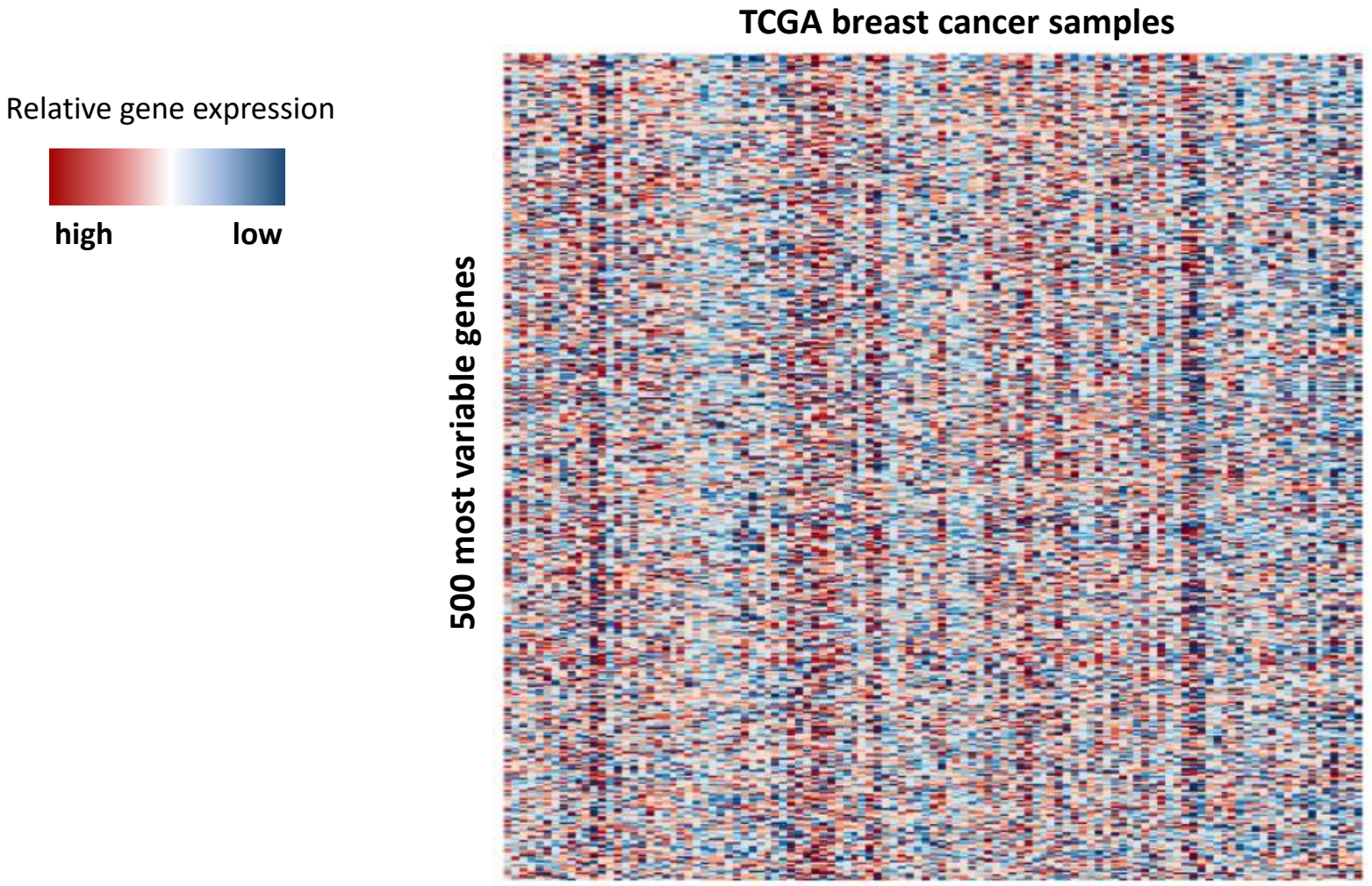
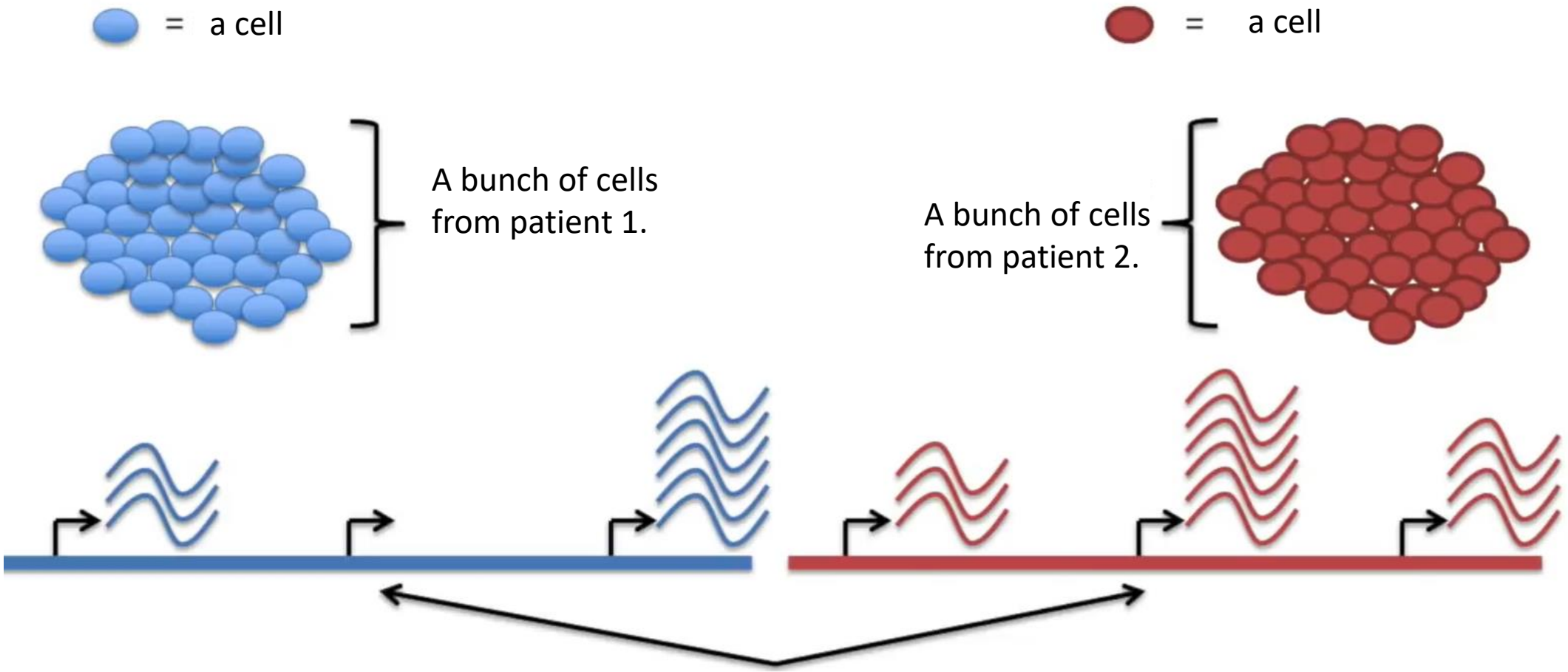
Heat map representation of gene expression levels across samples

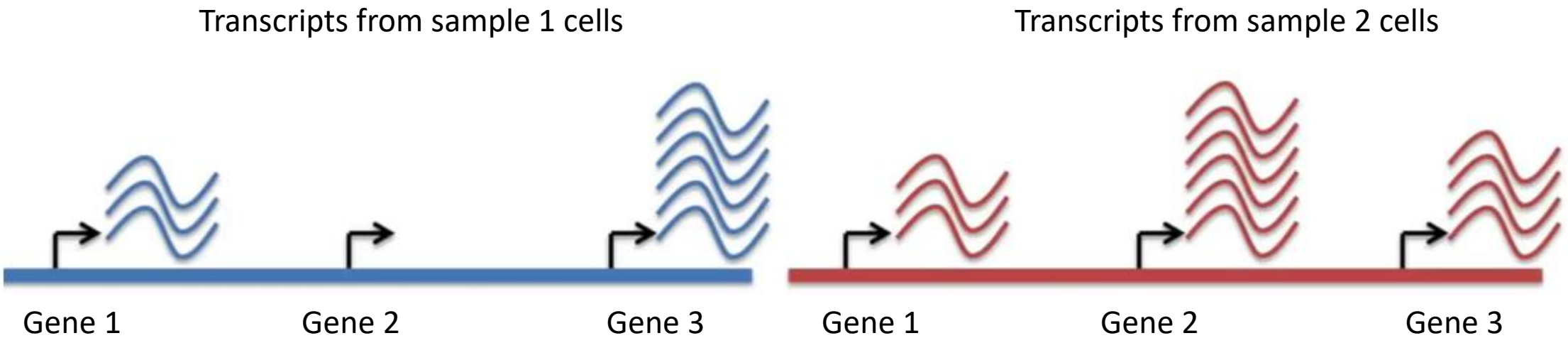


Gene expression data tells us how many copies of each gene in a sample (bunch of cells).

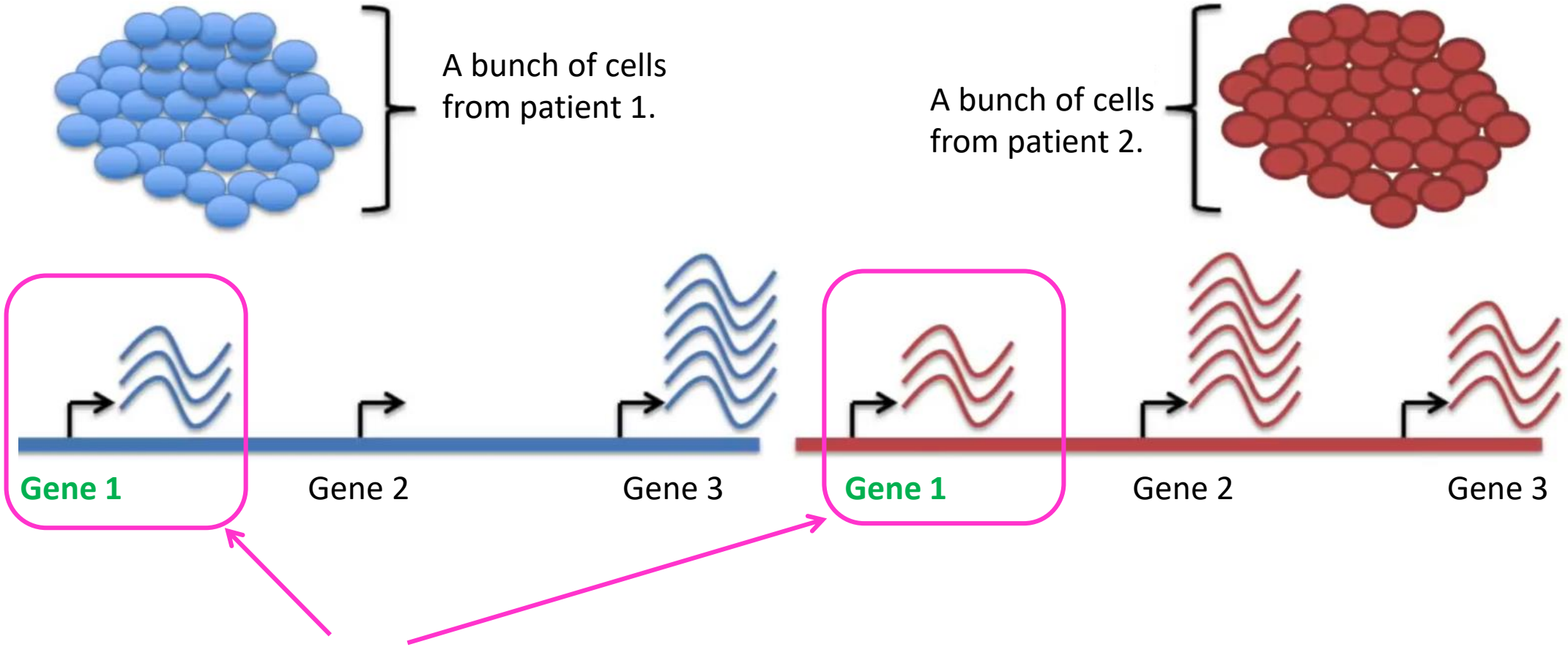


We compare different patient samples and figure out what‘s different in the two samples.

Gene expression data tells us how many copies of each gene in a sample (bunch of cells).

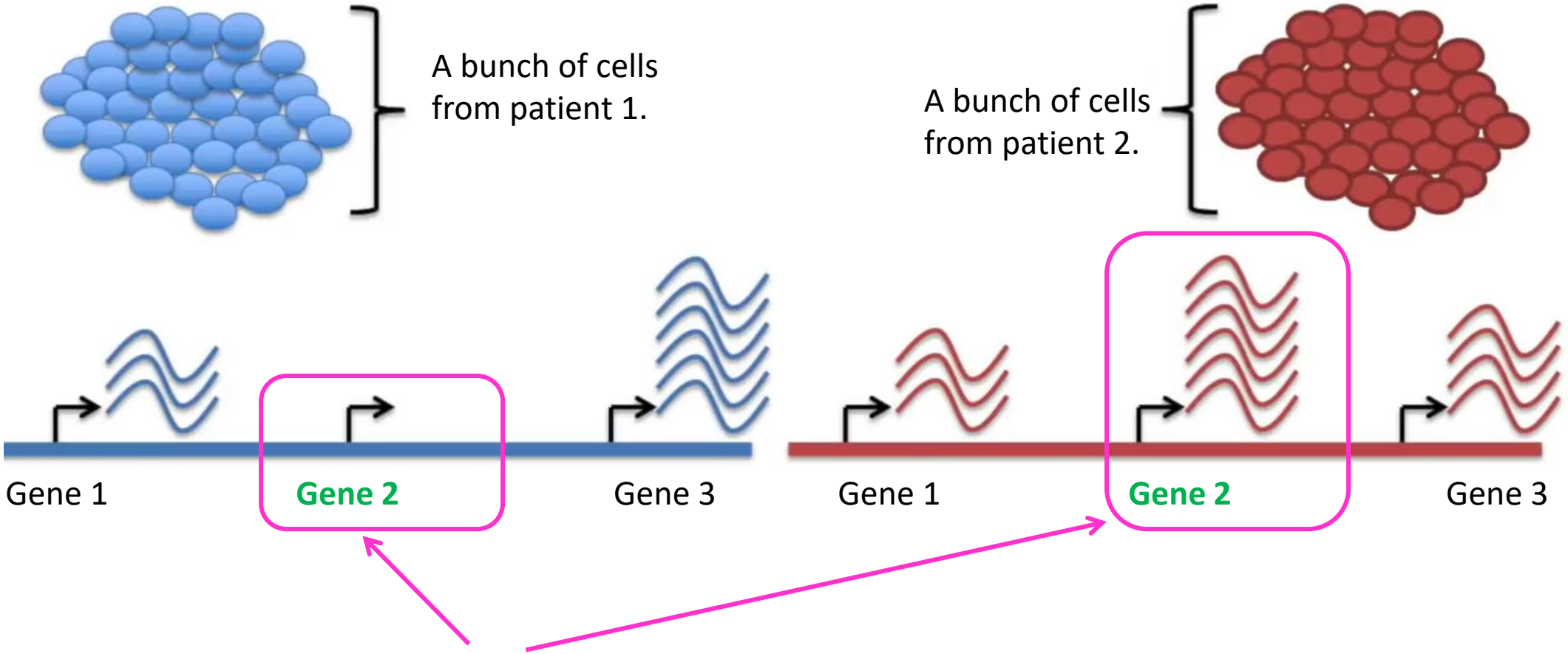


Gene expression data tells us how many copies of each gene in a sample (bunch of cells).



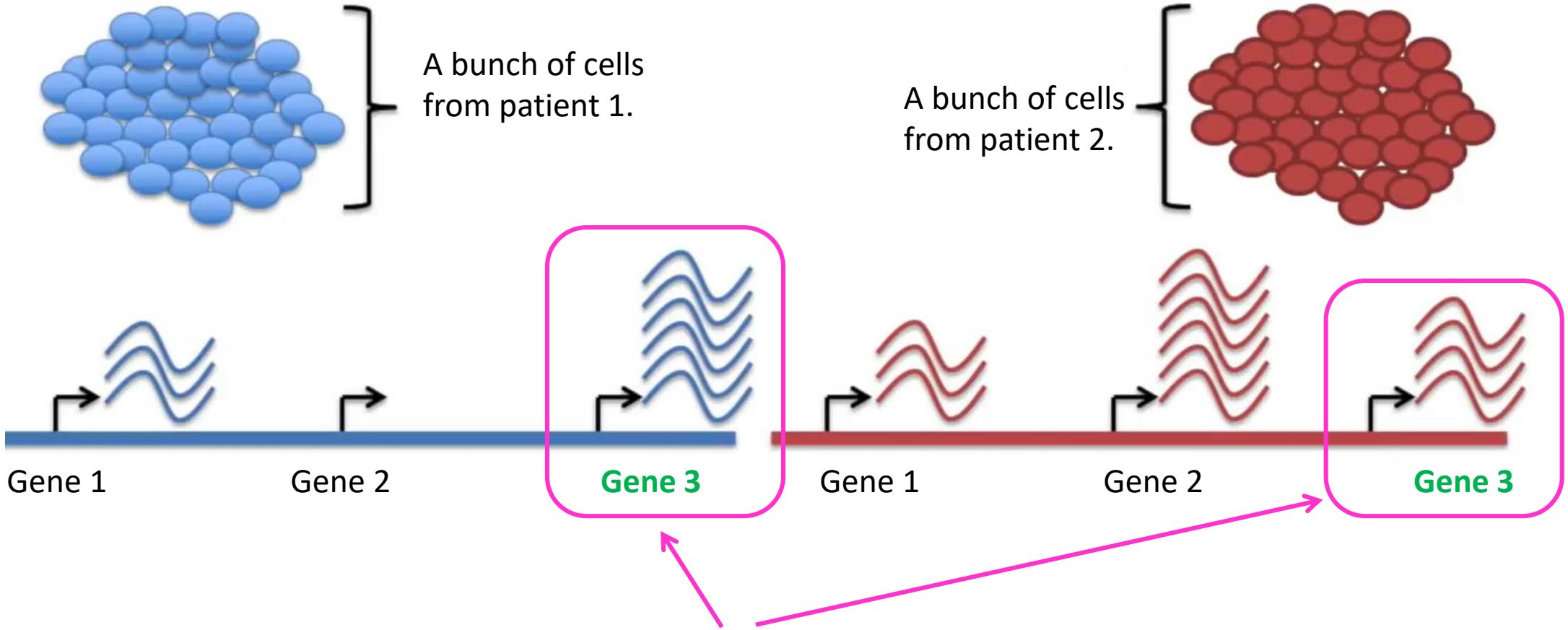
No difference in the amount of **Gene 1** between **sample 1** and **sample 2**.

Gene expression data tells us how many copies of each gene in a sample (bunch of cells).



A BIG difference in the amount of Gene 2 between sample 1 and sample 2.

Gene expression data tells us how many copies of each gene in a sample (bunch of cells).

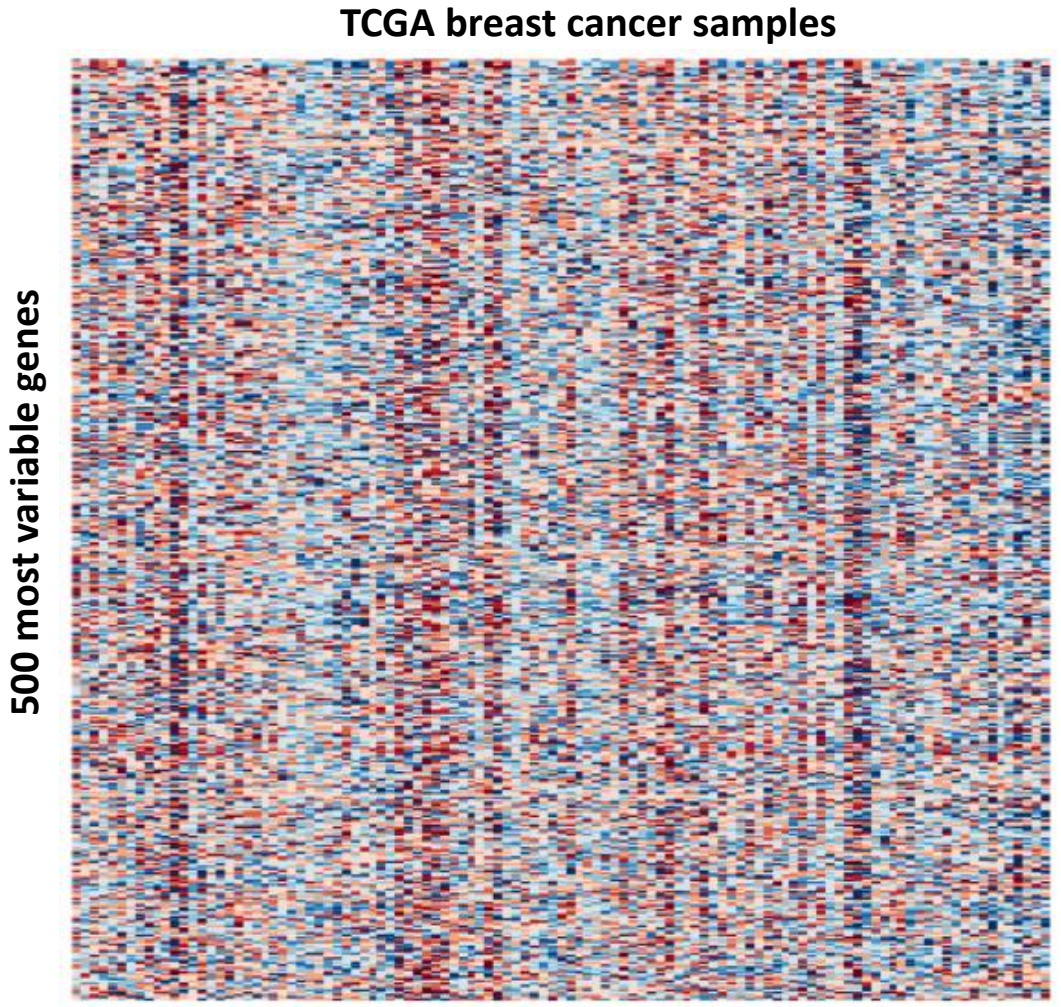


A subtle difference in the amount of **Gene 3** between **sample 1** and **sample 2**.

Heat map representation of gene expression levels across samples

Expression relative to the median across samples

high low

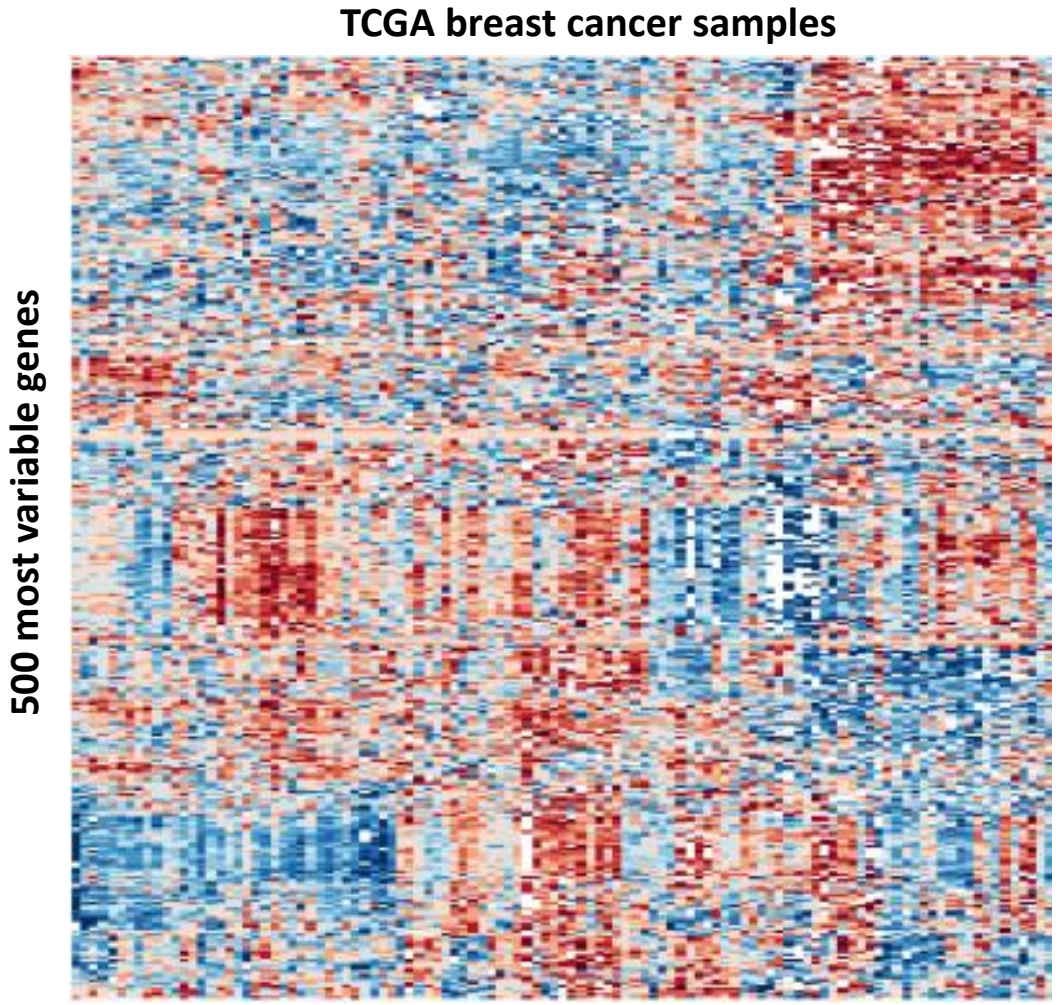


Clustering rearranges the rows and columns according to similarity.

Heat map representation of gene expression levels across samples

Expression relative to the median across samples

high low



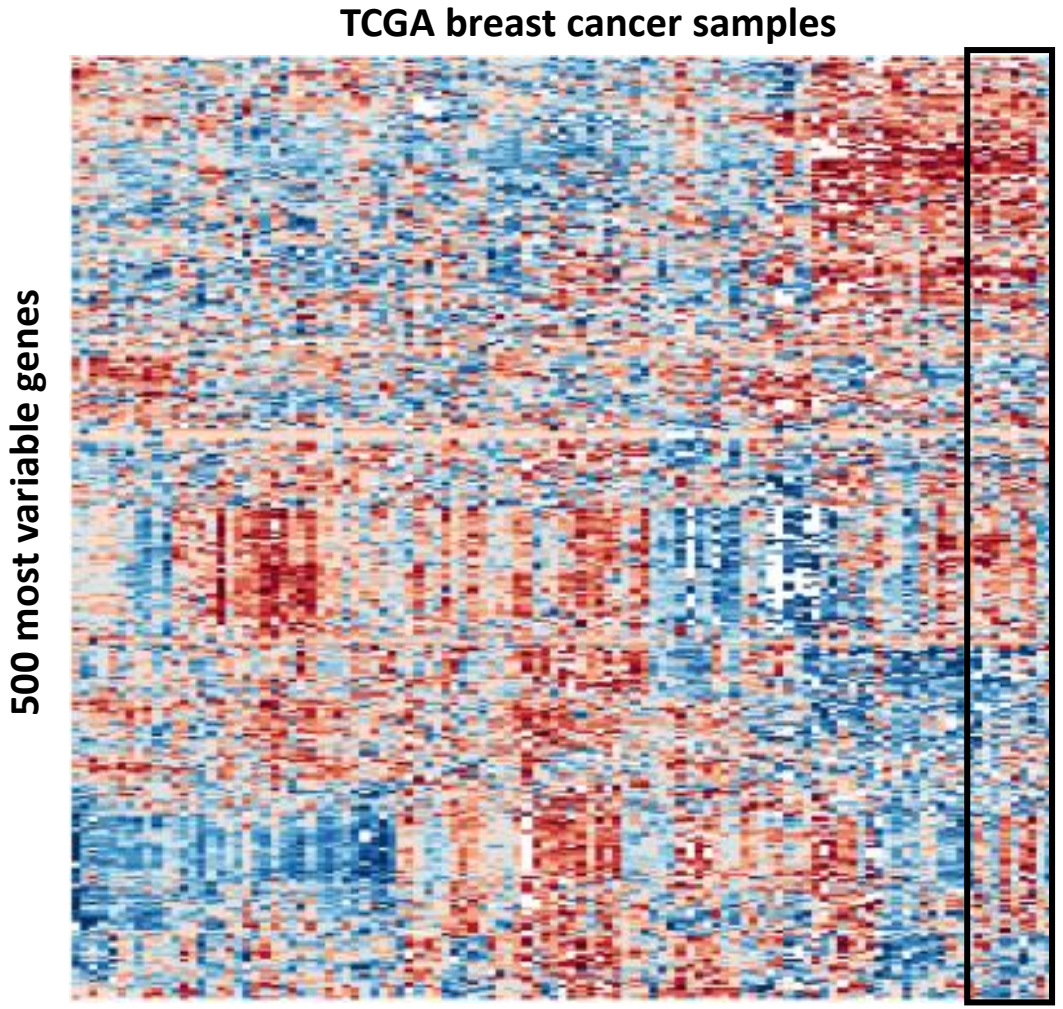
Clustering rearranges the rows and columns according to similarity.

It easy to see patterns in the clustered data.

Heat map representation of gene expression levels across samples

Expression relative to the median across samples

high low

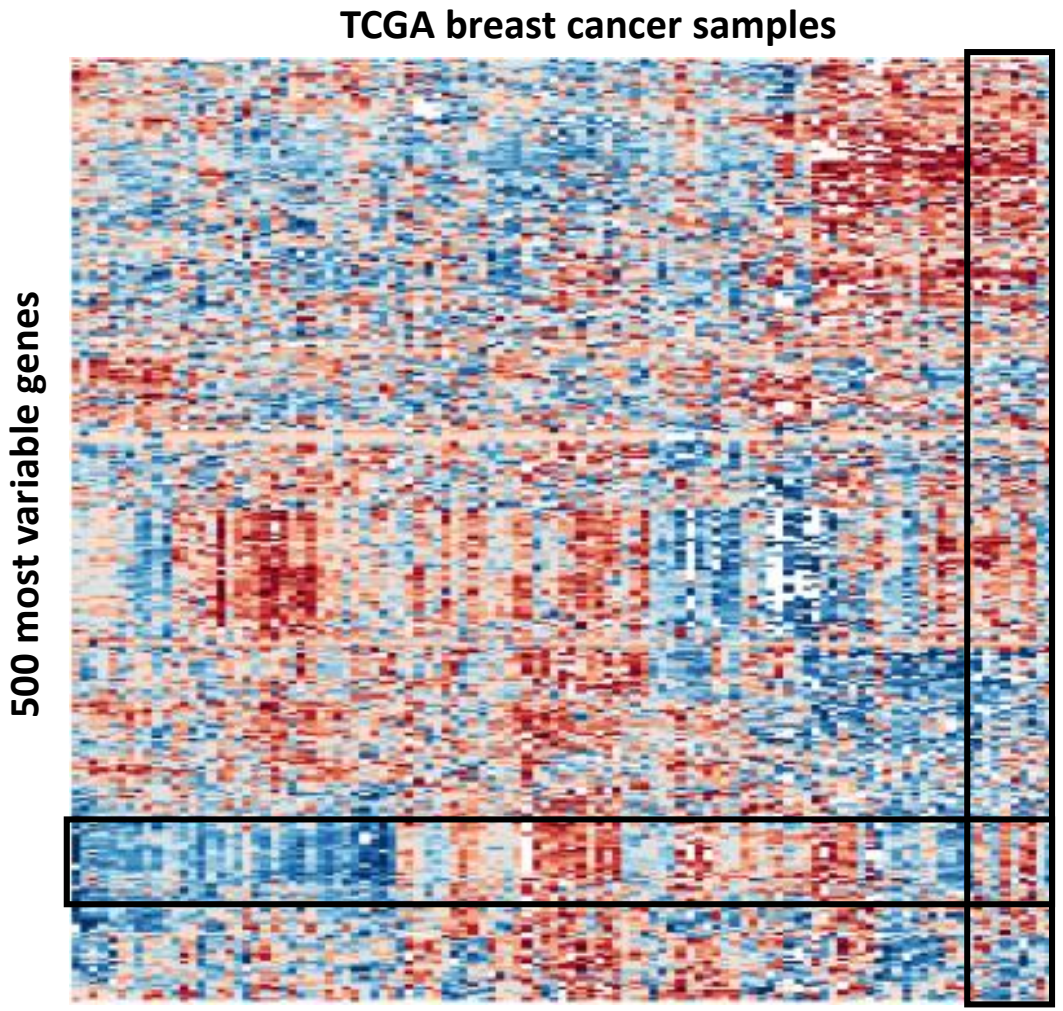


These samples express the similar genes.

Heat map representation of gene expression levels across samples

Expression relative to the median across samples

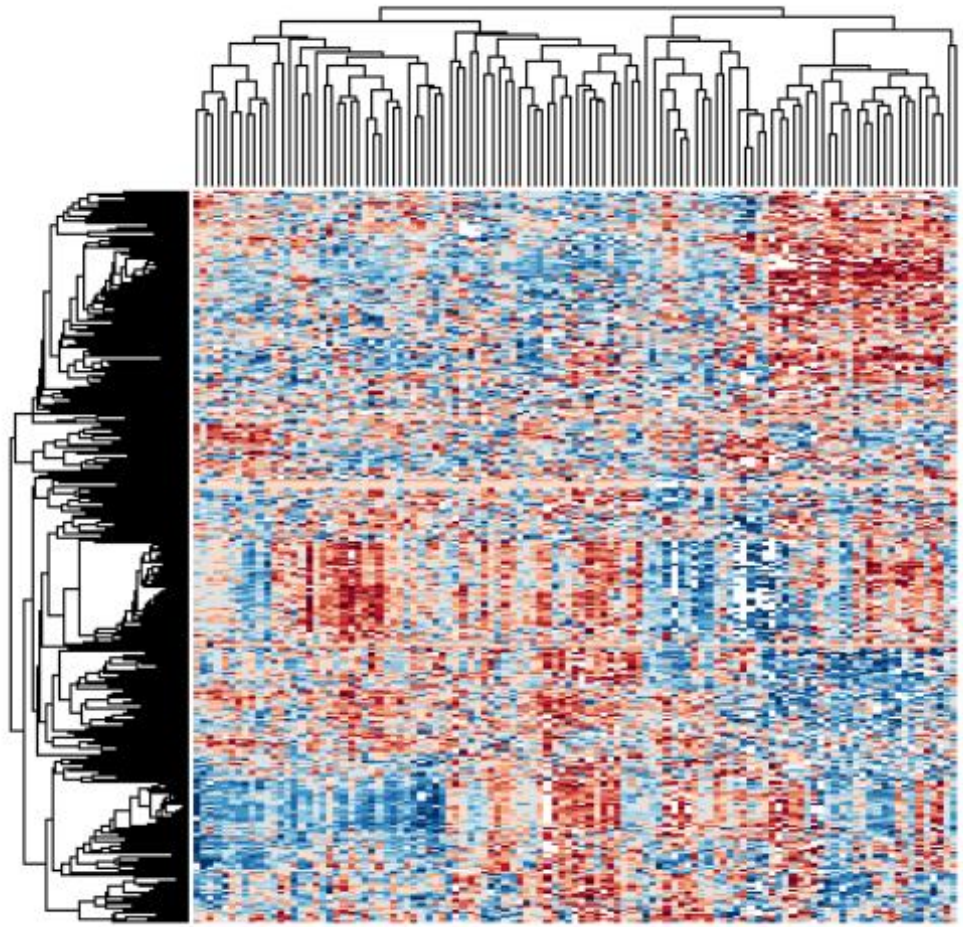
high low



These genes behave similarly across the samples.

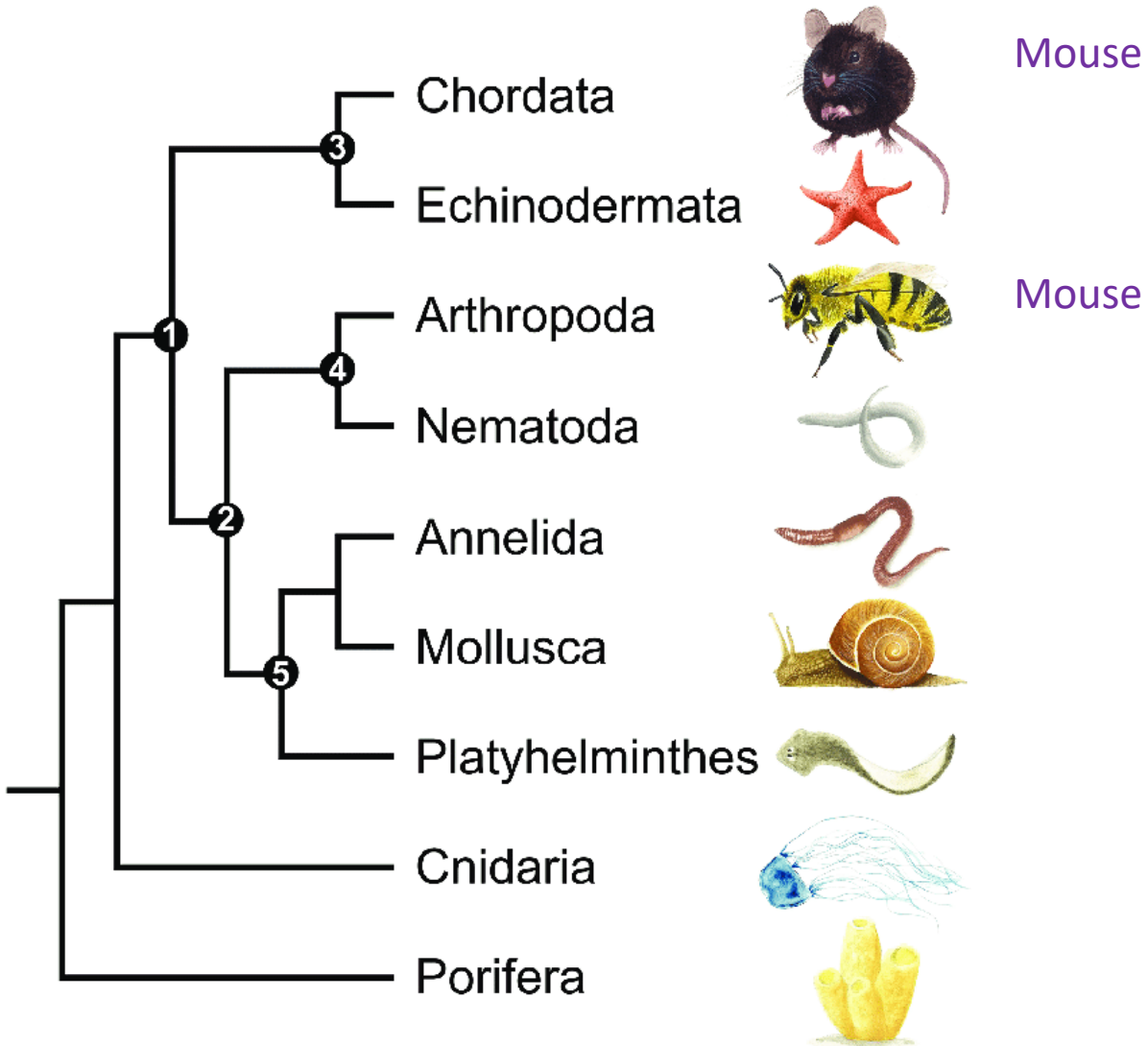
These samples express the same genes.

Heat maps often come with *dendrograms.*

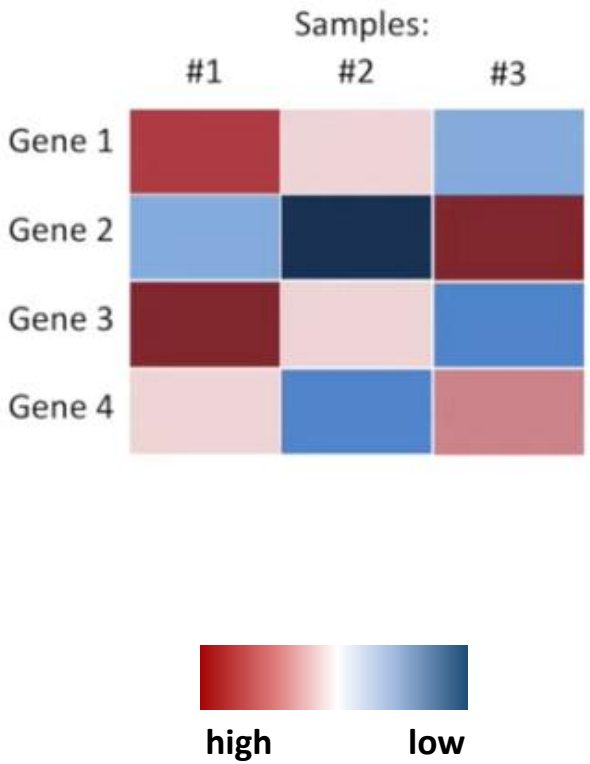


Dendrograms are **tree structures** that show how similar things (samples or genes) are to each other.

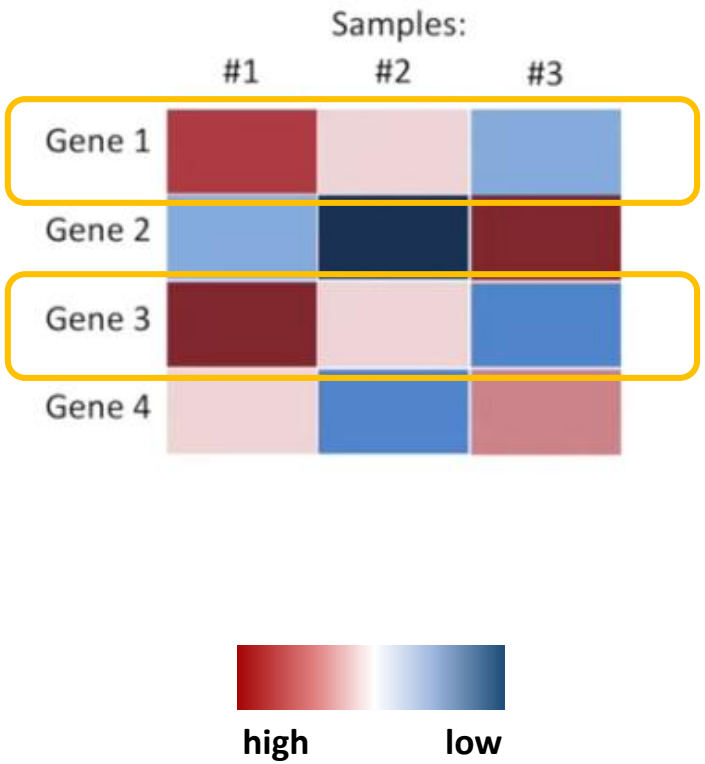
A “phylogenetic tree” is an example of a dendrogram.



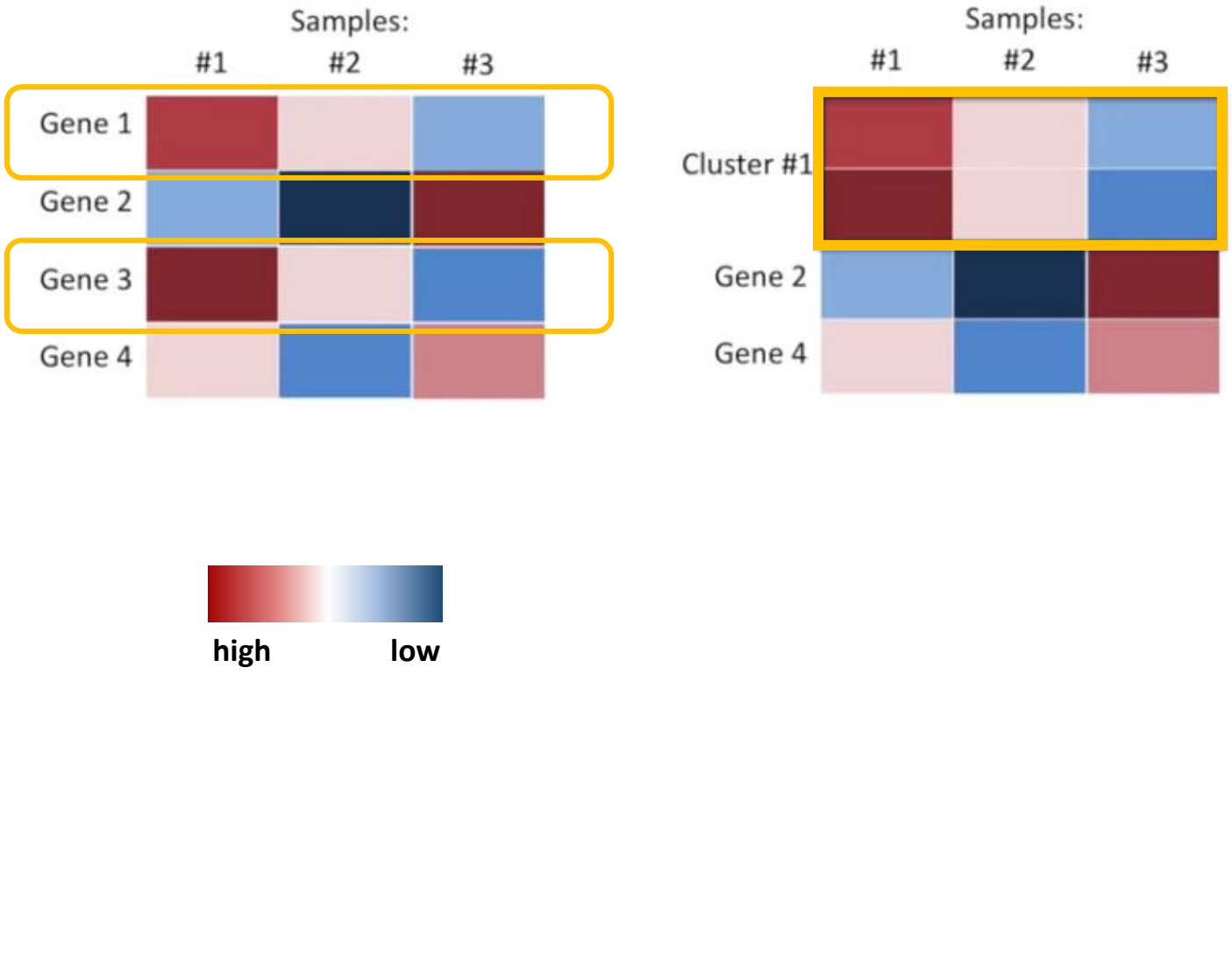
Heat map for expression values of four genes in three samples.



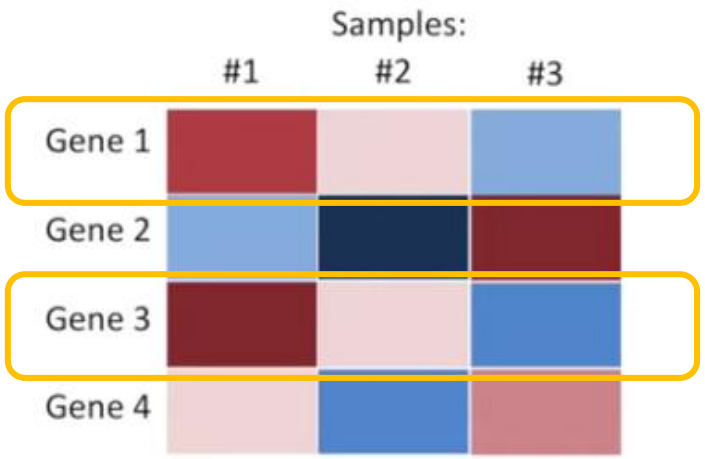
Gene 1 and Gene 3 are most similar to each other.



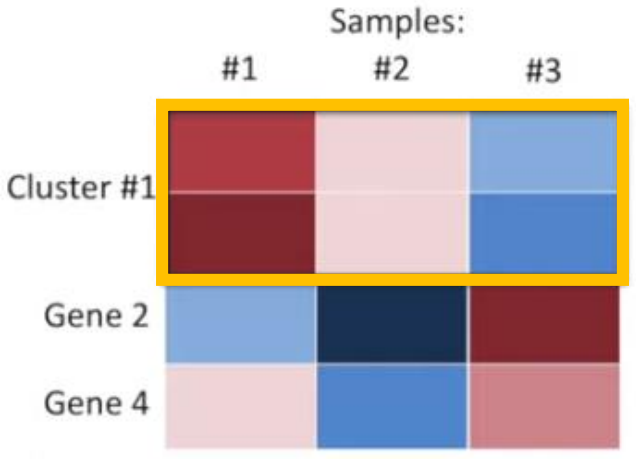
Gene 1 and Gene 3 become **Cluster #1.**



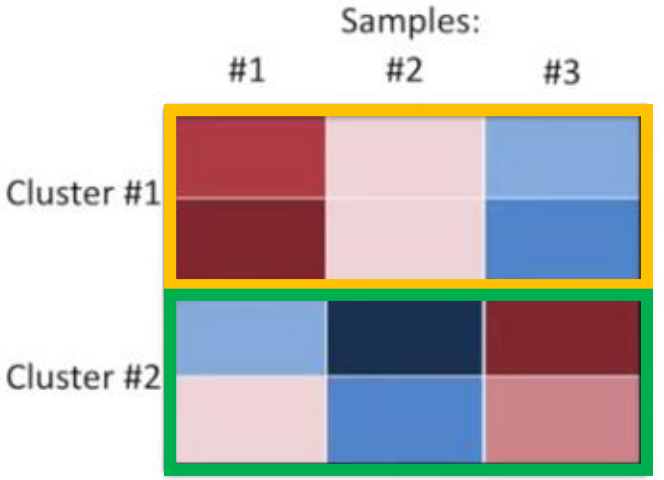
Genes 1 and 3 are most similar.



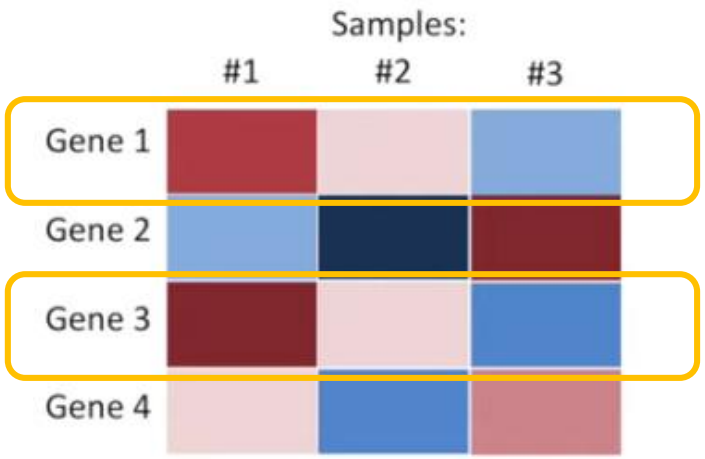
Genes 1 and 3 become **Cluster #1**.



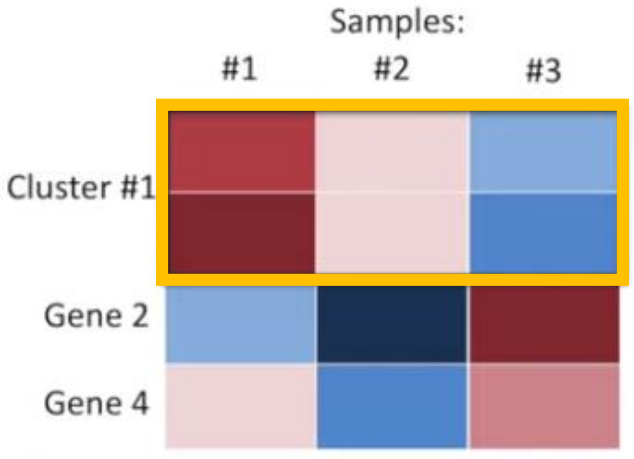
Genes 2 and 4 become **Cluster #2**.



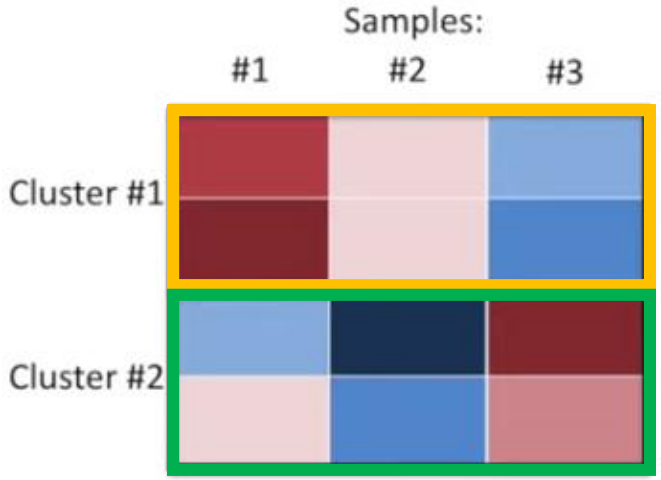
Genes 1 and 3 are most similar.

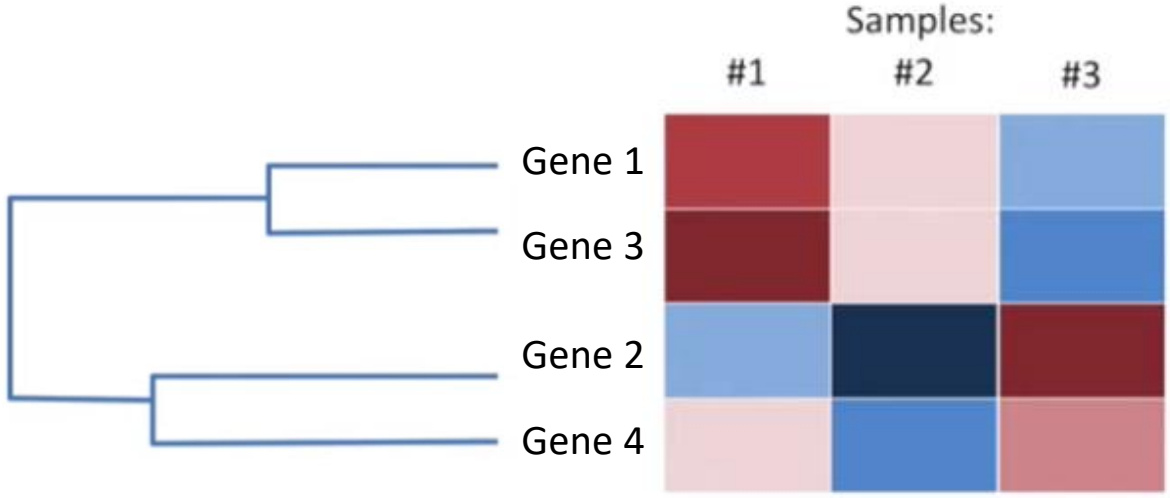


Genes 1 and 3 become **Cluster #1**.



Genes 2 and 4 become **Cluster #2**.



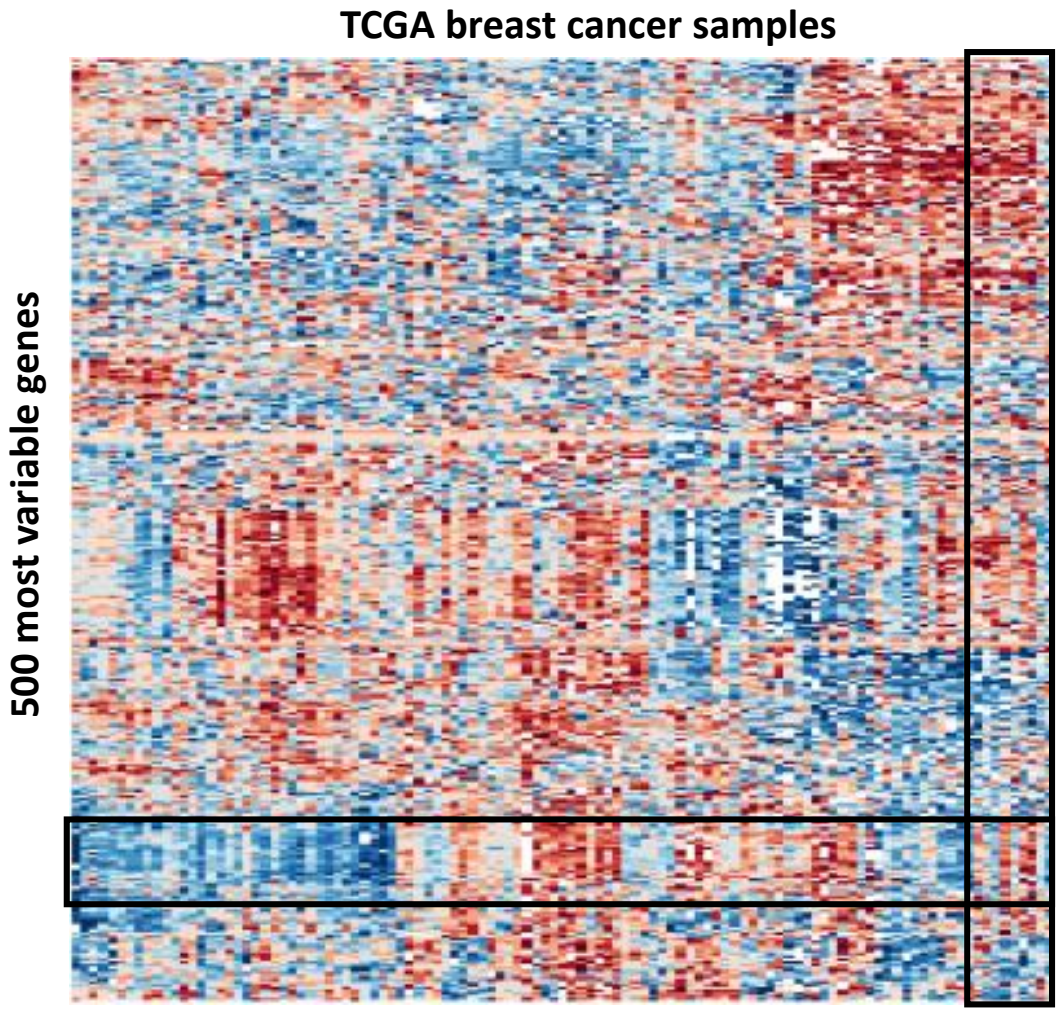


The dendrogram tree shows how the close the genes and clusters are to each other.

Heat map representation of gene expression levels across samples

Expression relative to the median across samples

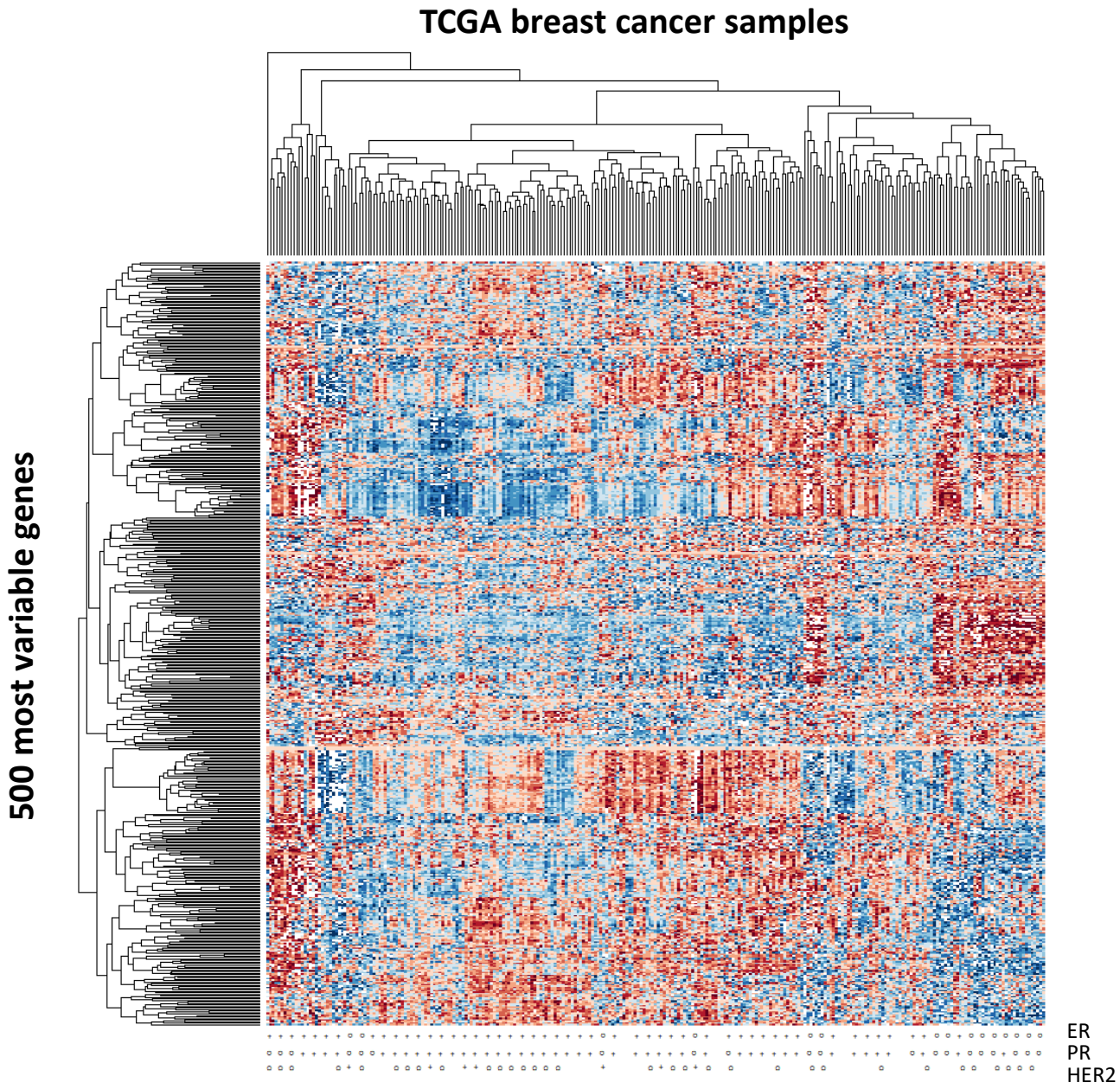
high low



These genes behave similarly across the samples.

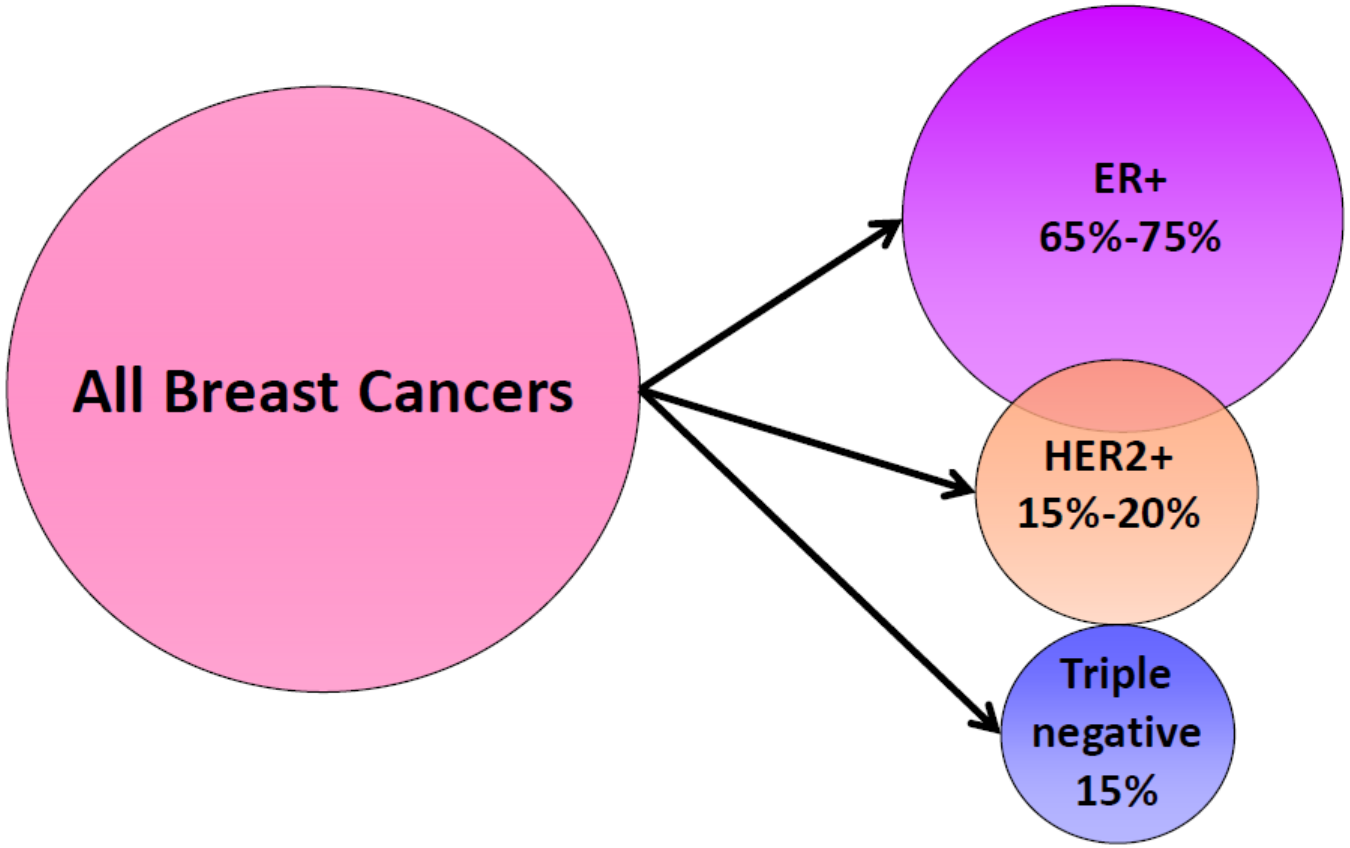
These samples express the same genes.

Clustered heat map and receptor status



ER: Estrogen receptor
PR: Progesterone receptor
HER2: Growth receptor

Invasive Breast Cancer Subsets Defined by IHC

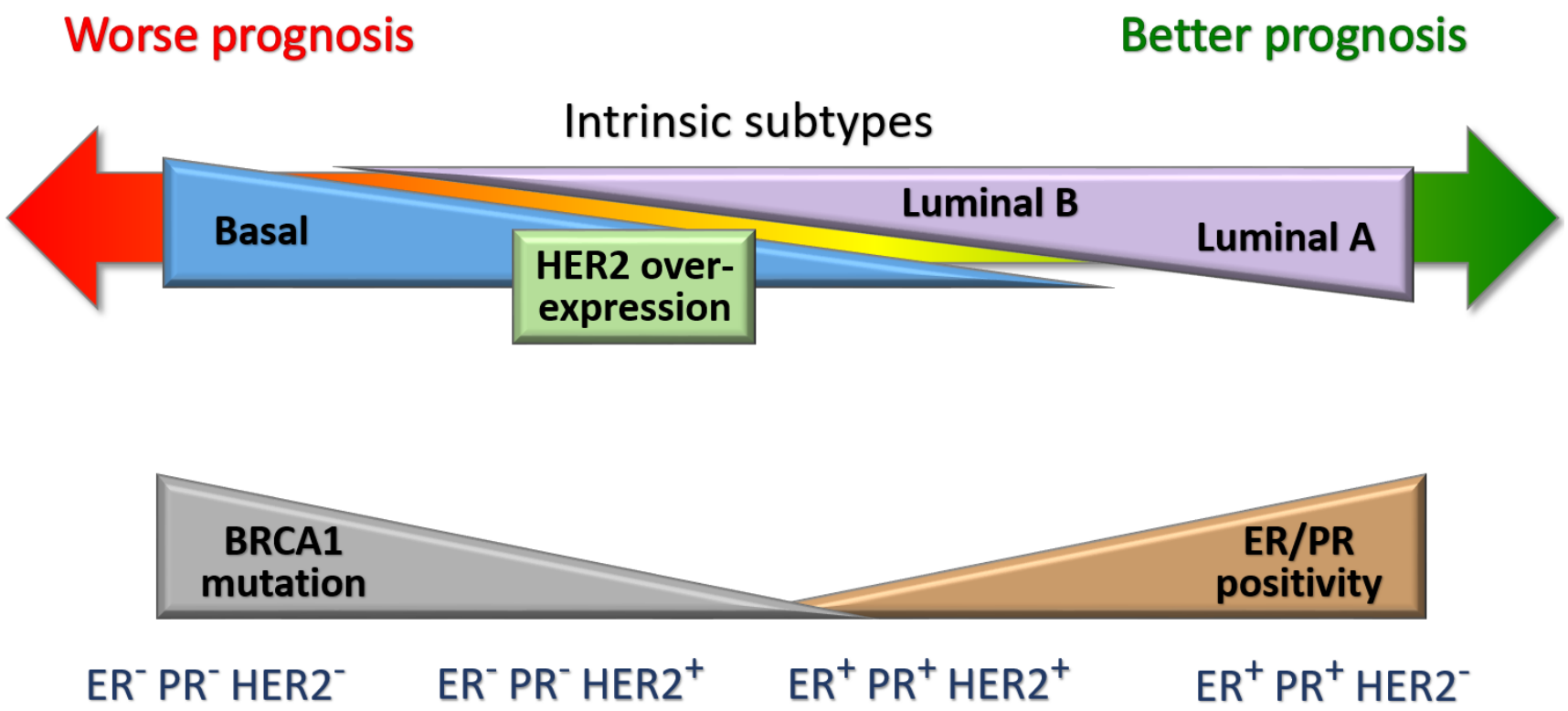


Patient outcomes based on breast cancer intrinsic (molecular) subtypes

Expand information used to stratify patients for prognosis:

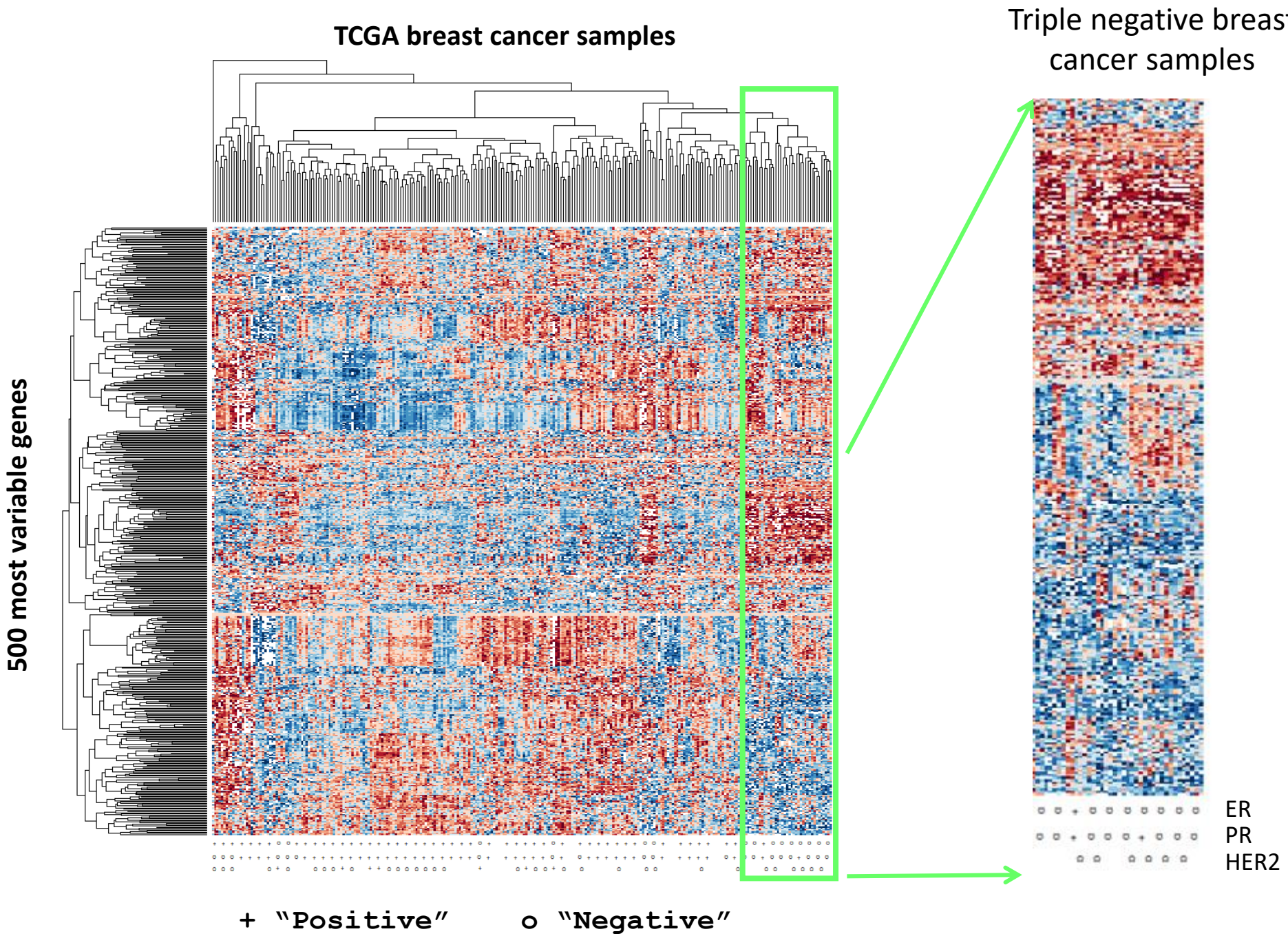
Classical clinical parameters age, node status, tumor size, histologic grade.

Pathologic markers ER, PR, and HER2.

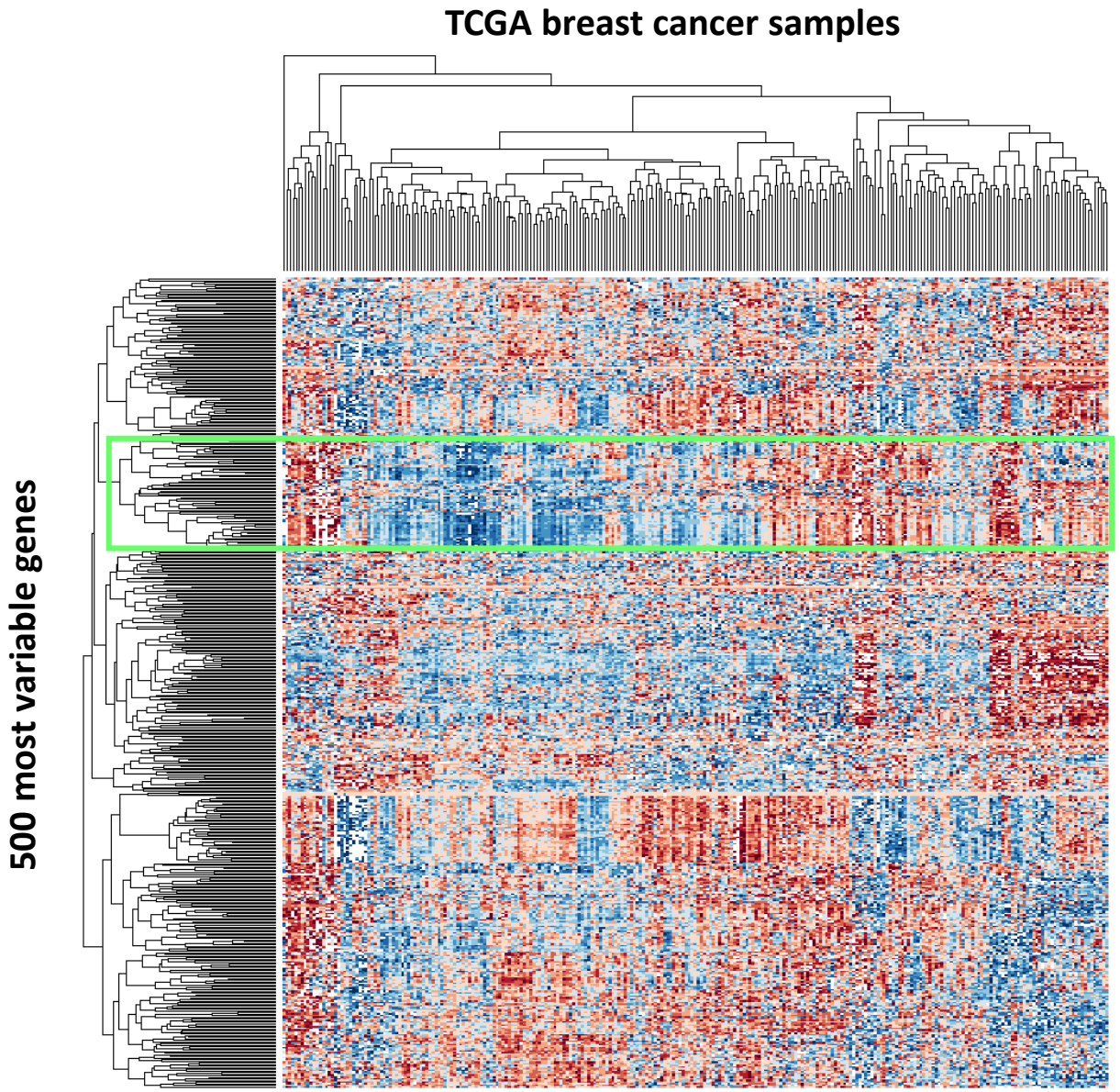


PMID 26693050

Clustered heat map and receptor status



Clustered heat map and gene clusters



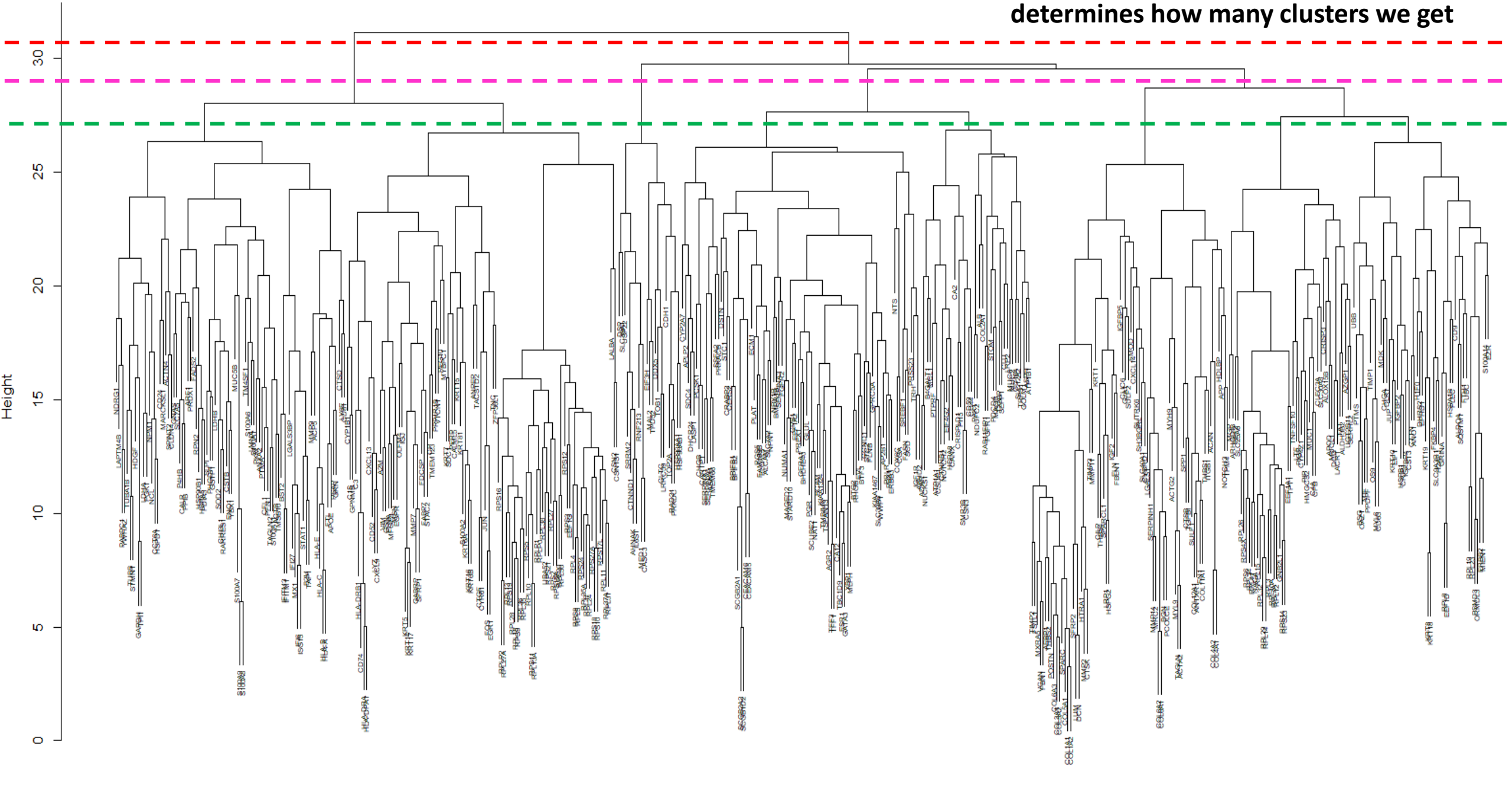
These genes behave similarly across the patient samples.

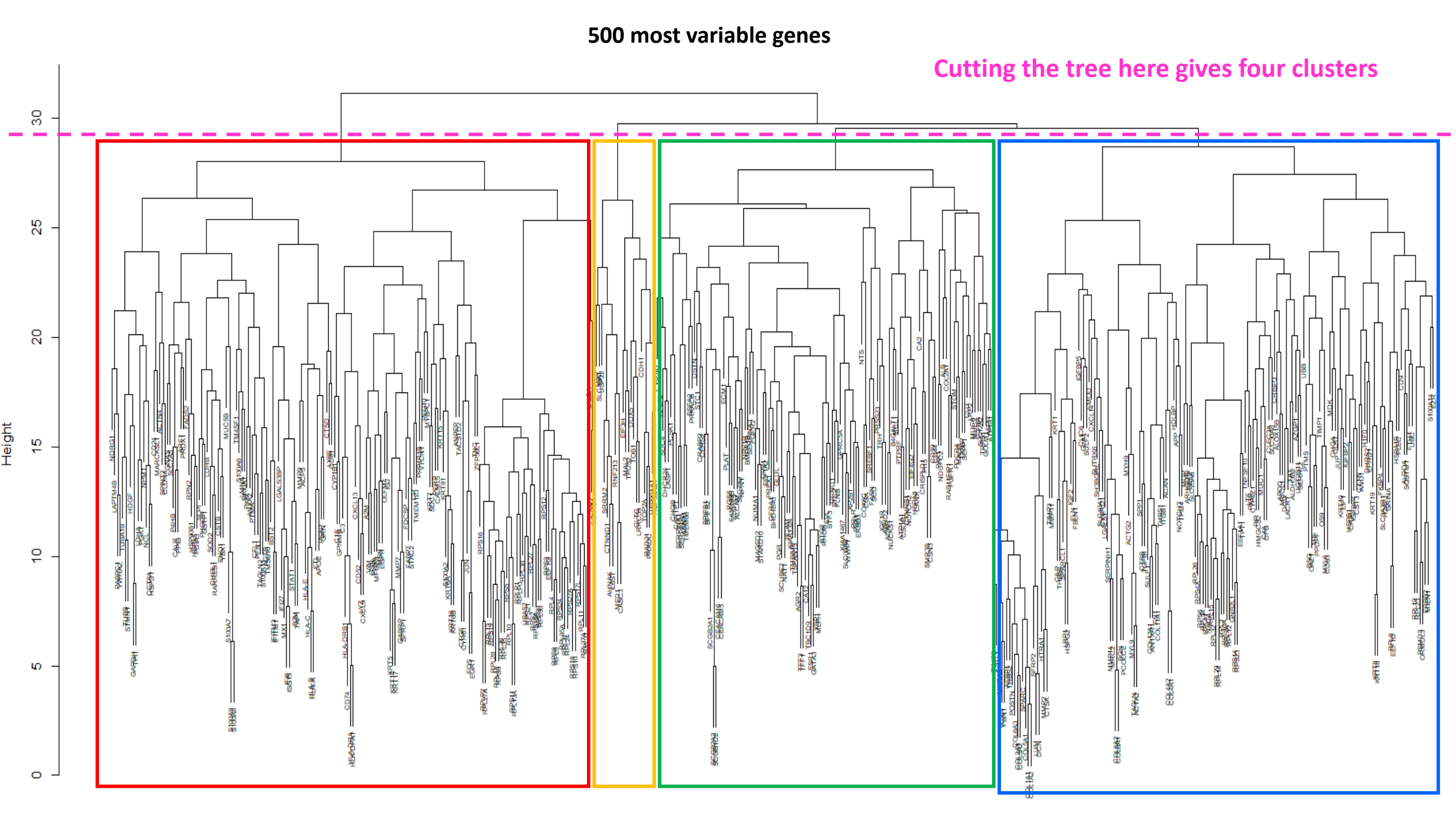
Do they perform similar functions in breast cancer cells??

500 most variable genes

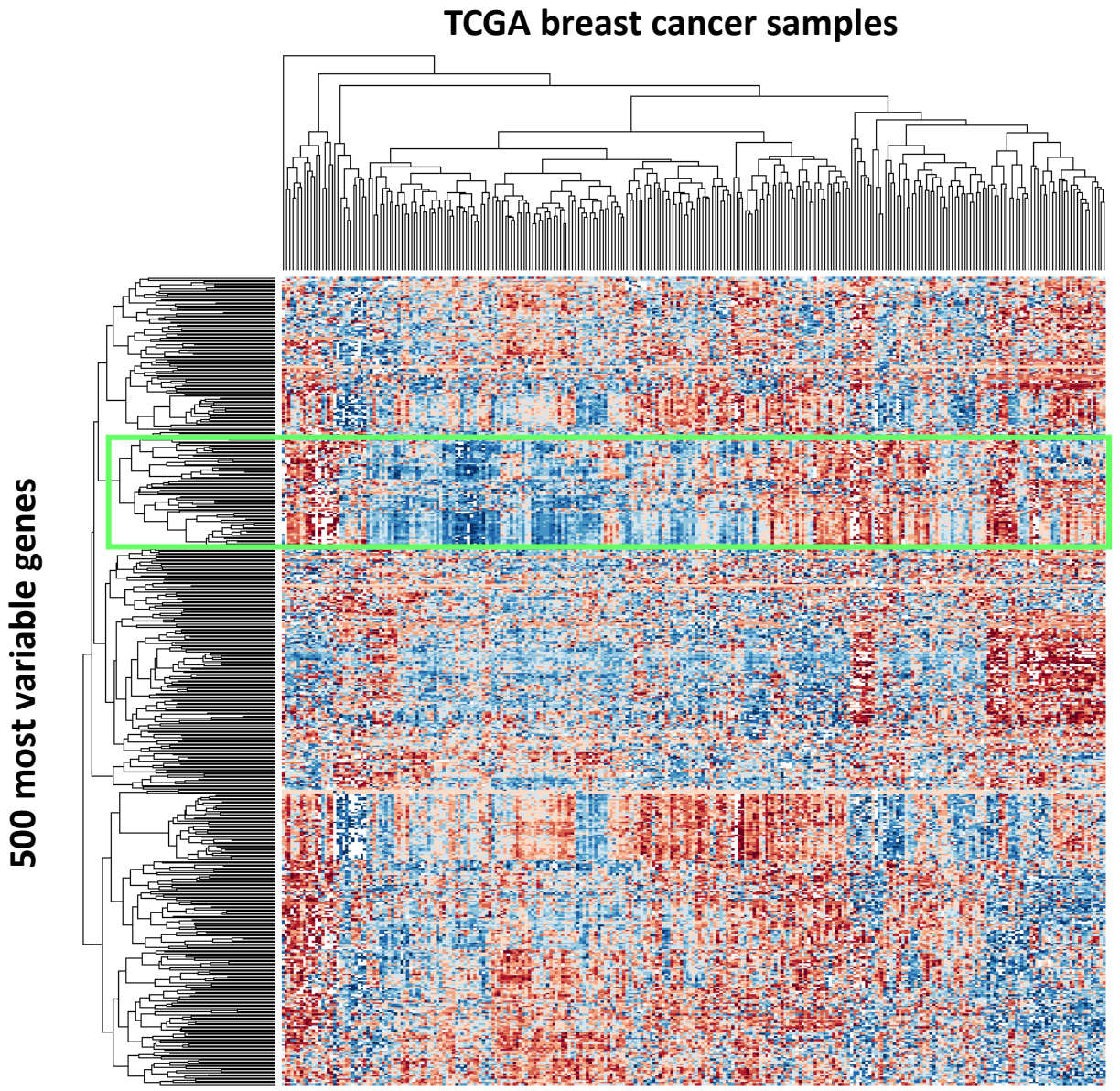
500 most variable genes

Where we “cut” the braches of the tree determines how many clusters we get




500 most variable genes
Cutting the tree here gives four clusters
Height
0
5
10
15
20
25
30

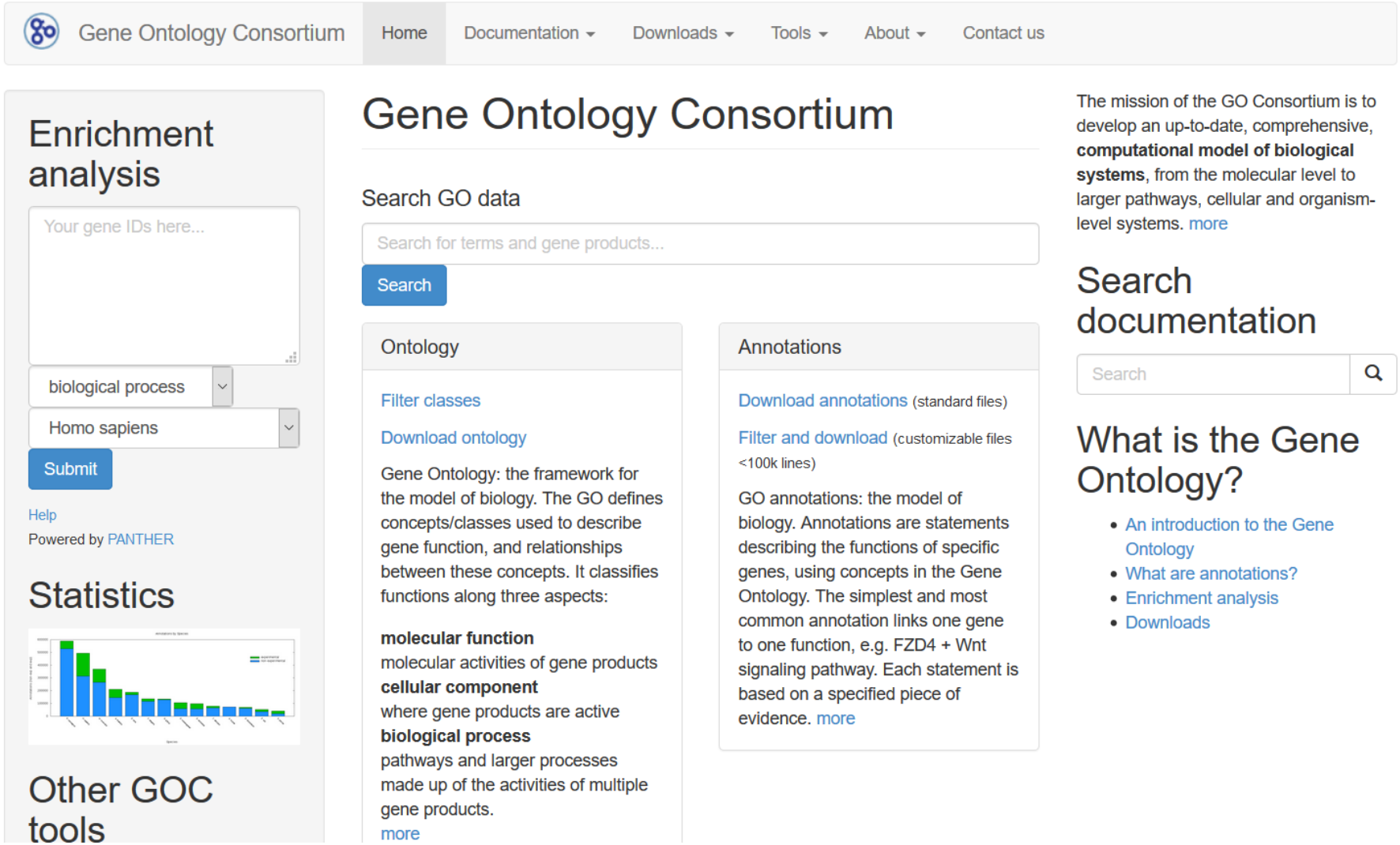
Clustered heat map and gene clusters



These genes behave similarly across the patient samples.

Do genes in the same cluster perform similar biological functions??

http://www.geneontology.org



on·tol·o·gy

/änˈtäləjē/

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"

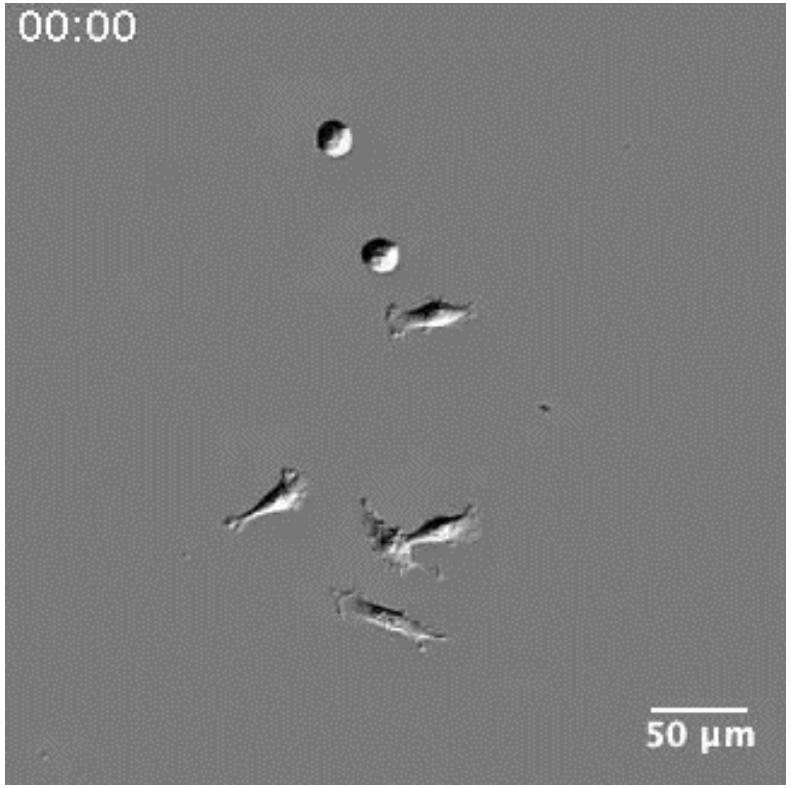
THE GENE ONTOLOGY RESOURCE

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.

https://www.youtube.com/watch?v=bdWRZd19swg

MDA-MB-231 cell migration

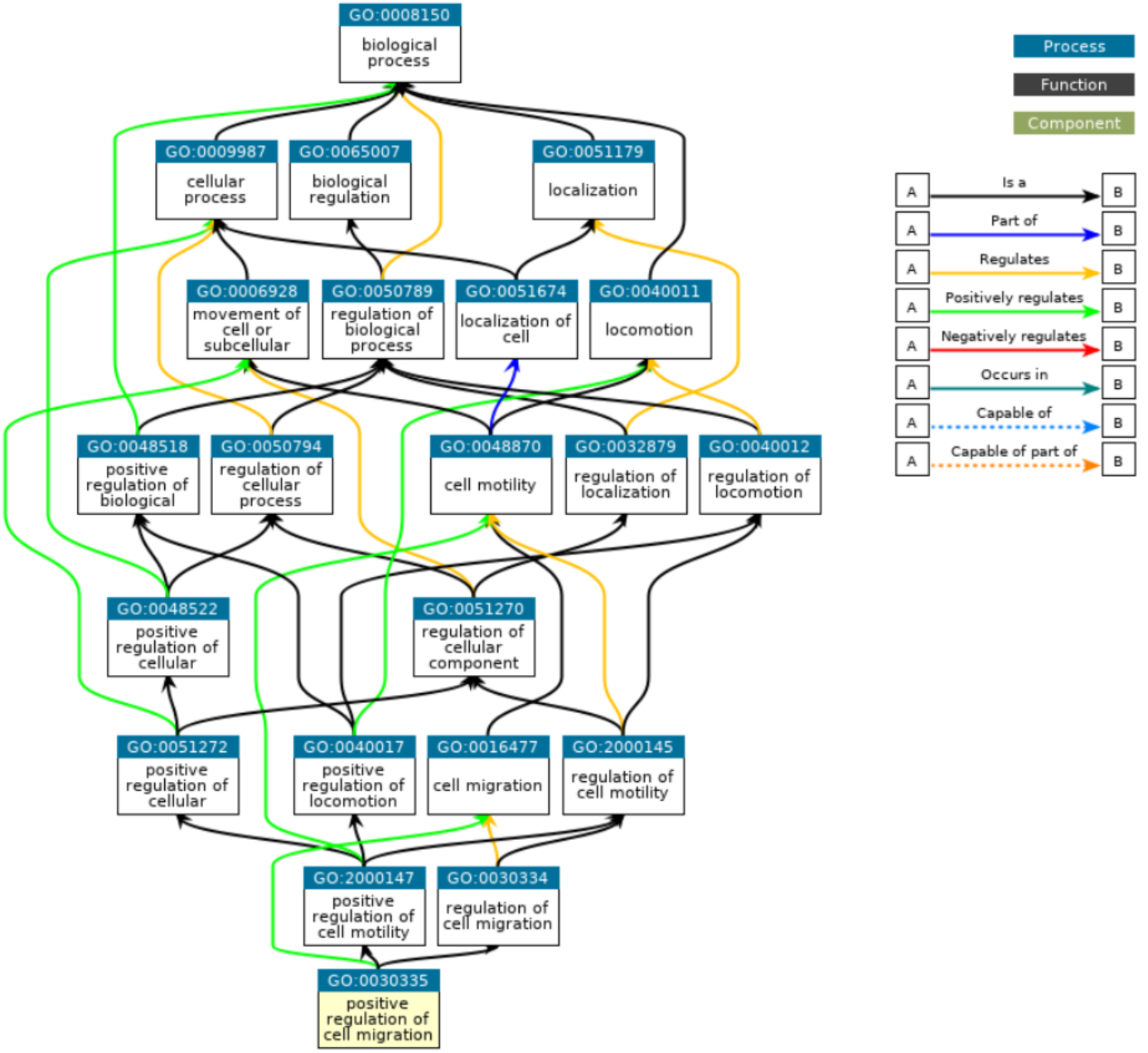


Terms for biological processes such as

positive regulation of cell migration

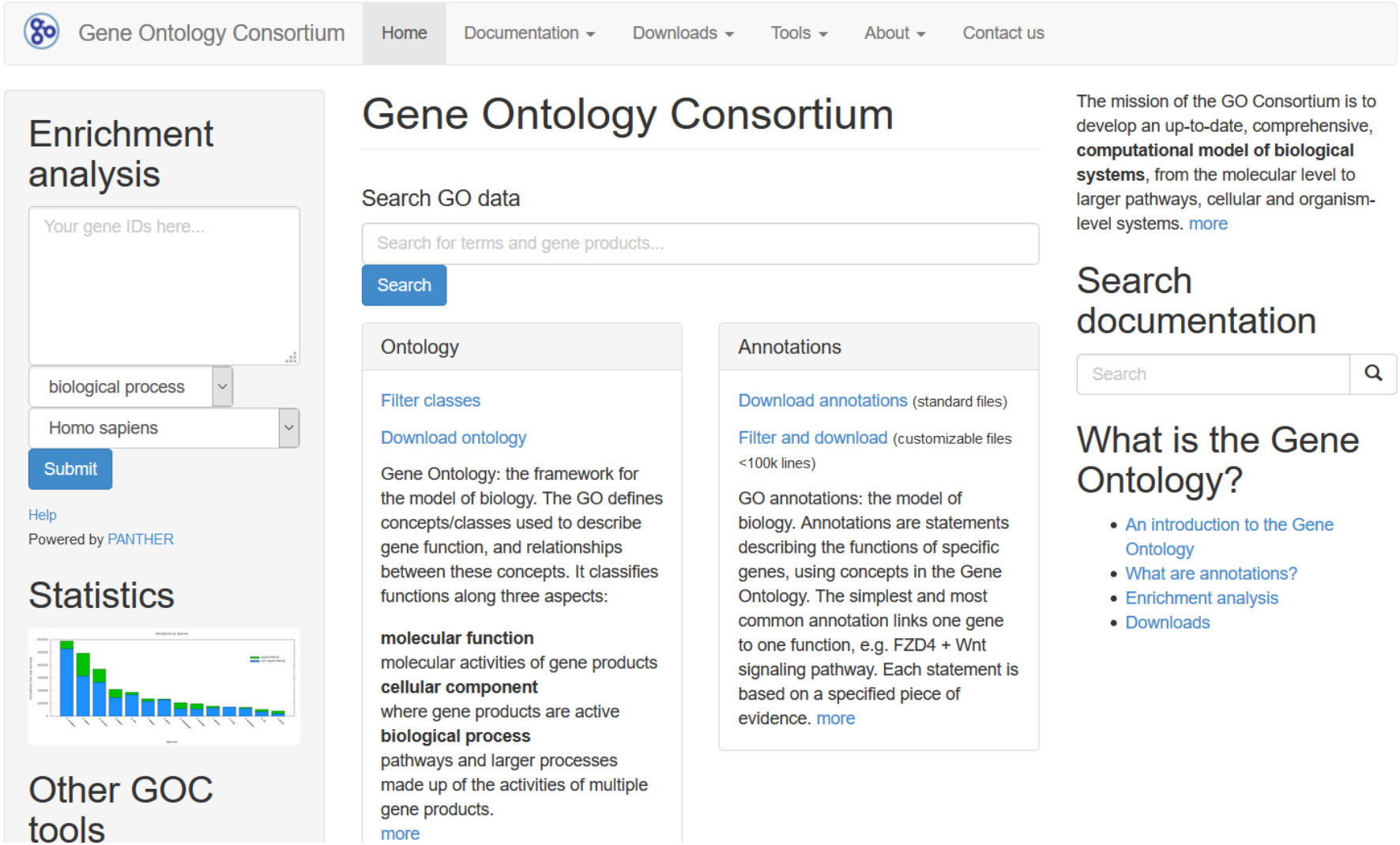
are carefully organized into an ontology

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

http://www.geneontology.org