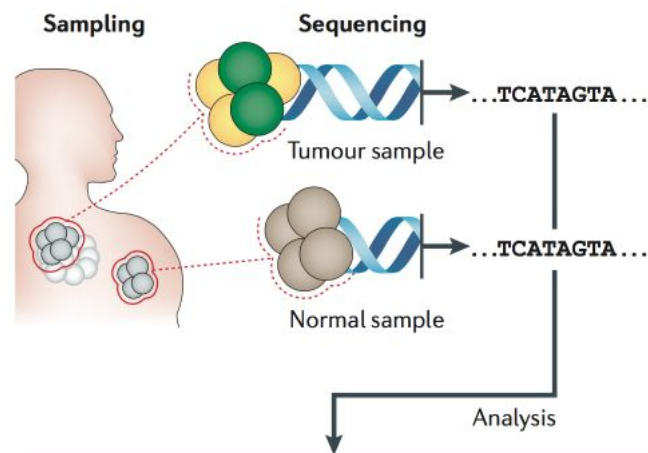


Lecture 27: Cancer genomics

Overview



Variant detection

SNVs and indels

Discover SNVs and small indels using WGS, exome sequencing and RNA-seq data

CNAs, SVs and gene fusions

Uncover large-scale CNAs, SVs and gene fusions using WGS and RNA-seq data

Example tools

VarScan	GATK	BreakDancer
SomaticSniper		Genome STRiP
Pindel	Strelka	ChimeraScan
MuTect	Bassovac	CREST
JointSNVMix		Hydra
		GASV-pro
		TIGRA
		deFuse

Variant annotation and interpretation

Level I

Annotation and analysis of individual genetic alterations

Example tools

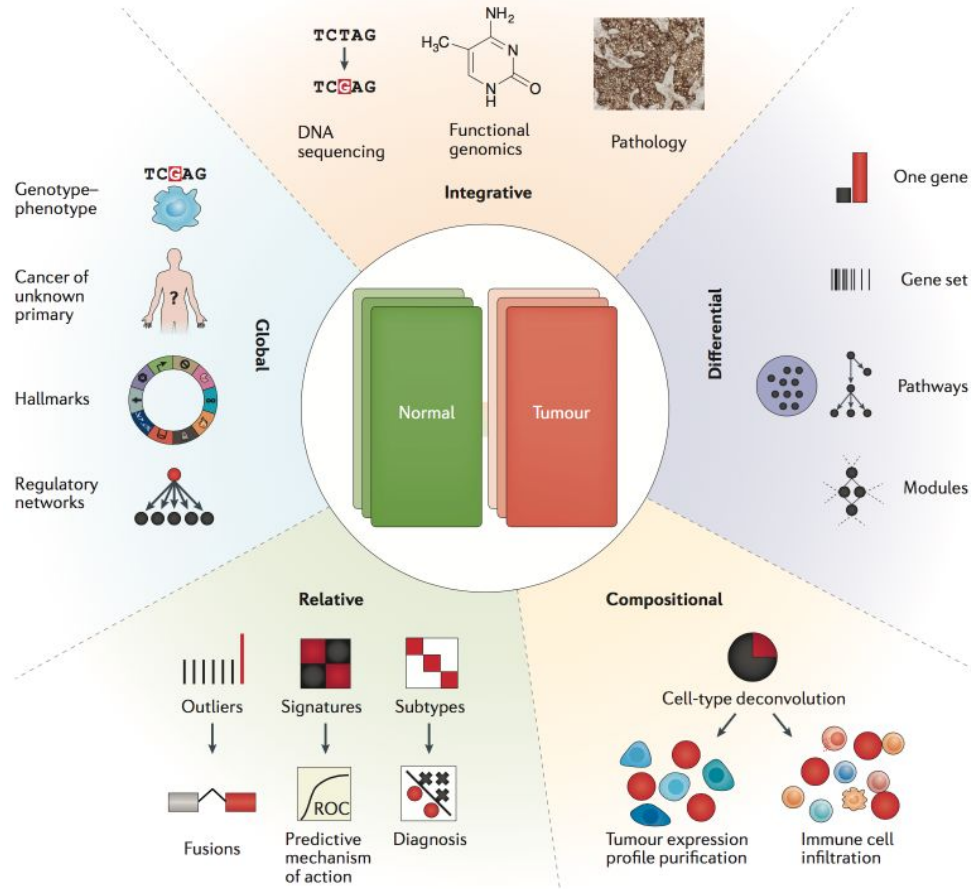
SNPeff	VEP
ANNOVAR	SIFT
PolyPhen2	CHASM
MutationAssessor	
ActiveDriver	

Level II

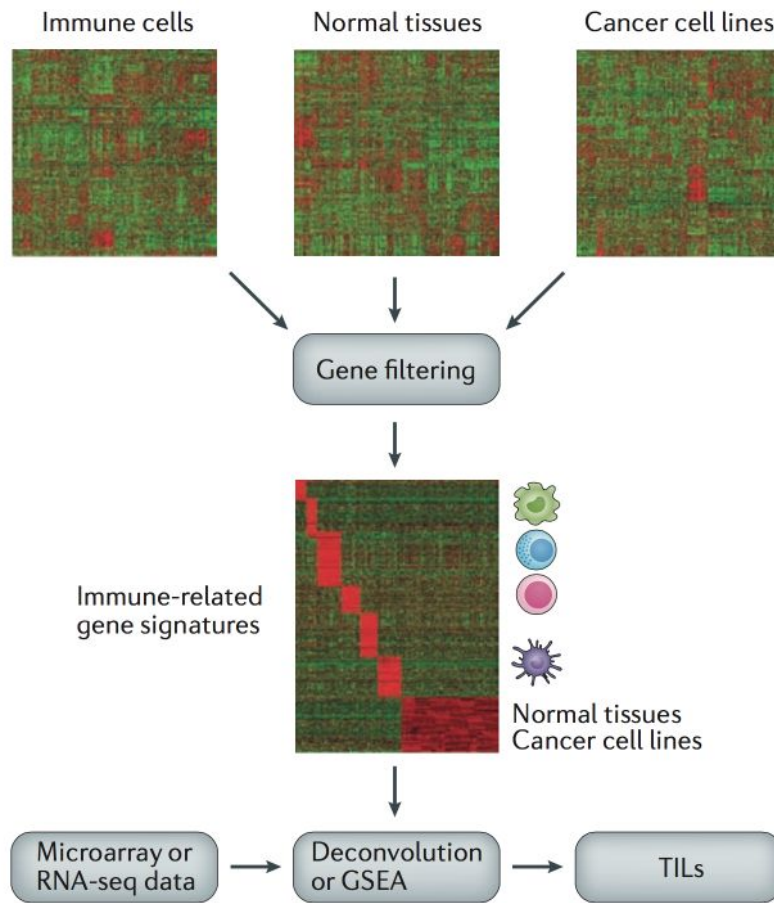
Population-based analysis of genetic alterations and identification of significant alterations, genes, pathways and networks

MuSiC	MutSig
Oncodrive	TieDIE
HotNet	PathScan
Dendrix	MEMo
PARADIGM	

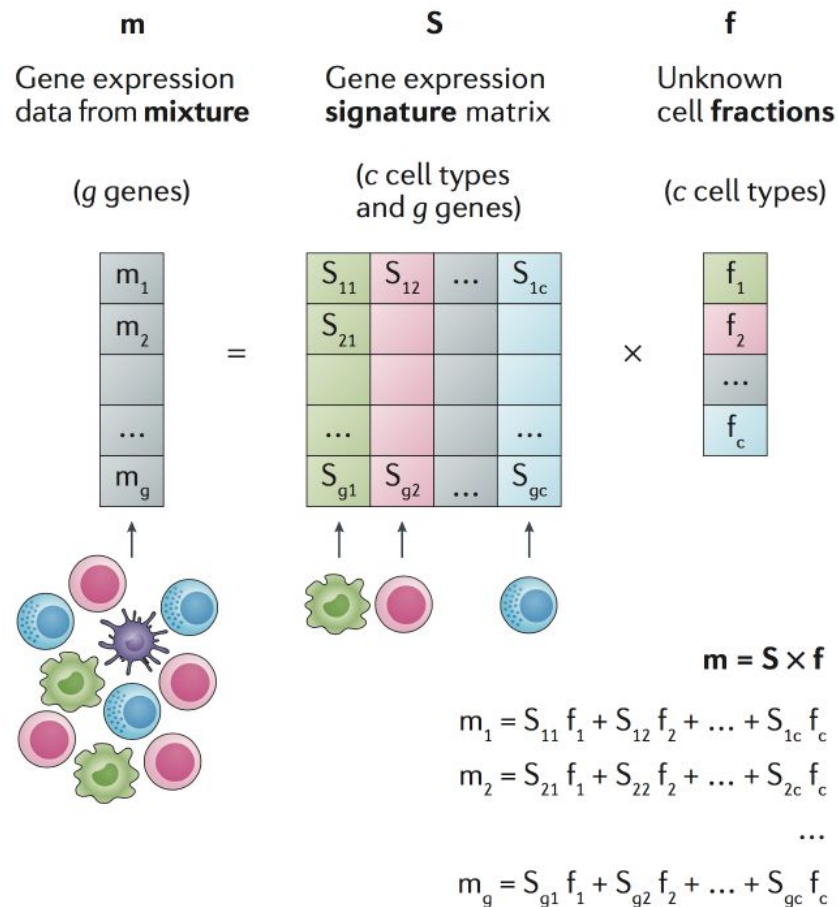
Uses of gene-expression assays in cancer genomics



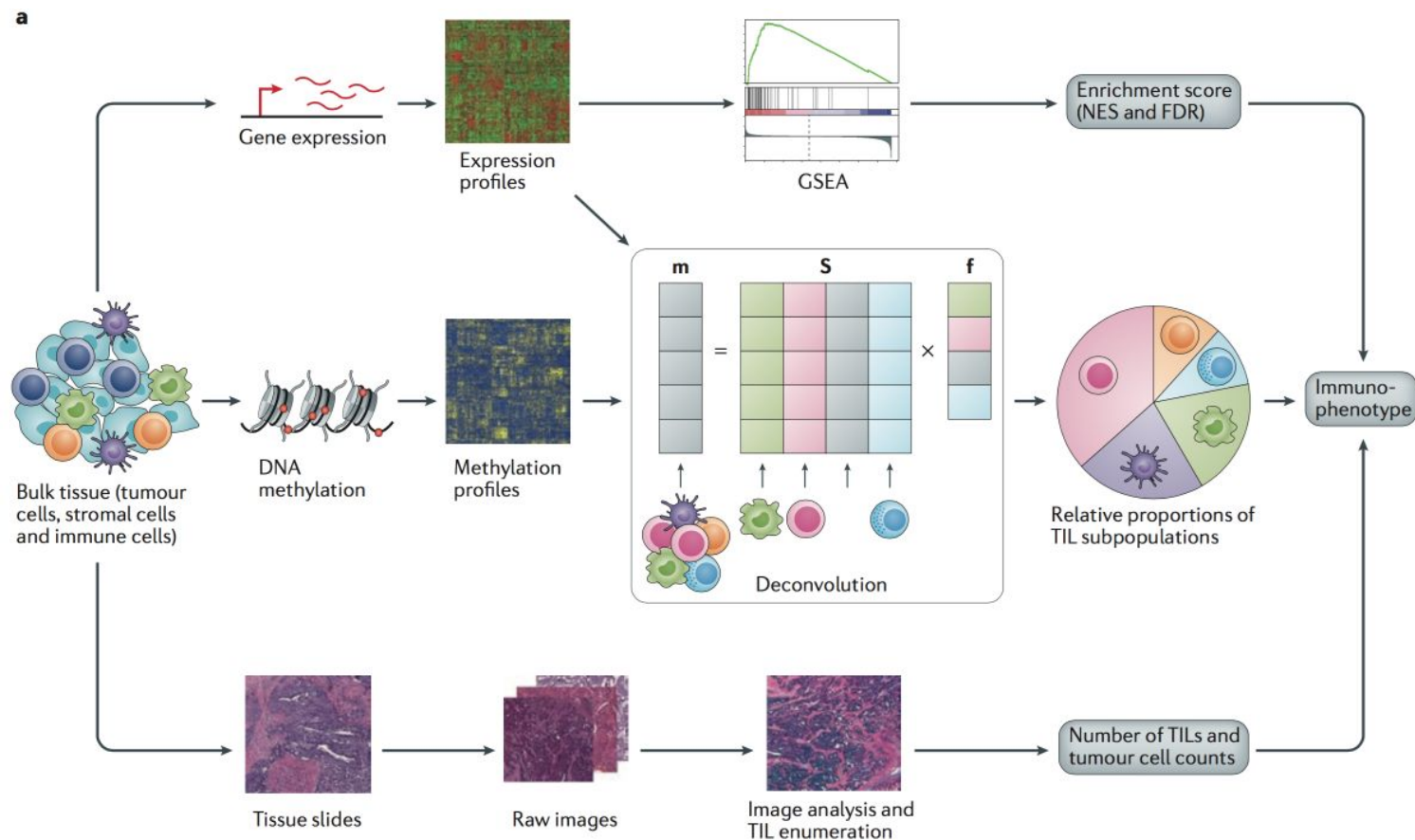
Deriving cell-type-specific gene signatures



Cell-type deconvolution from bulk tissue data

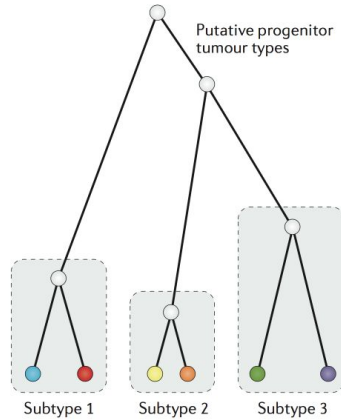
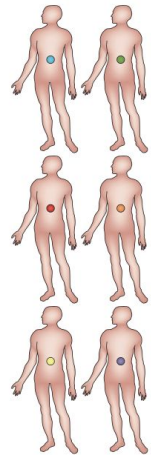


Combining these analyses

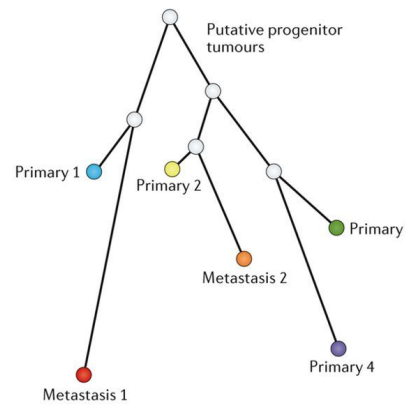
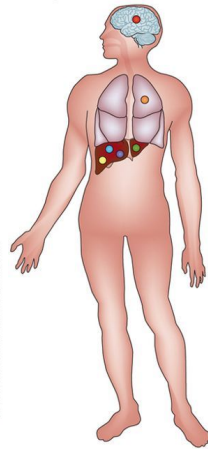


Cancer evolution

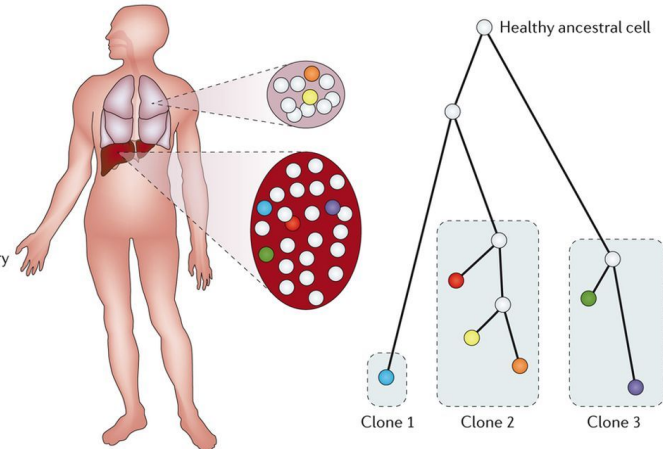
Cross-sectional (oncogenetic)



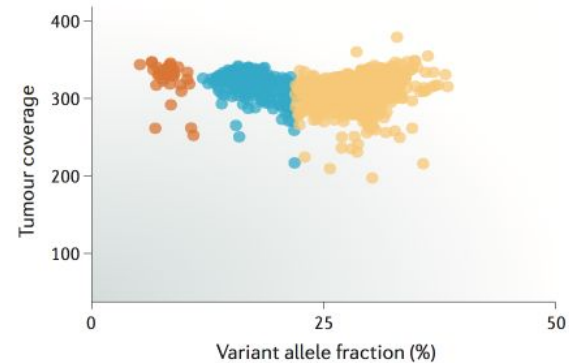
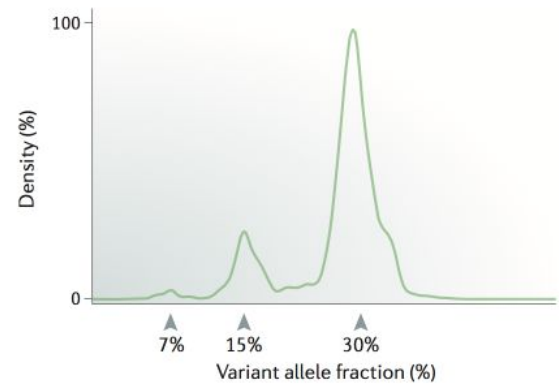
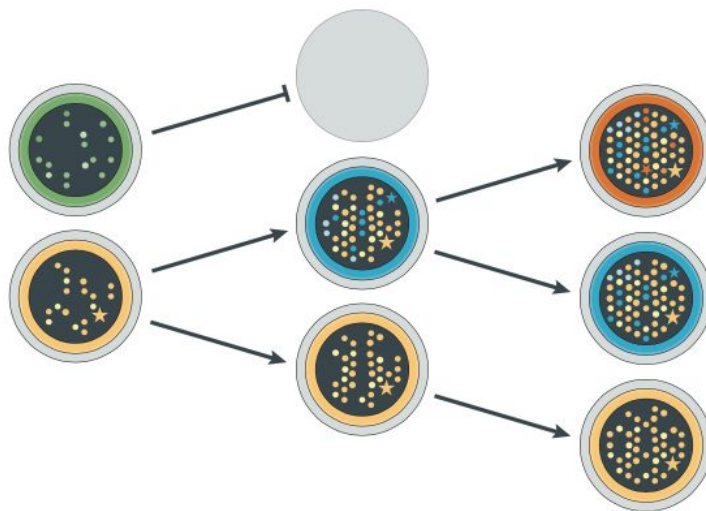
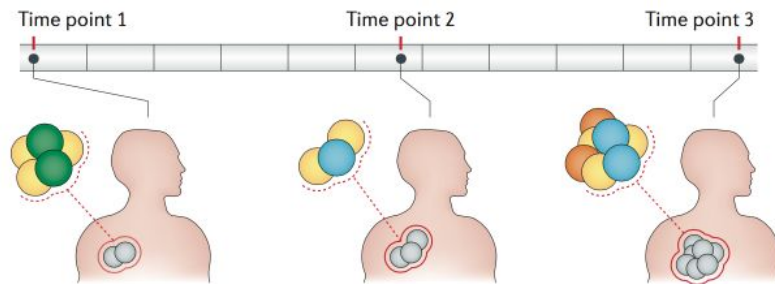
b Regional bulk



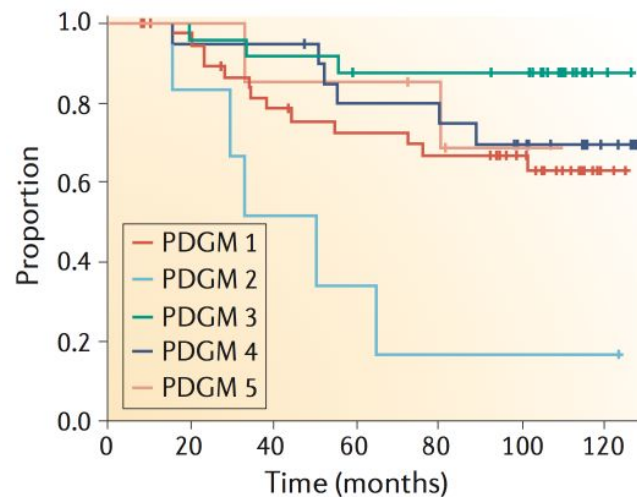
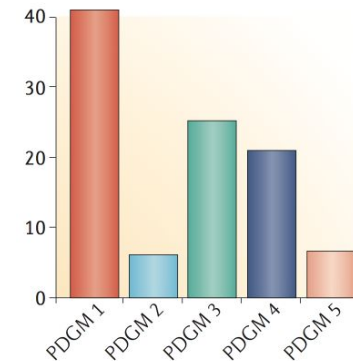
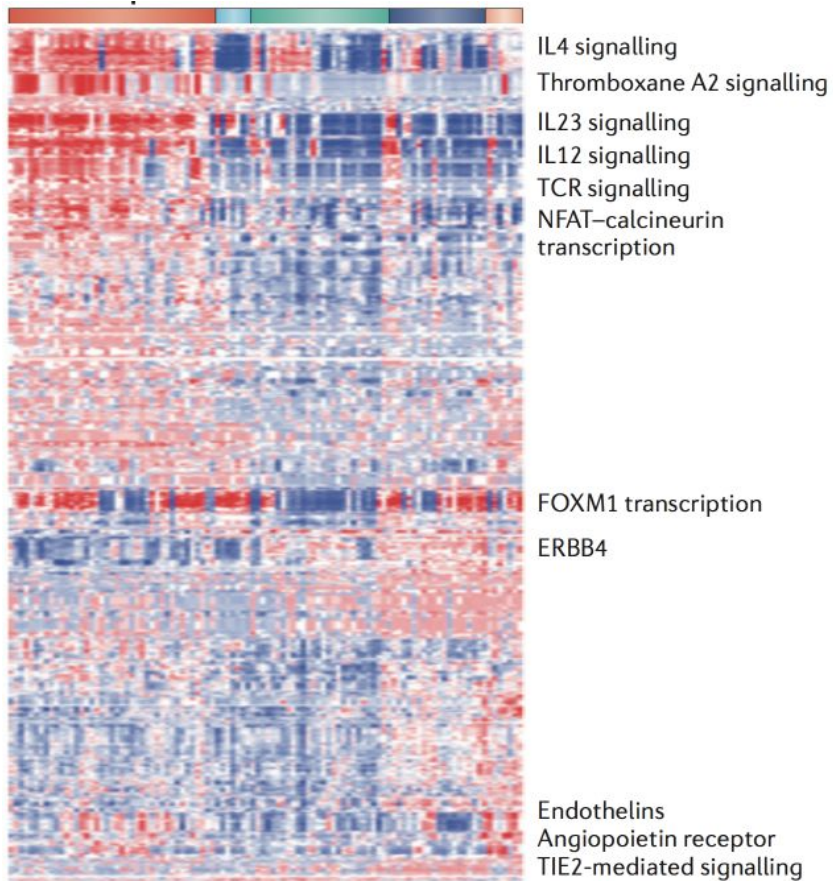
c Single cell



Cancer evolution

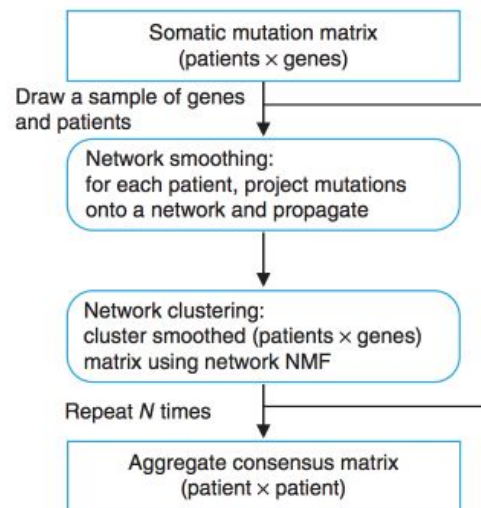


Tumor subtyping

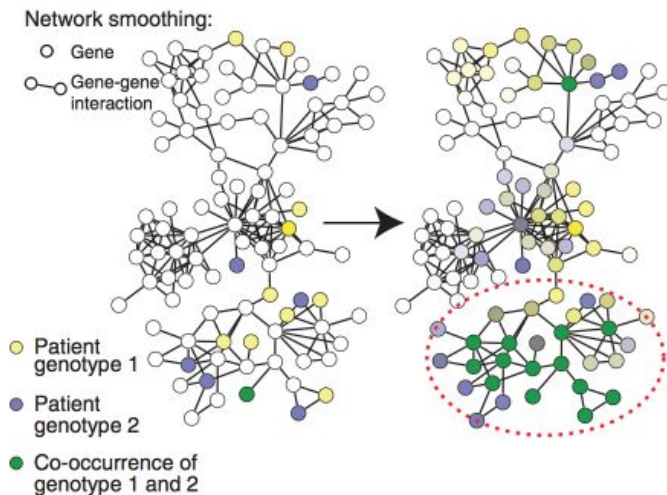


Tumor subtyping

a

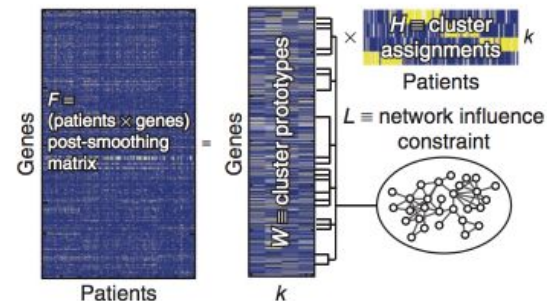


b



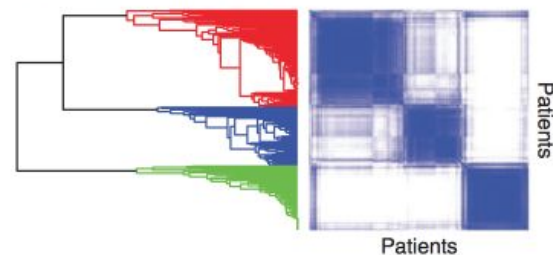
c

$$\text{Network NMF: } \min_{W, H > 0} \|F - WH\| + \gamma \|W^T L\|_F$$

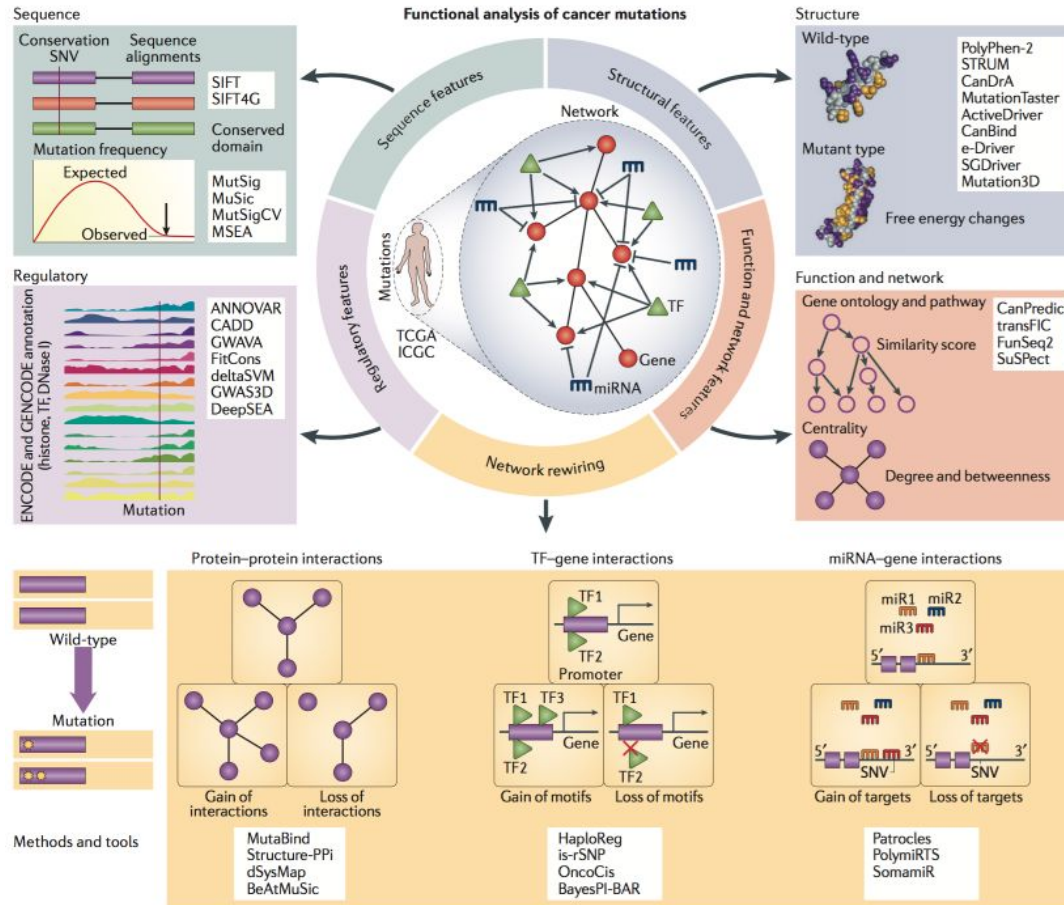


d

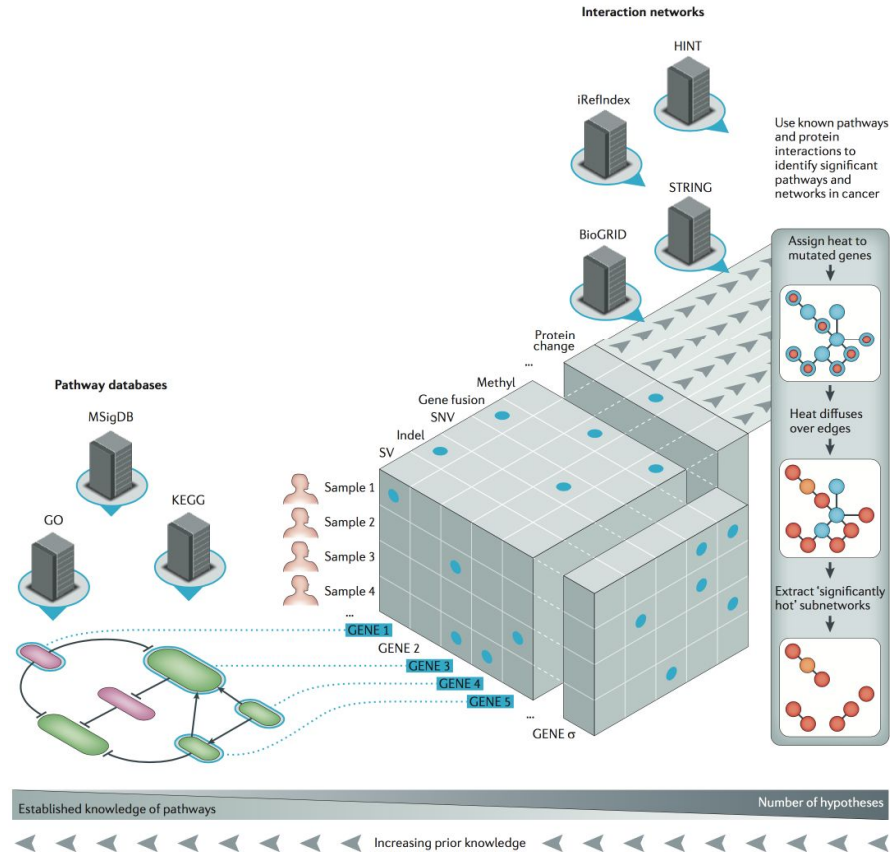
Network-based stratification



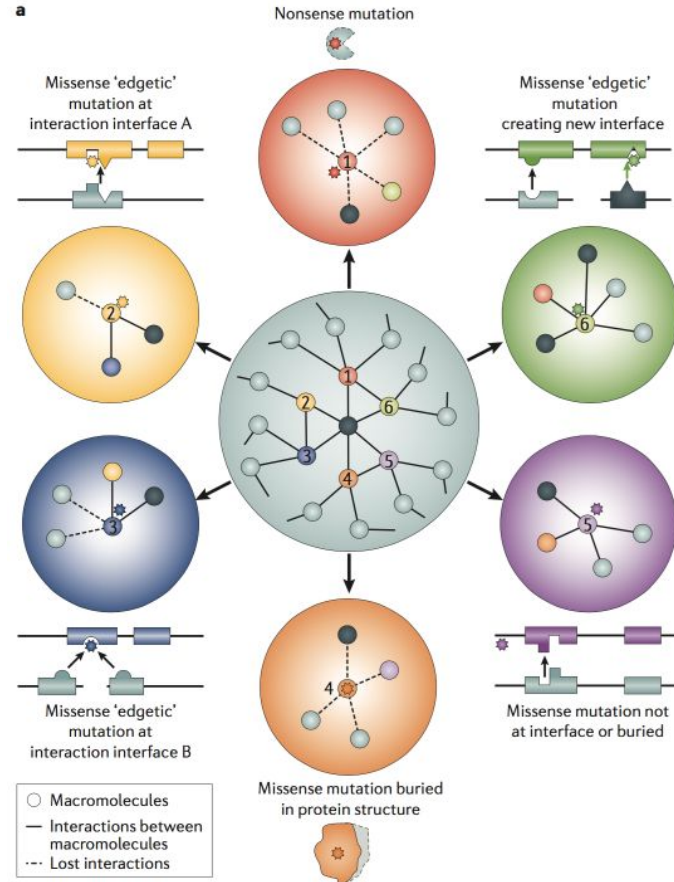
Functional analysis of cancer mutations



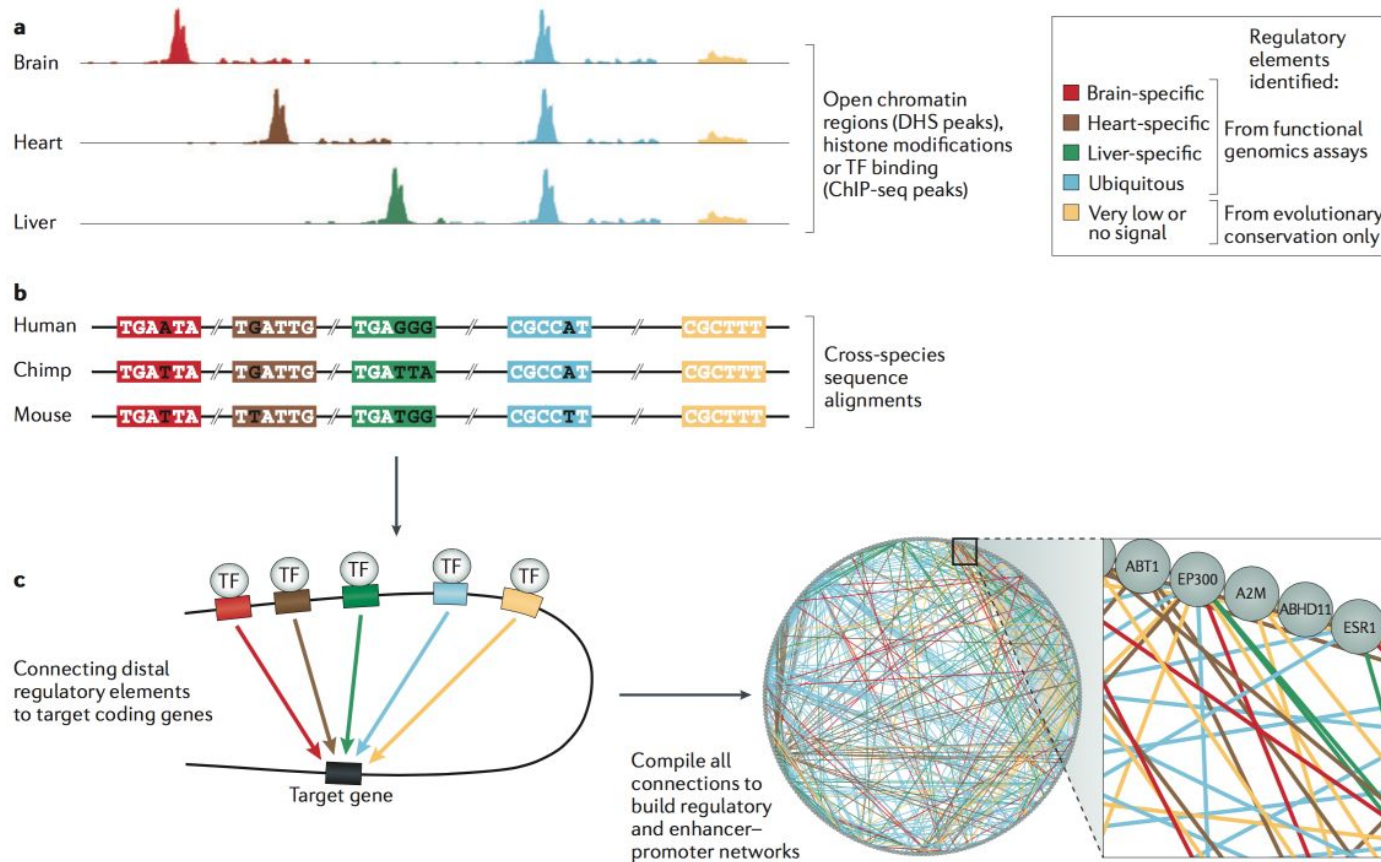
Genes, pathways, & networks



Genes, pathways, & networks

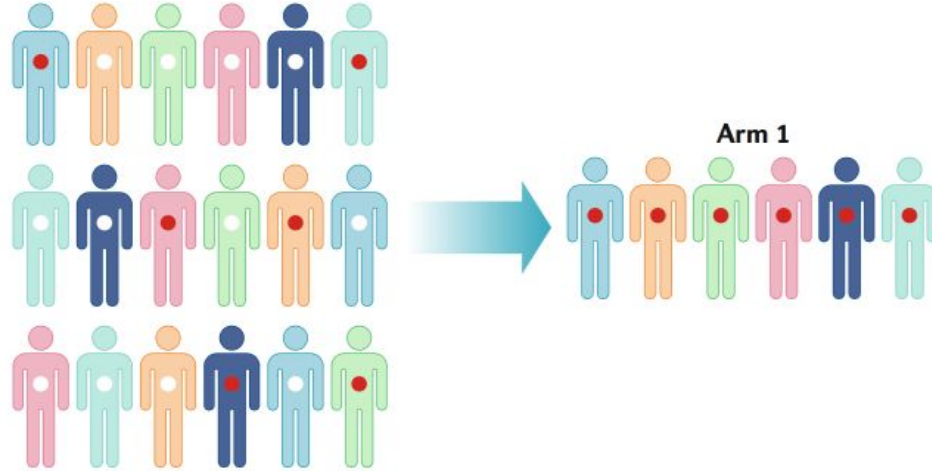


Non-coding variants



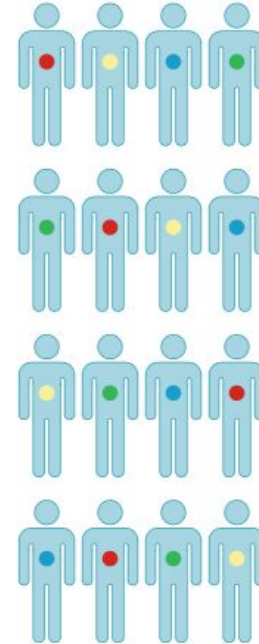
Clinical trial designs informed by genomics

a
Different tissue of origin, same target gene driver
(in a subset of patients)

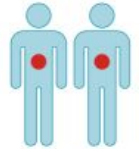


● Targetable alteration
○ No targetable alteration

b
Same tissue of origin, different target gene drivers



Targeted therapy 1



Targeted therapy 2



Targeted therapy 3



Integrative data generation & analysis of breast cancer

