068479
MIEN1	GO:0030335    positive regulation of cell migration	ECO:0000314  IDA	PMID:21628459

GENE	DGE
Gene 3	6
Gene 1	3
Gene 4	-9
Gene 2	-15



Gene 3: Apoptosis, Migration, Calcium sensing, extracellular matrix

Gene 1: Migration, extracellular matrix, cell growth, wound repair

Gene 4: Adhesion, duct development, tight junction

Gene 2: Adhesion, oxidation, tight junction, calcium sensing

GENE	DGE
Gene 3	6
Gene 1	3
Gene 4	-9
Gene 2	-15



Gene 3: Apoptosis, **migration**, calcium sensing, **extracellular matrix**

Gene 1: **Migration**, **extracellular matrix**, cell growth, wound repair

Gene 4: **Adhesion**, duct development, **tight junction**, apoptosis

Gene 2: **Adhesion**, oxidation, **tight junction**, calcium sensing

Genes most highly expressed in “fast” cell line versus “slow” cell line

VIM	LDHB	SERPINE1	MSN	GPX1	CAV1	GSTP1	FOSL1	AXL	F3	CST1
9.7	8.8	8.7	8.7	8.7	8.5	8.4	8.1	8.0	8.0	7.9
PLAT	MMP14	AKR1B1	PLAU	NT5E	CAV2	TGM2	CTGF	DKK1		
7.8	7.8	7.7	7.7	7.6	7.6	7.5	7.3	7.3		

Genes most highly expressed in “slow” cell line versus “fast” cell line

PREX1	CLDN3	HOXC10	FXYD3	IGFBP2	ST14	AZGP1	KRT23	FOXA1	OLFM1	RAB25
-6.6	-6.7	-6.8	-6.9	-6.9	-6.9	-7.4	-7.5	-7.8	-7.9	-8.0
AGR3	IGFBP5	CDH1	STC2	CRABP2	SERPINA6	CRIP1	PIP	MGP		
-8.3	-8.4	-8.6	-8.6	-8.8	-9.4	-9.6	-11.9	-12.3		

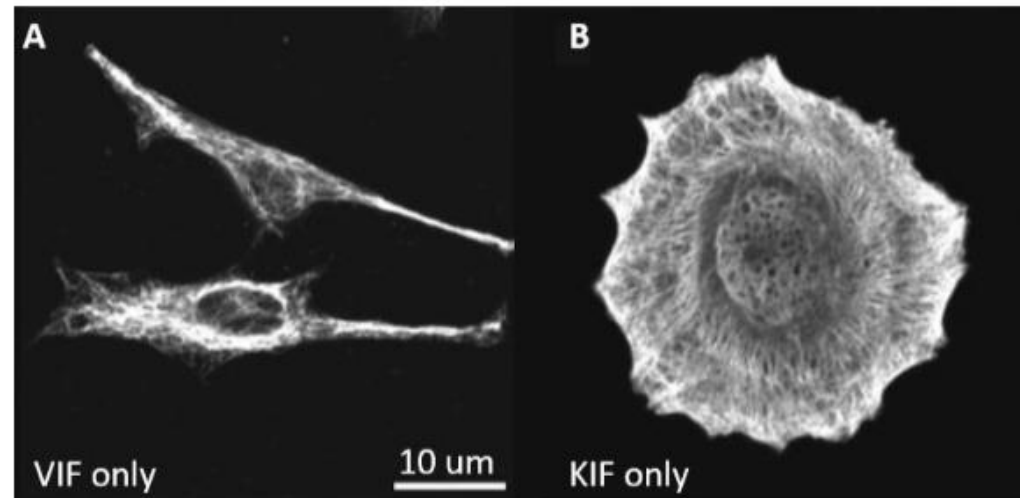
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VIM	LDHB	SERPINE1	MSN	GPX1	CAV1	GSTP1	FOSL1	AXL	F3	CST1
9.7	8.8	8.7	8.7	8.7	8.5	8.4	8.1	8.0	8.0	7.9
PLAT	MMP14	AKR1B1	PLAU	NT5E	CAV2	TGM2	CTGF	DKK1		
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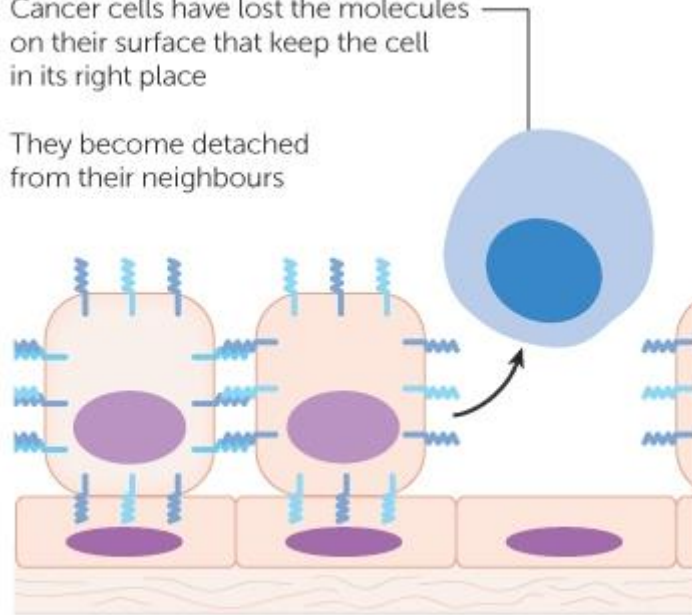
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AGR3	IGFBP5	CDH1	STC2	CRABP2	SERPINA6	CRIP1	PIP	MGP		
-8.3	-8.4	-8.6	-8.6	-8.8	-9.4	-9.6	-11.9	-12.3		

Vimentin intermediate filaments (VIF)
keratin intermediate filaments (KIF)



Cancer cells have lost the molecules on their surface that keep the cell in its right place

They become detached from their neighbours



Cancer Research UK

