

Molecular Biology

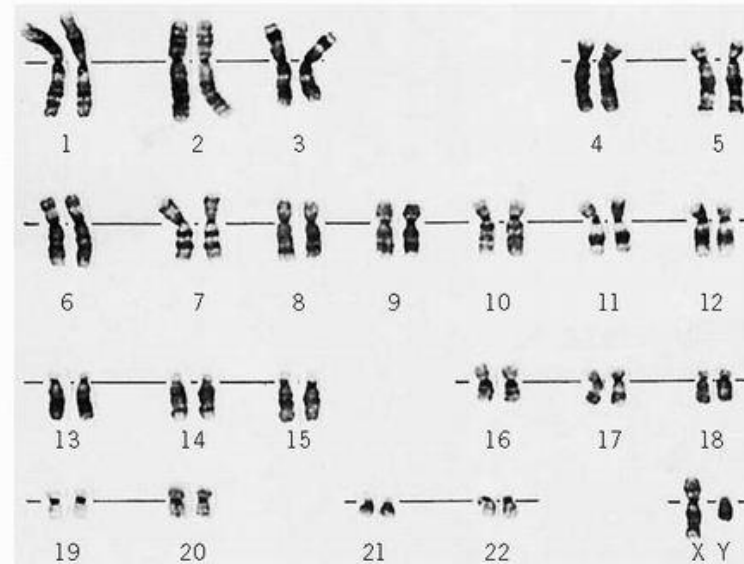
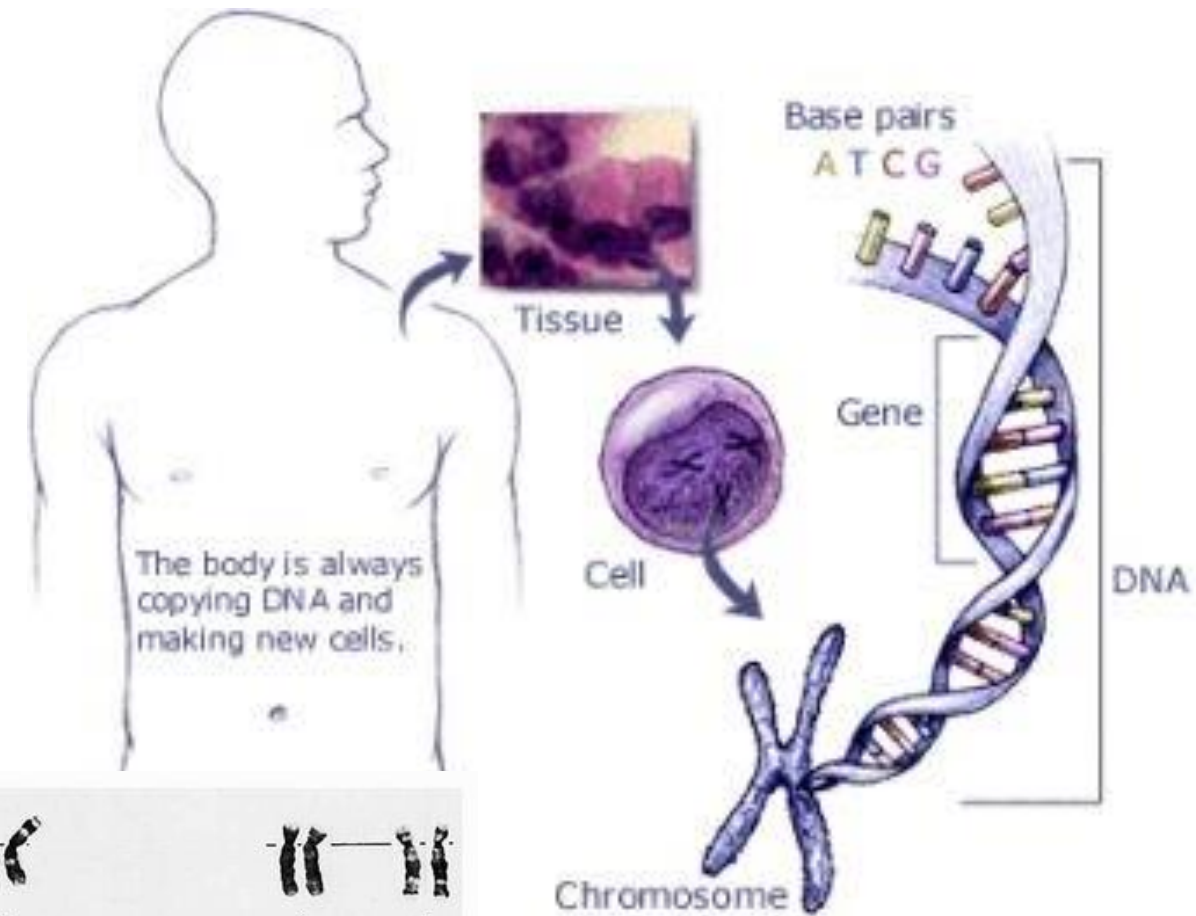
Rogier van Wijck

29-5-2018

Internal Medicine, ErasmusMC

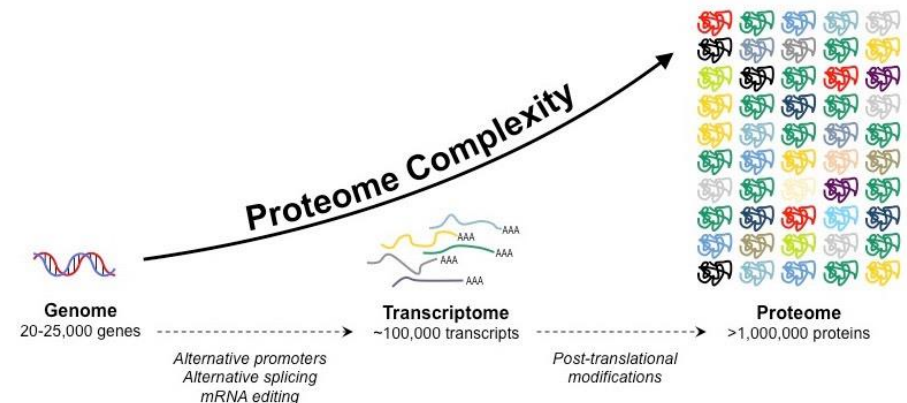
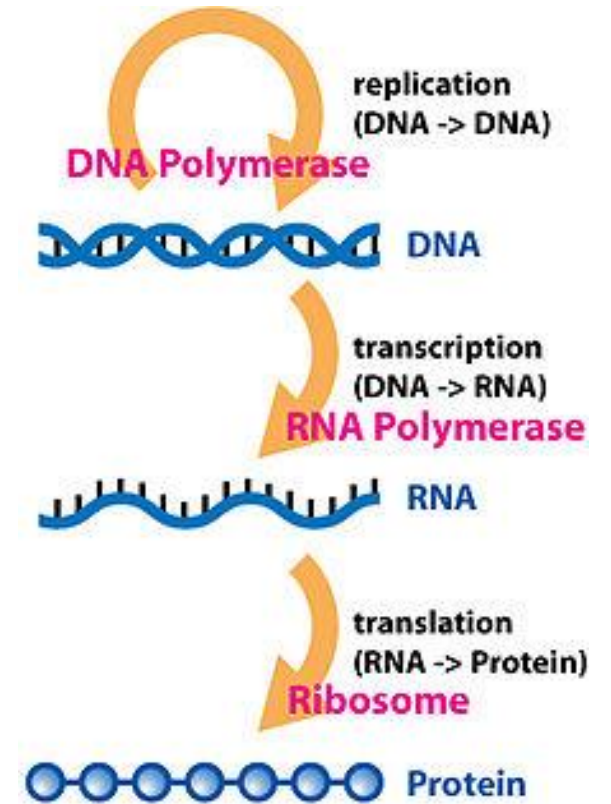
Inside the human body

- Different tissues/cell types
 - All cells have the same DNA
 - 46 chromosomes
 - 23 from your mother
 - 23 from your father
 - Yet different cell types
 - Unique cell environment
 - Gene expression profiles



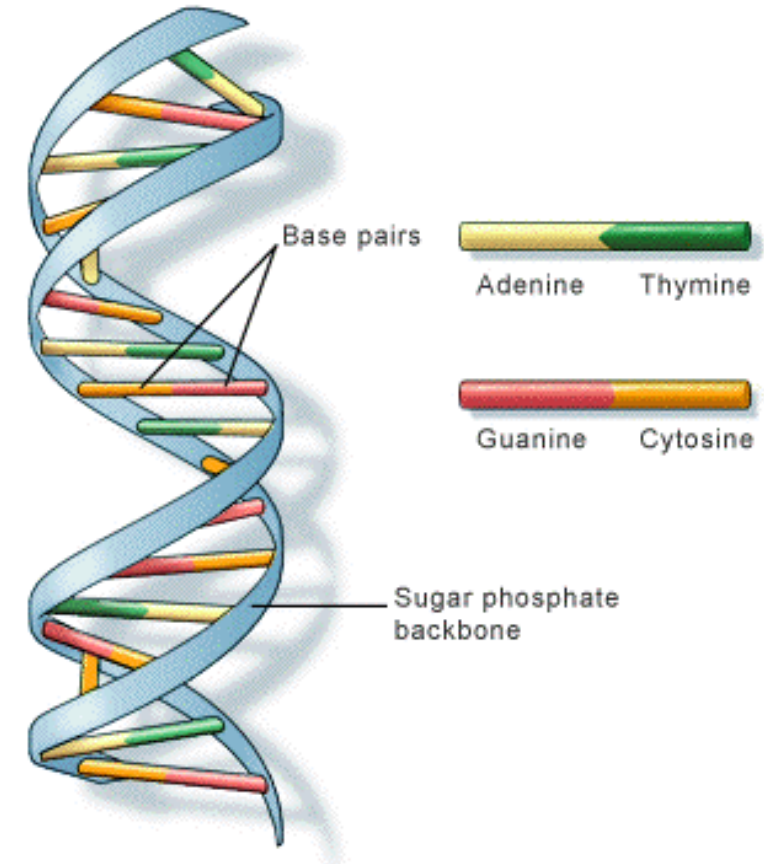
Central Dogma of molecular biology

- DNA (~23,000)
 - Harbours the genetic information
 - Coded blueprint for all processes essential for life
- RNA (~100,000)
 - Derivative of DNA
 - Different forms of RNA with different functions
 - Gene Expression Profiles
- Protein (~1,000,000)
 - Molecules that perform the processes
 - Each protein has a function or multiple functions
 - Protein Expression Profile



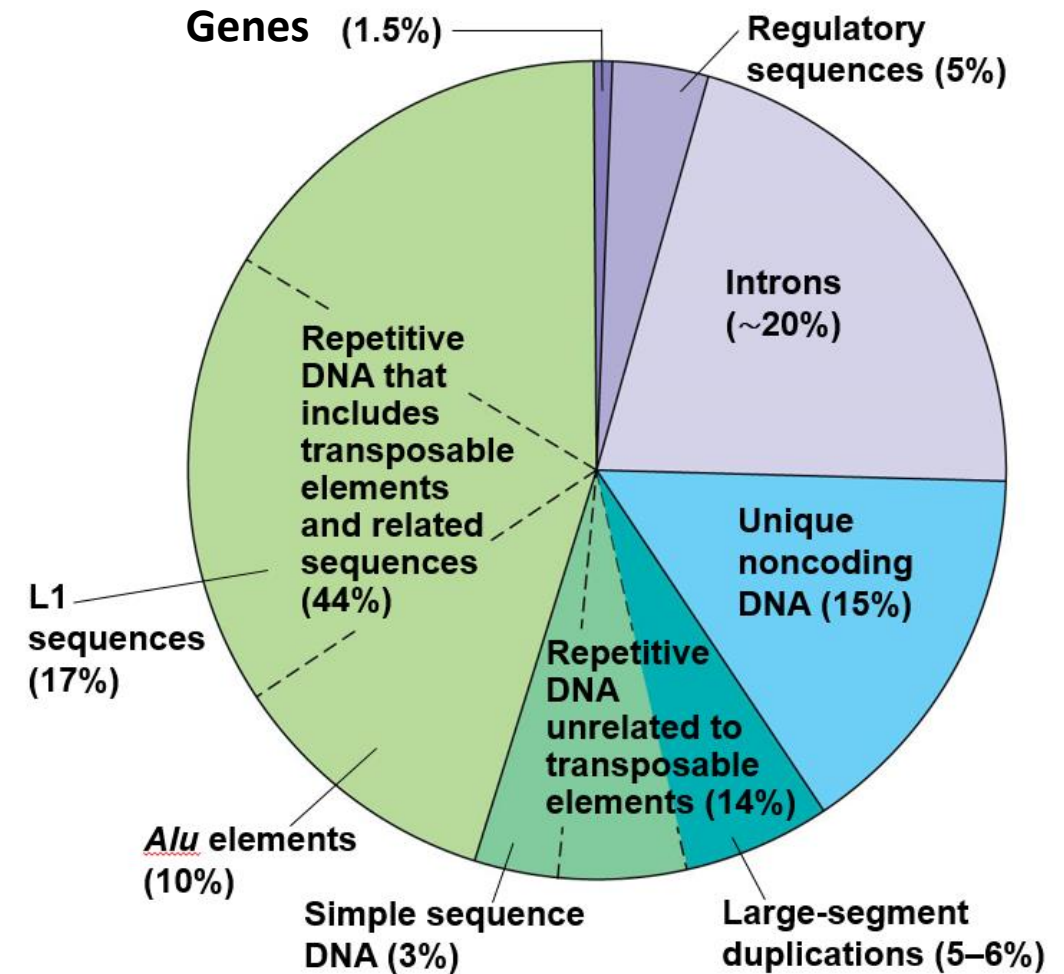
DNA

- Four buildingblocks
 - Adenosine (A), Thymine (T), Guanine (G), Cytosine (C)
- Built of two strands
 - Two strands are complementary
 - If A on the one strand, T on the other
 - If C on the one strand, G on the other
 - Combination of AT/CG is called a base pair
- The sequence of these is the genetic information
 - ~3 billion base pairs
 - Unique for each individual
 - ~150,000 differences between random persons



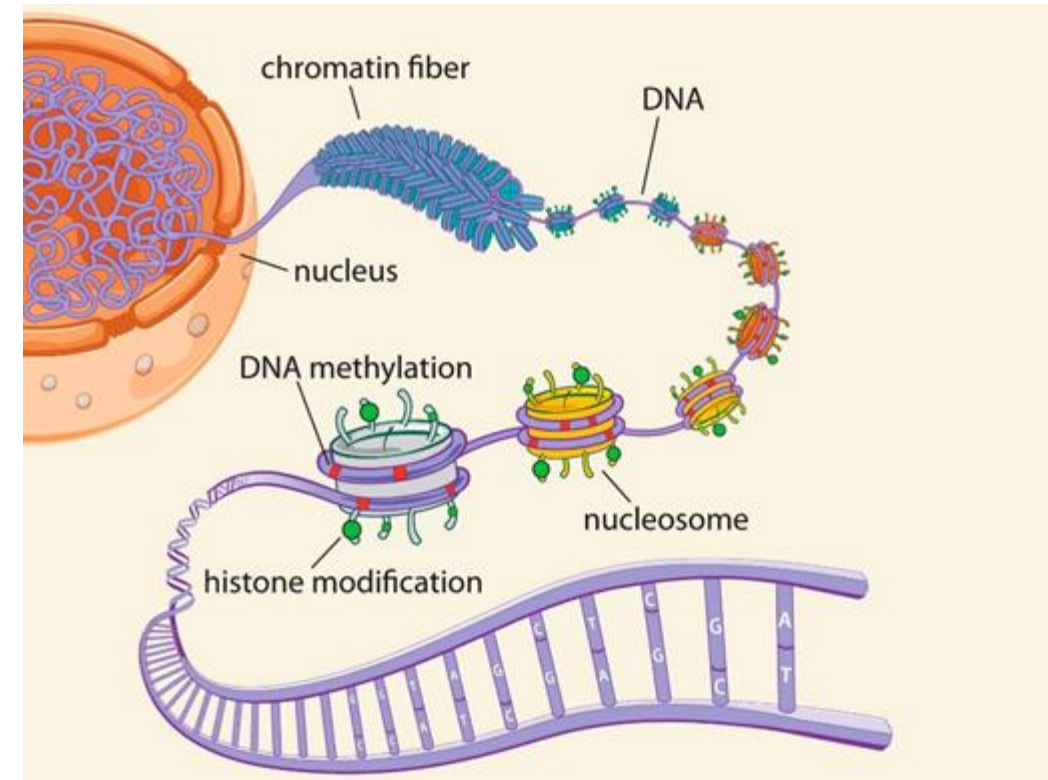
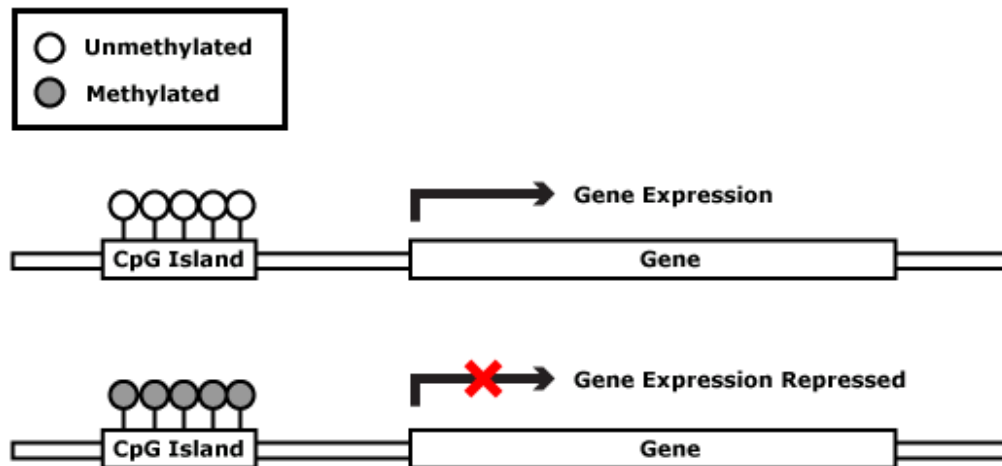
The Genome

- The collection of all basepairs (AT/GC) is called the genome
 - Non-coding (~98%)
 - Regulation
 - Coding part (~1.5%)
 - Genes
 - Chromosomal location
 - DNA that gives rise to all proteins
 - One gene gives rise to one protein



Methylation

- Molecules added on DNA
- Involved in gene expression regulation
 - Methylated: gene switched off
 - Unmethylated: gene switched on



Methylation

- Methylated
 - The pillar is above ground so cars are blocked
 - You can not reach your destination (gene)

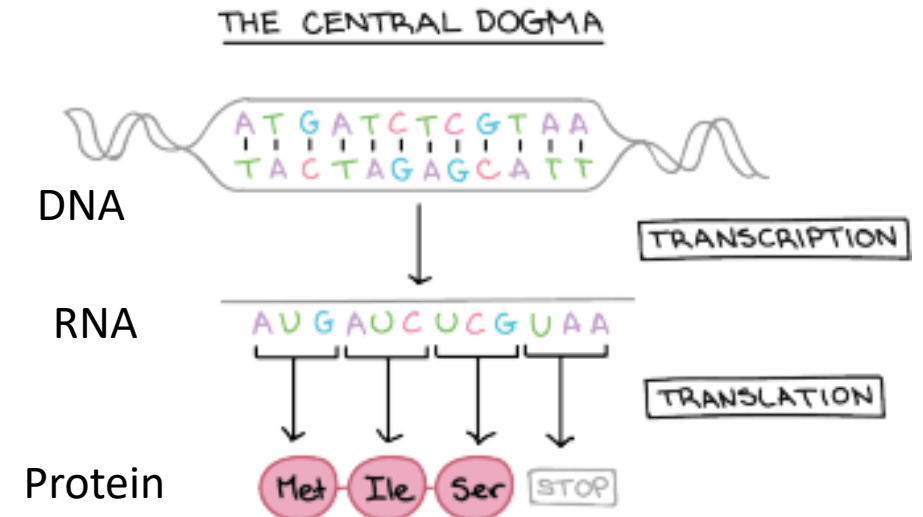


- Unmethylated
 - The pillar is below ground so cars can pass
 - You can reach your destination (gene)



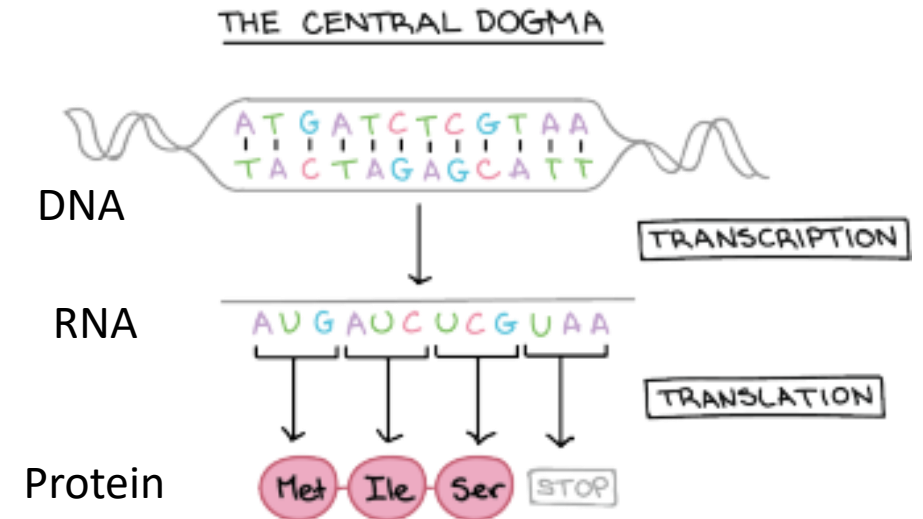
RNA

- Similar to DNA, but only one strand
- Four building blocks
 - Adenosine (A), Uracil (U), Guanine (G), Cytosine (C)
 - U is basically the T
- DNA to RNA (Transcription)
 - DNA is 'copied' to RNA (Only the coding part)
 - A on DNA becomes U on RNA
 - T on DNA becomes A on RNA
 - C on DNA becomes G on RNA
 - G on DNA becomes C on RNA

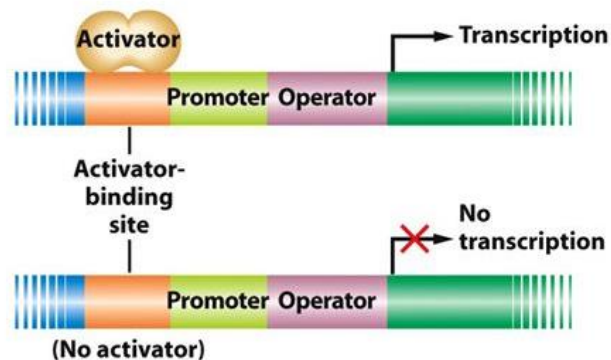


Proteins

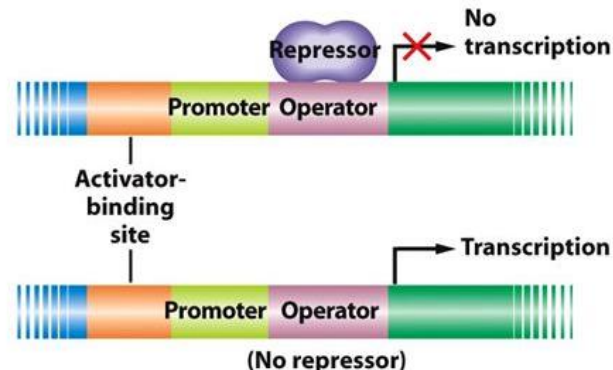
- Decoded from RNA (Translation)
 - Three letters correspond to aminoacid
 - Same aminoacids with different combination
 - Proteins are sequences of aminoacids
- Proteins play the most important role in all processes
 - Regulation on DNA, RNA, Proteins



Positive regulation

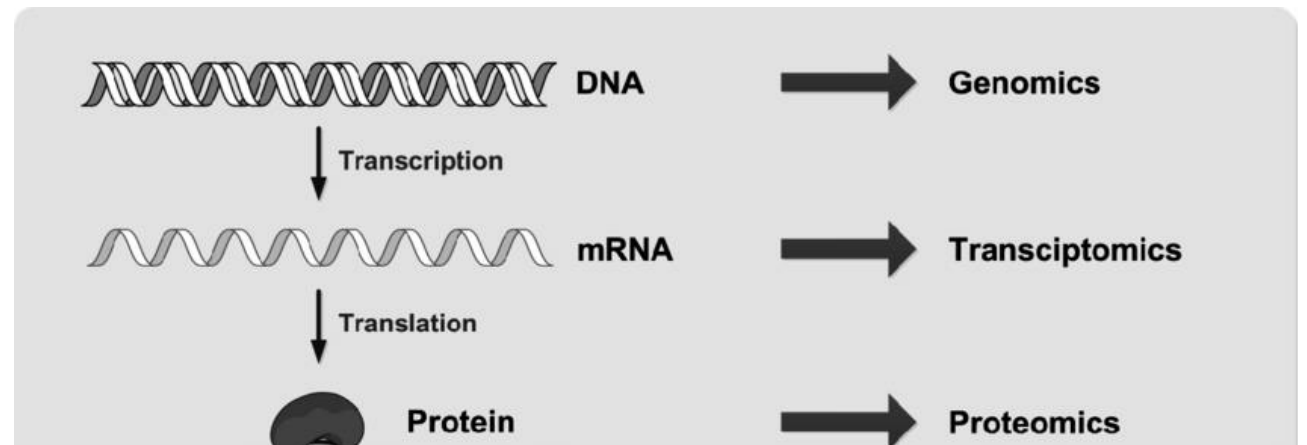
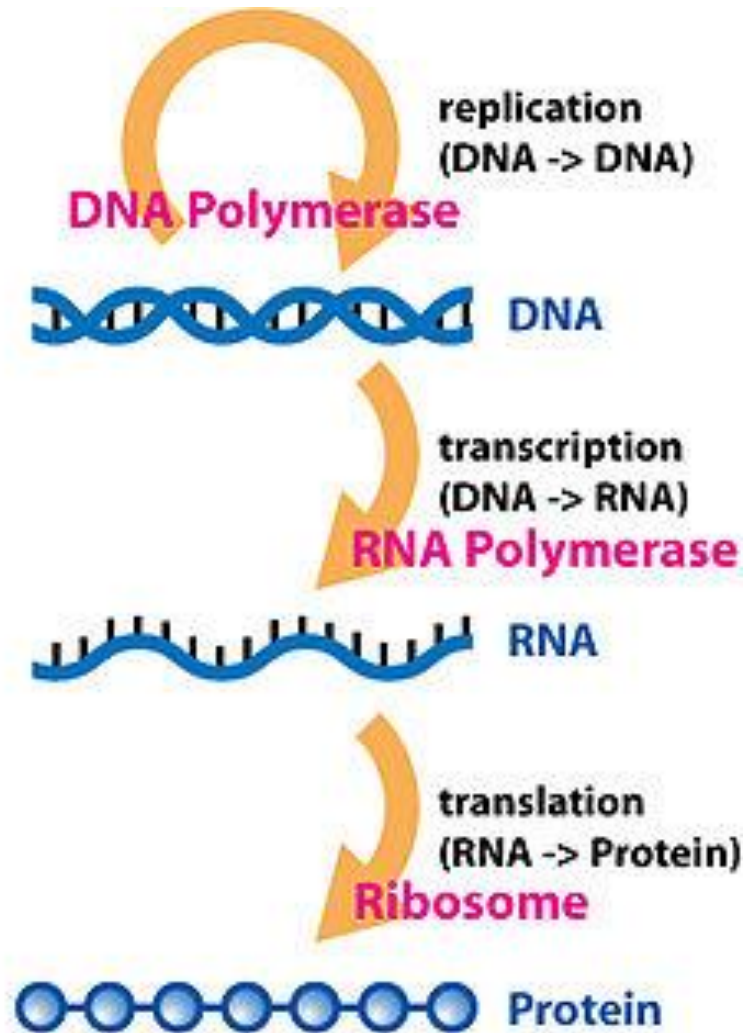


Negative regulation

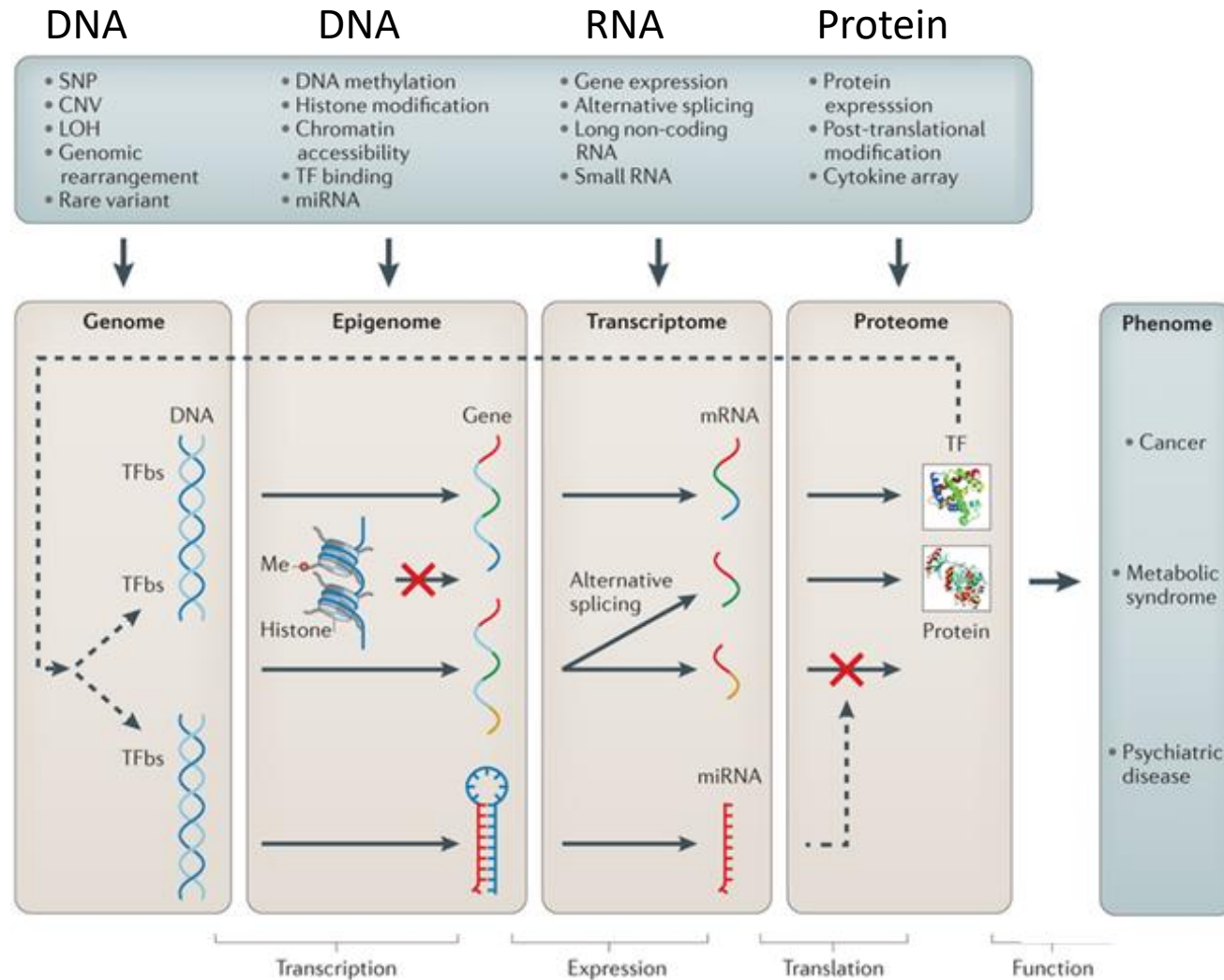


		Second letter				
		U	C	A	G	
First letter	U	UUU } Phe UUC } UUA } UUG } Leu	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA STOP UAG STOP	UGU } Cys UGC } UGA STOP UGG Trp	U C A G
	C	CUU } CUC } CUA } CUG } Leu	CCU } CCC } CCA } CCG } Pro	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } CGA } CGG } Arg	U C A G
	A	AUU } Ile AUC } AUA } AUG Met	ACU } ACC } ACA } ACG } Thr	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }	U C A G
	G	GUU } Val GUC } GUA } GUG }	GCU } GCC } GCA } GCG } Ala	GAU } Asp GAC } GAA } Glu GAG }	GGT } GGC } GGA } GGG } Gly	U C A G

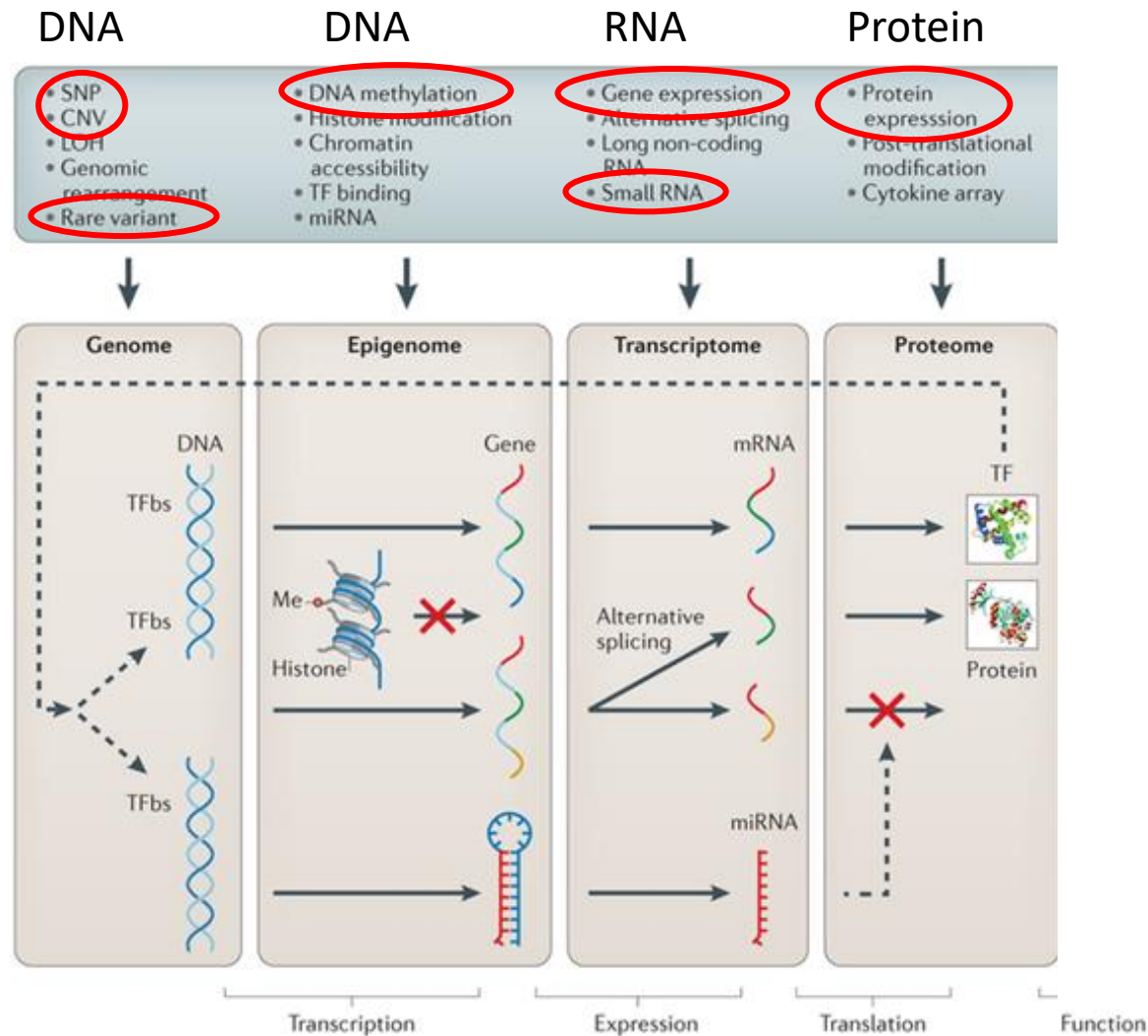
Central Dogma to the Omics



What can you measure?

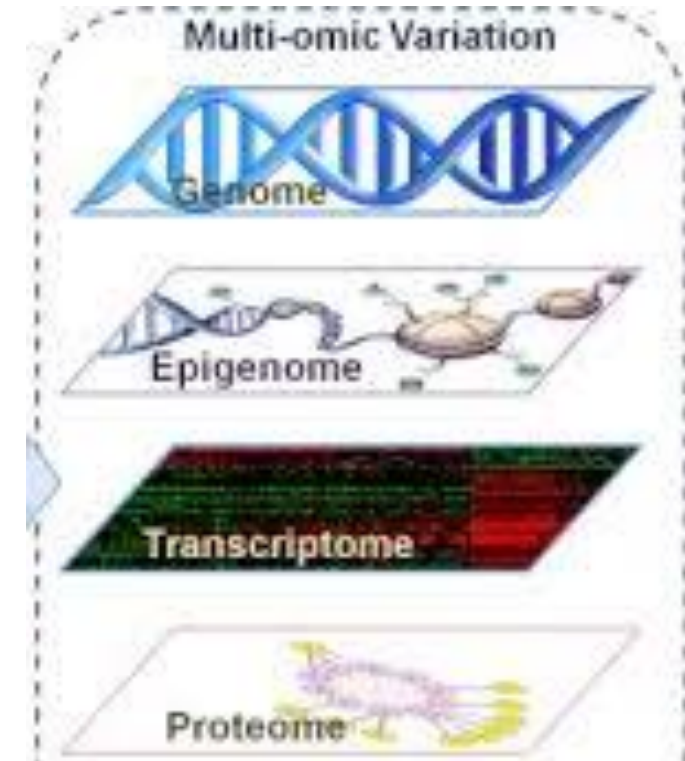
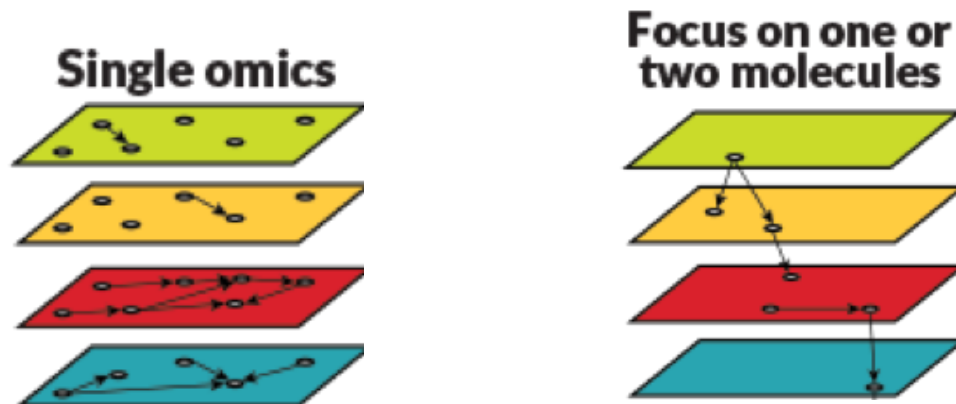


What data will you get at the hackathon?

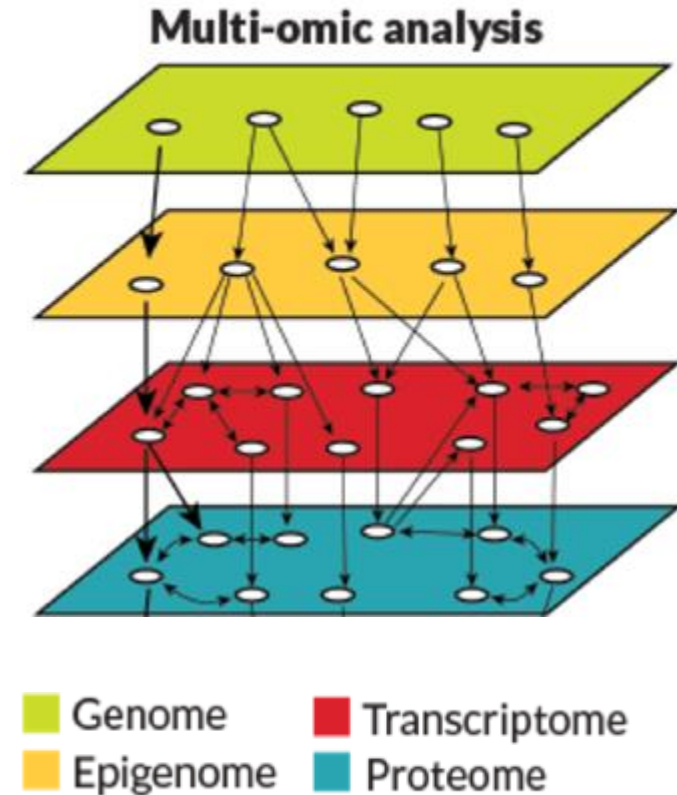
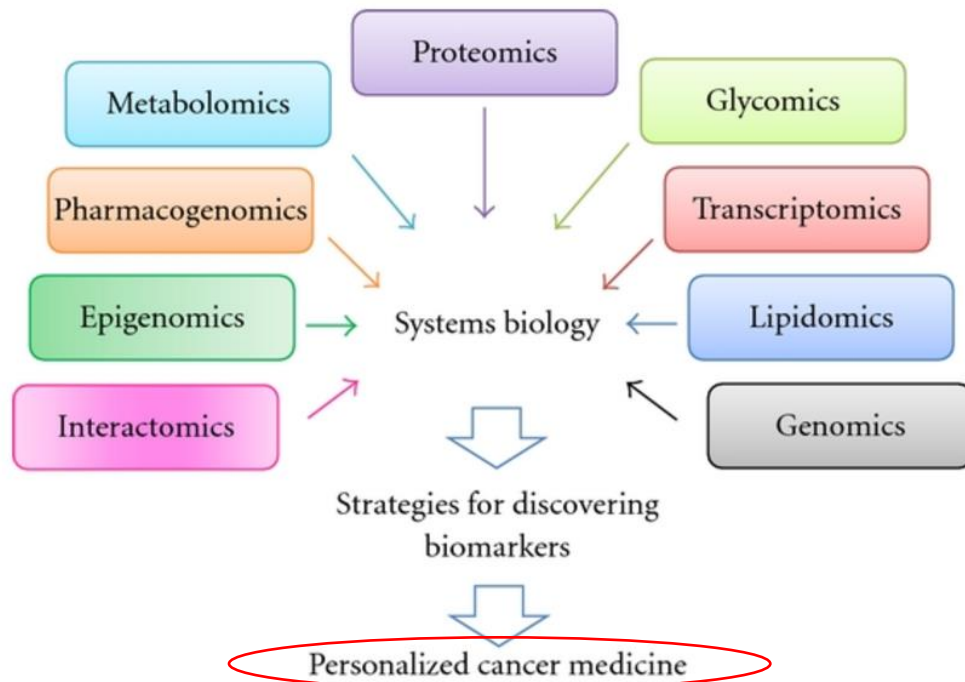


Omics – What we do

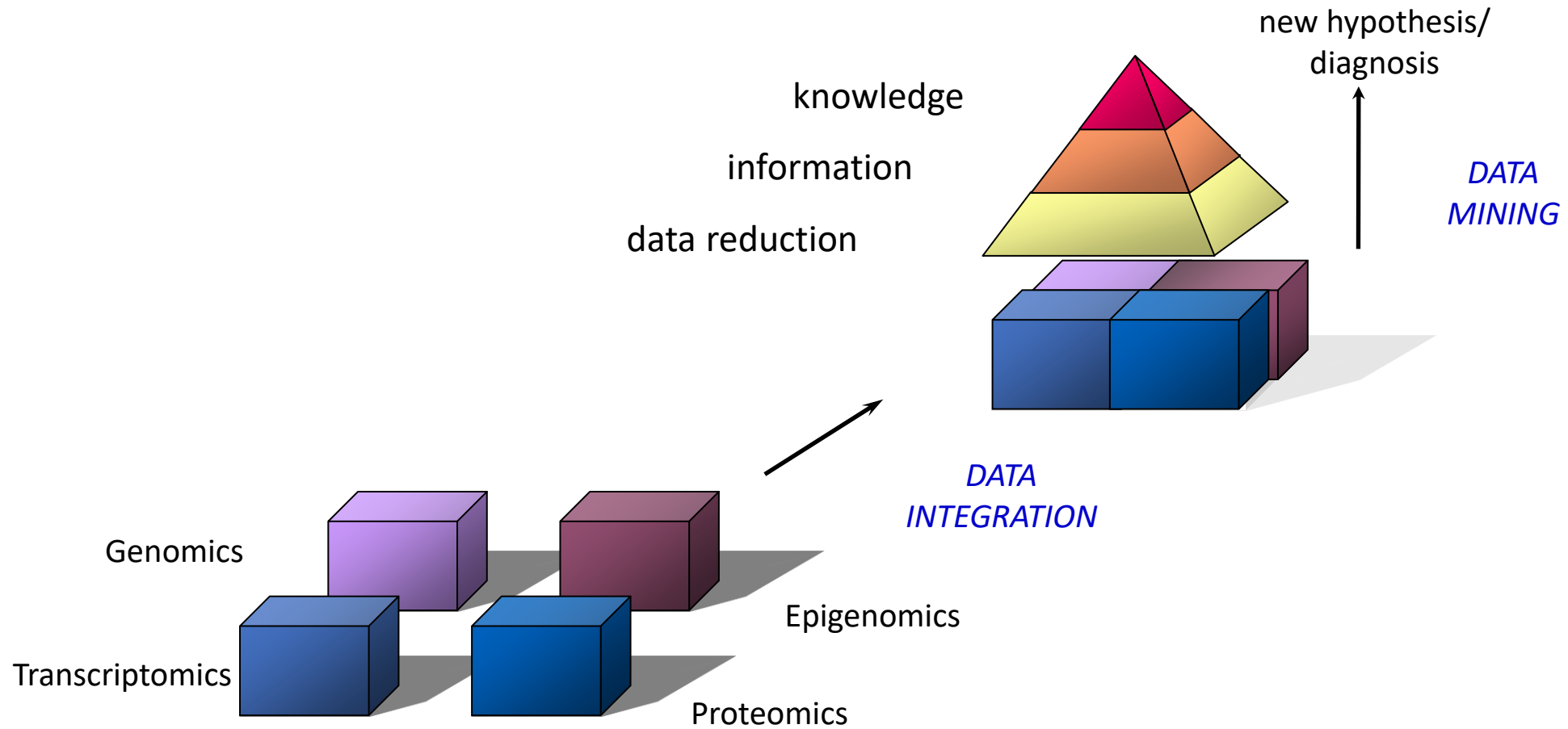
- Because DNA, RNA and Protein are related
 - you see changes in each omic separately
 - you can follow a gene through the omics



Omic – What we want

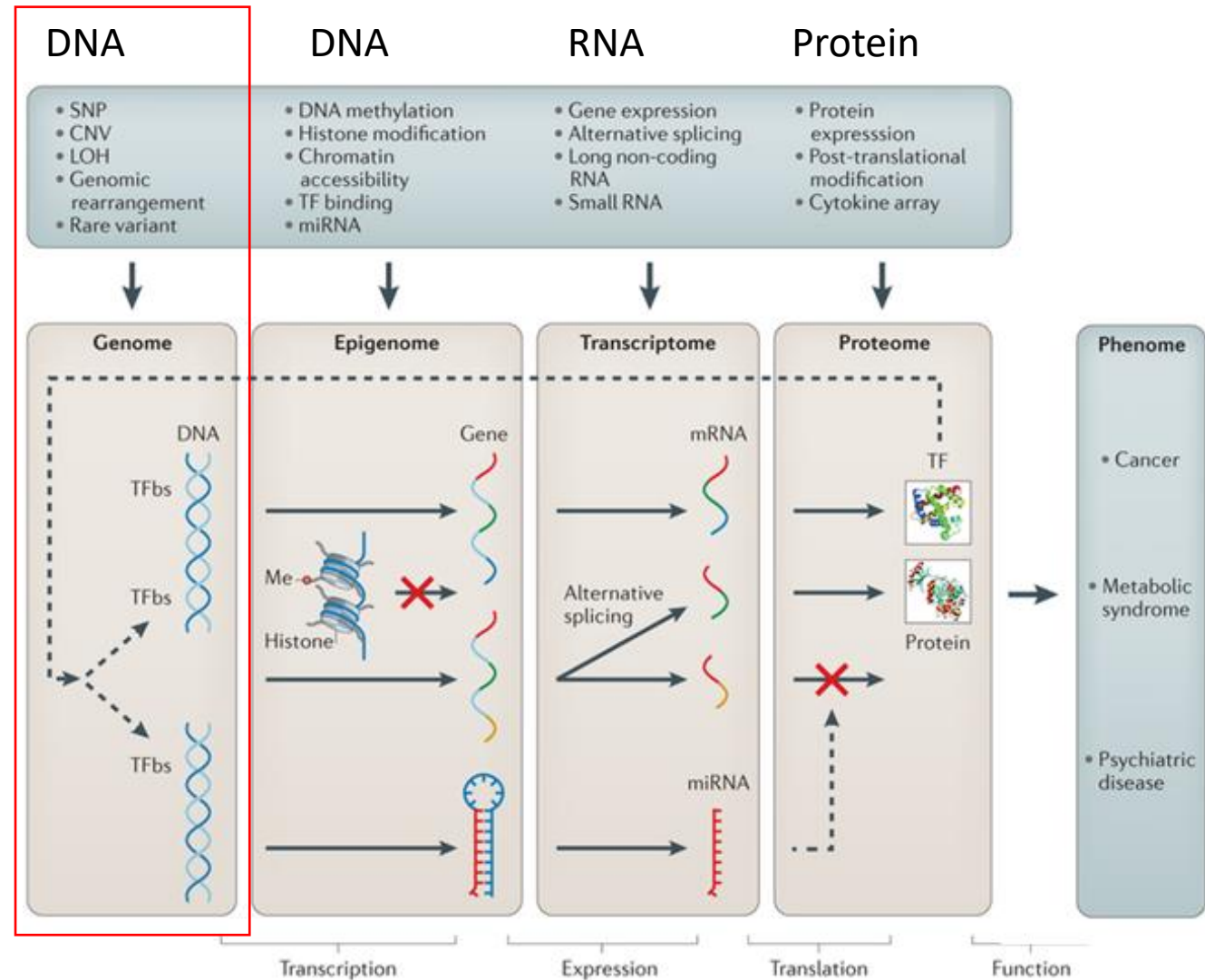


Omics – Integration



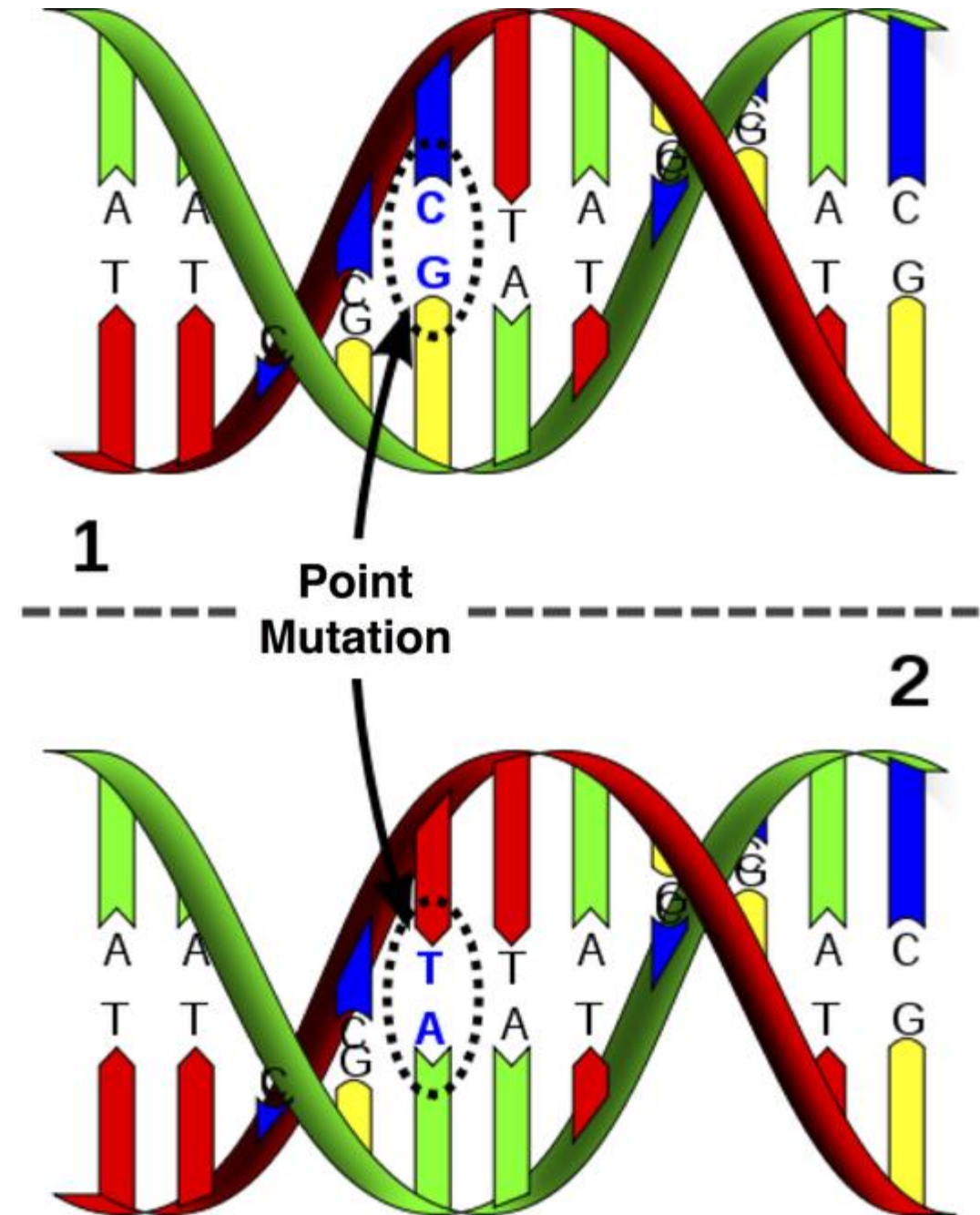
Genomics

- Focusses on DNA itself
 - Base Pairs
 - The amount of DNA



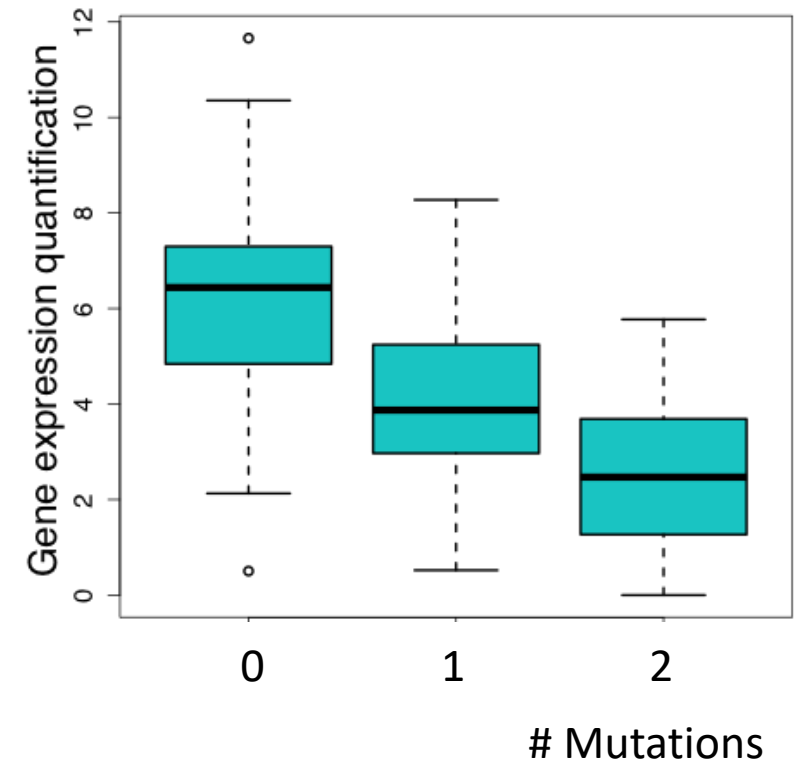
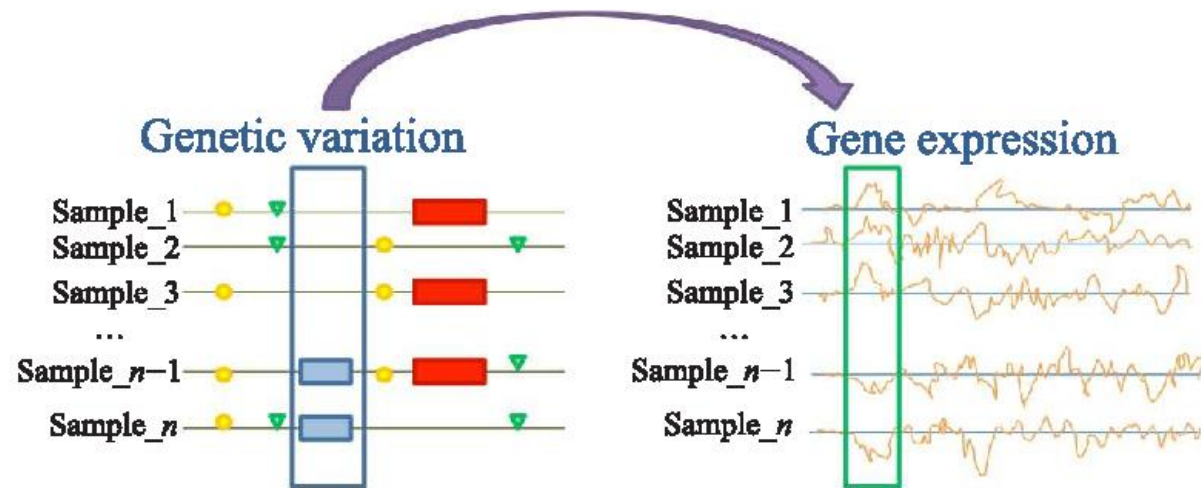
Genomics – Base pairs

- Changes in base pair
 - Mutation
 - Not all mutations will give rise to disease
 - Dependent on function of a gene
 - Can alter gene expression
 - Can change protein function



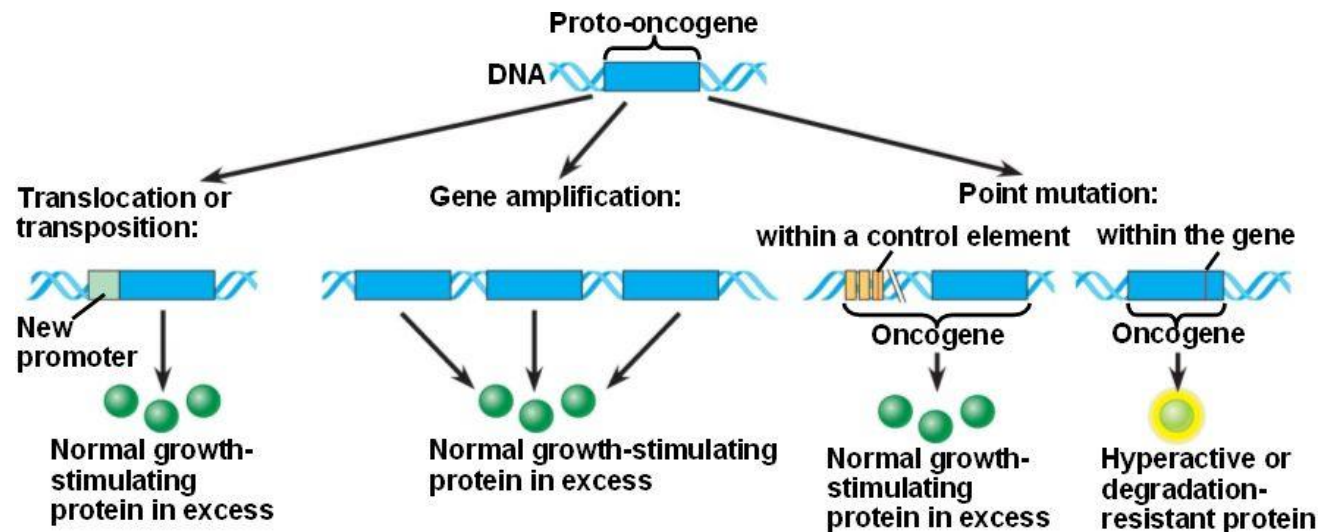
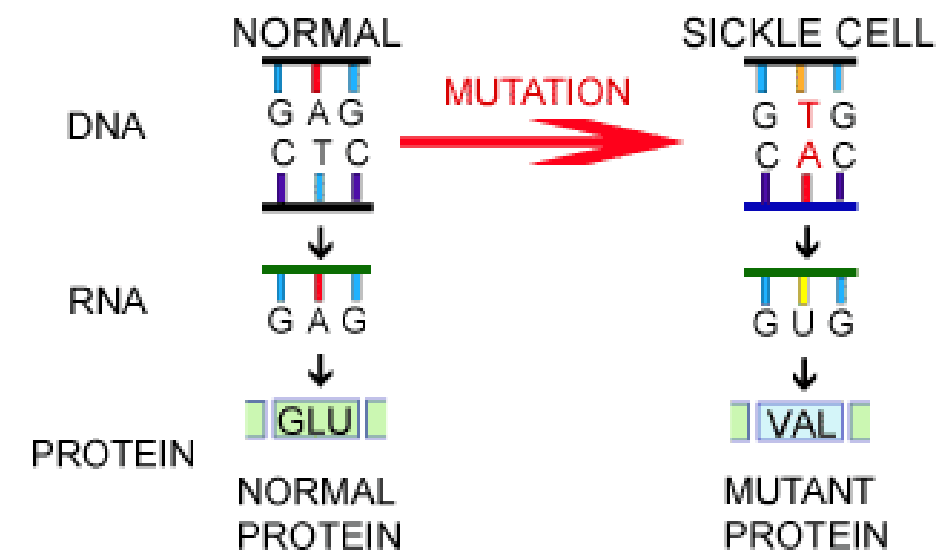
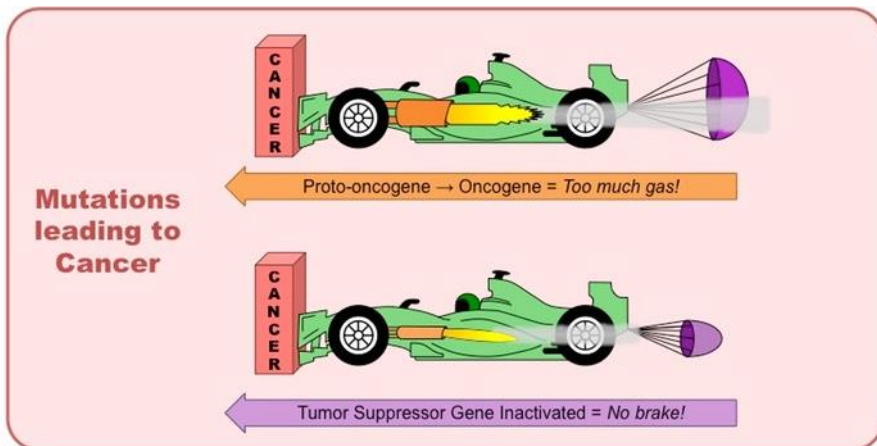
Genomics – Gene Expression

- Changes in gene expression



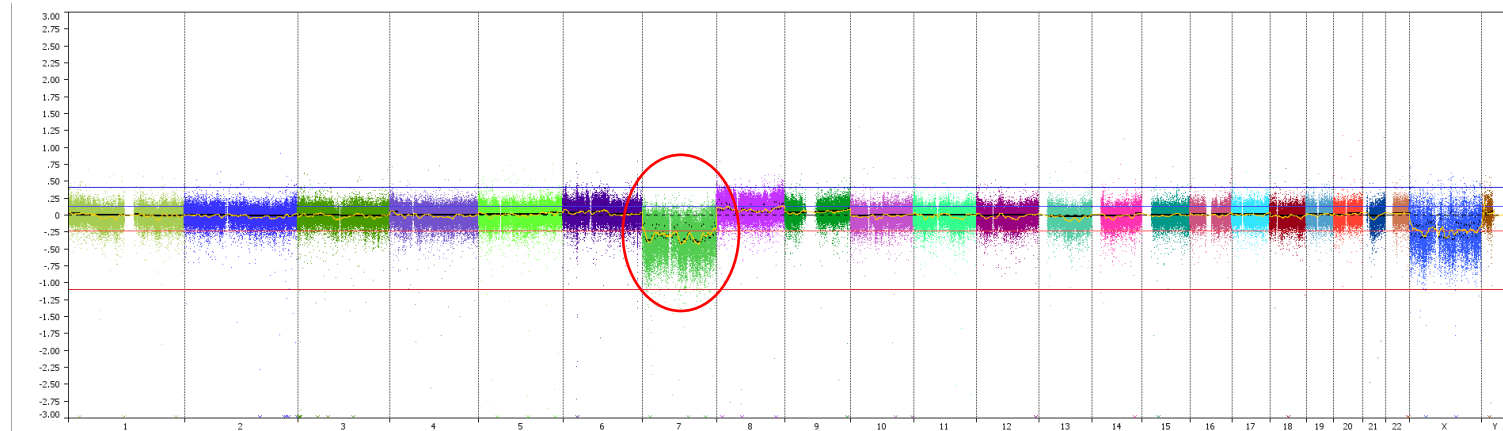
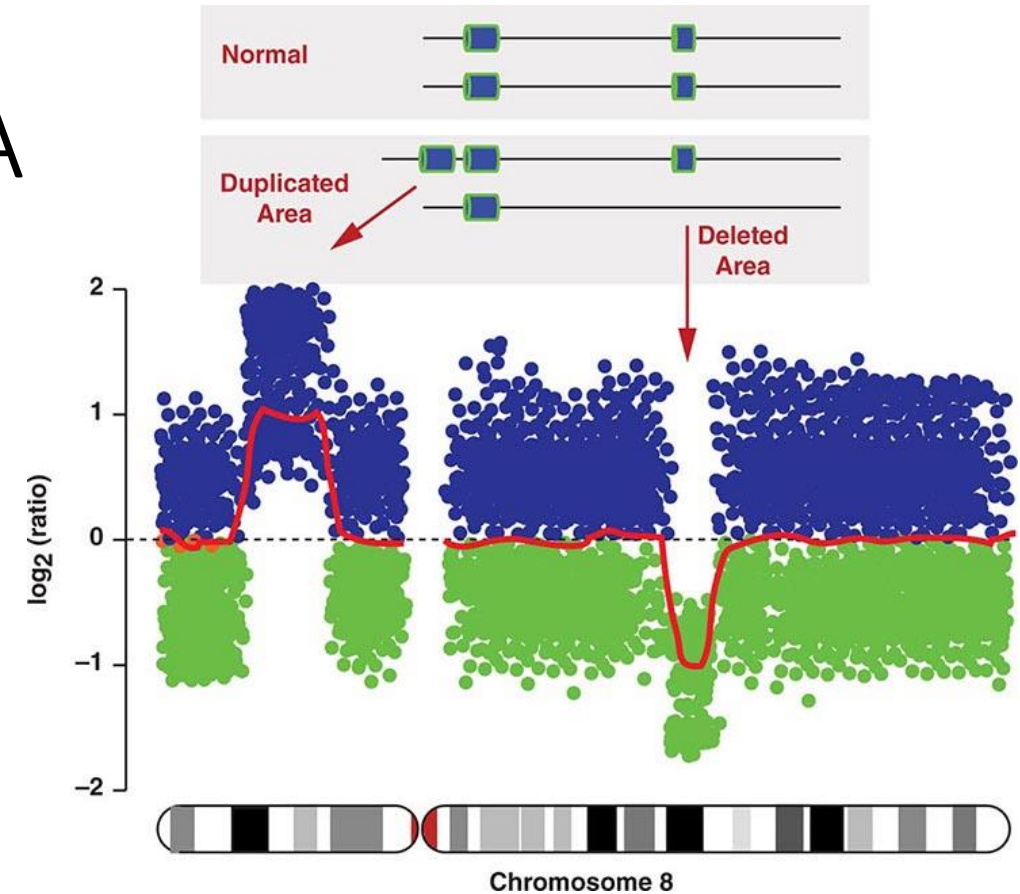
Genomics – Protein function

- Big changes in protein function
 - Dependent on severity of mutation
 - Dependent on function of gene
 - Proto-oncogene
 - Activates cell division/cell survival
 - Tumor suppressor gene
 - Inhibits cell division/cell survival



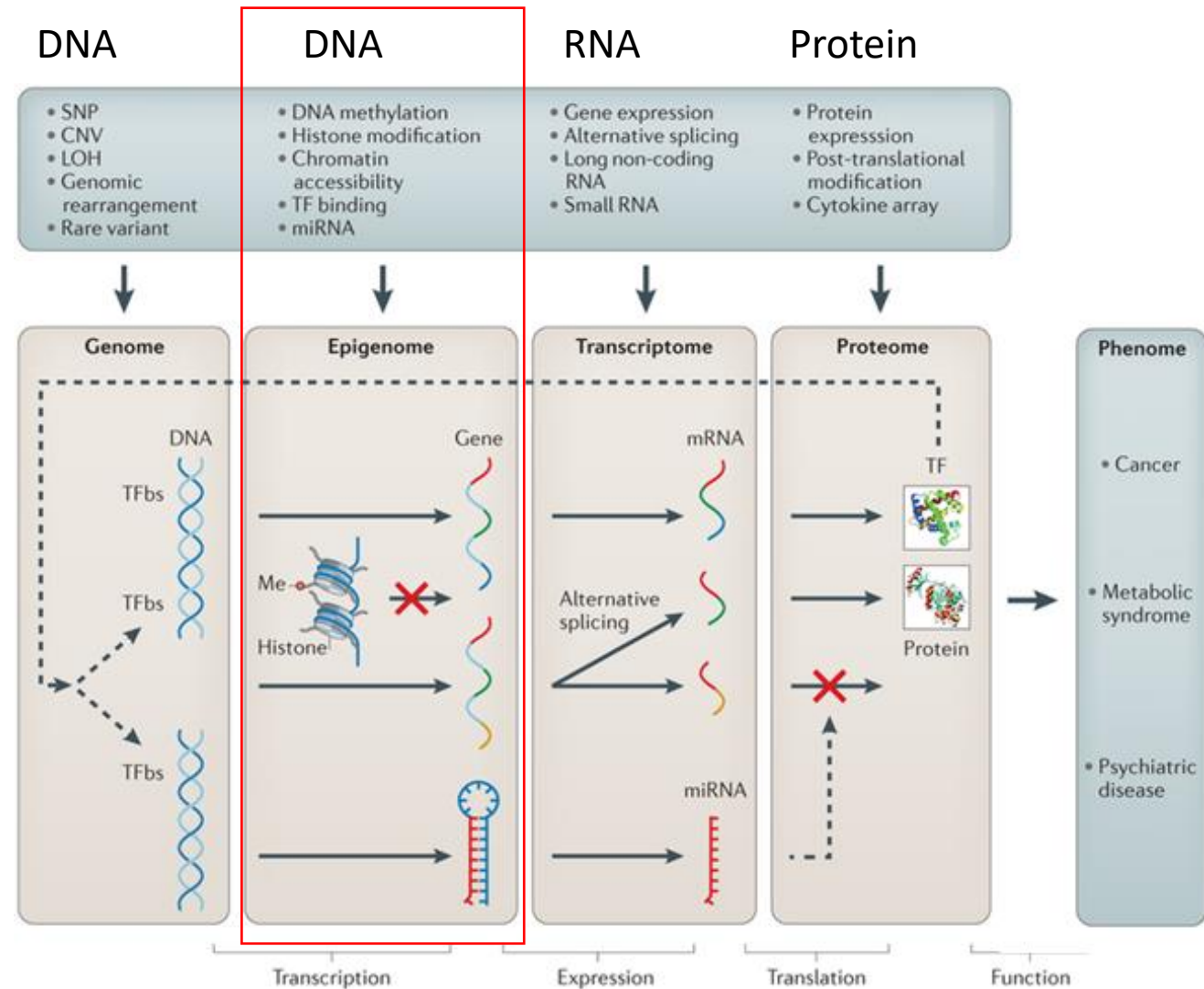
Genomics – Amount of DNA

- Copy Number Variation (CNV)
 - Normal at every position two copies
 - One each from your mother and father
 - Small aberrations
 - Deletions
 - Amplifications
- Chromosomal aberrations
 - Deletions
 - Acute Myeloid Leukemia
 - Monosomy 7
 - Amplifications
 - Down Syndrome
 - Trisomy 21



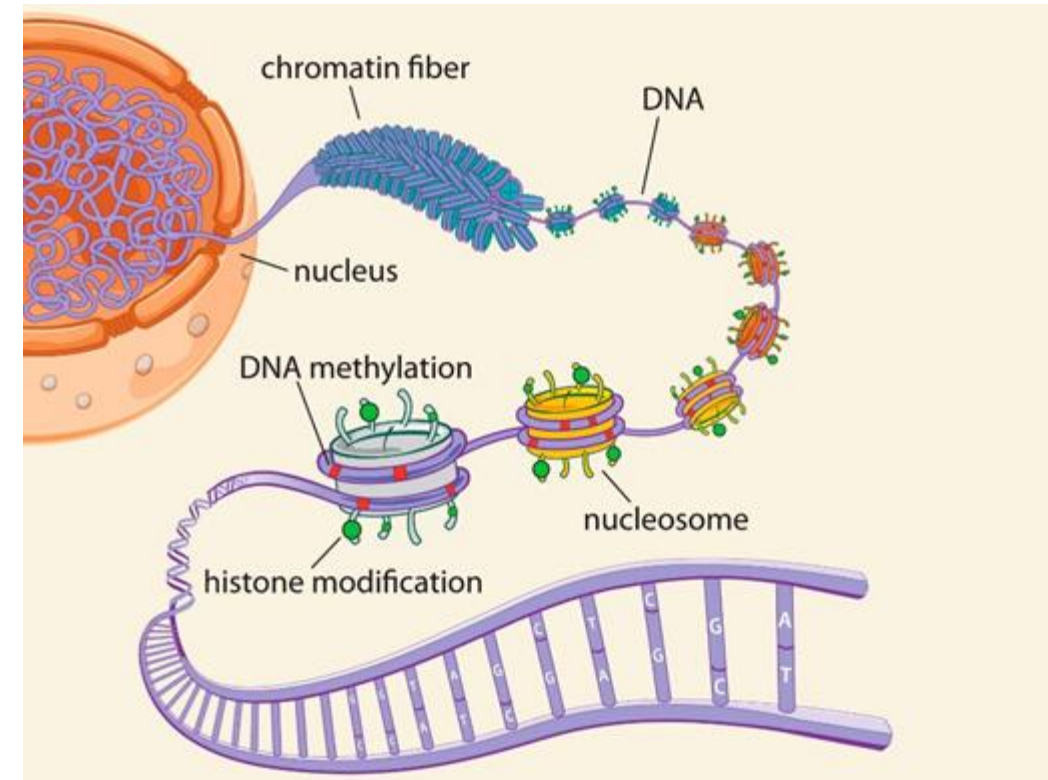
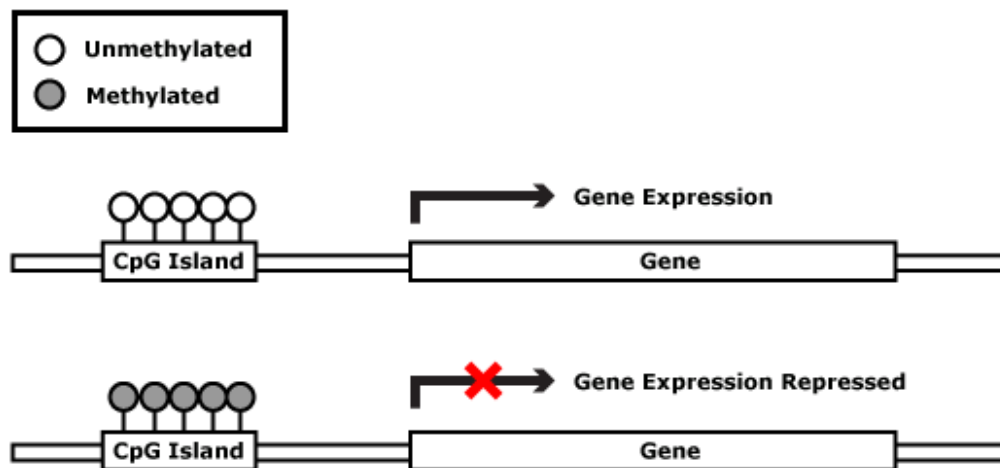
Epigenomics

- Focusses on what is happening on the DNA
 - Methylation



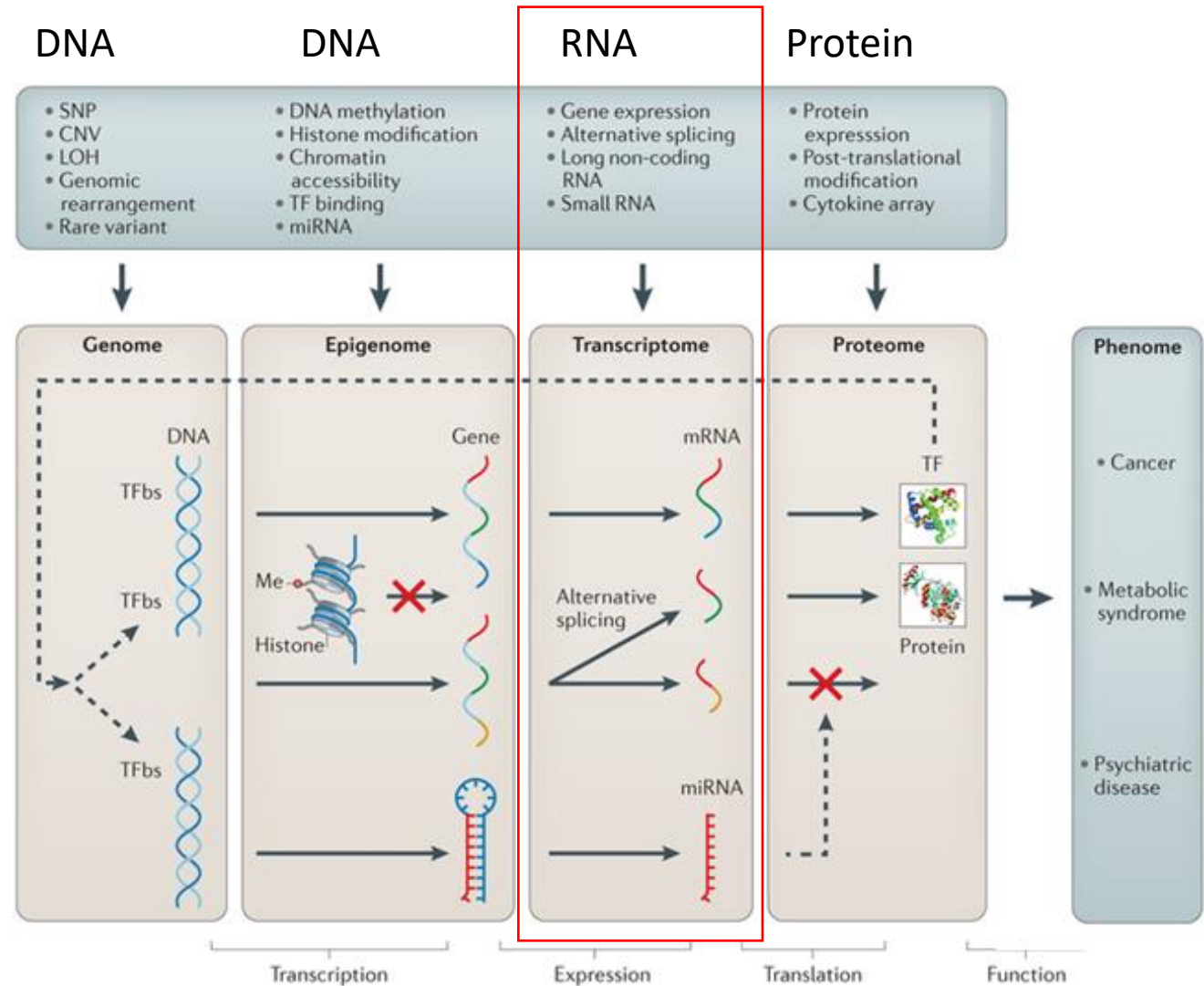
Methylation

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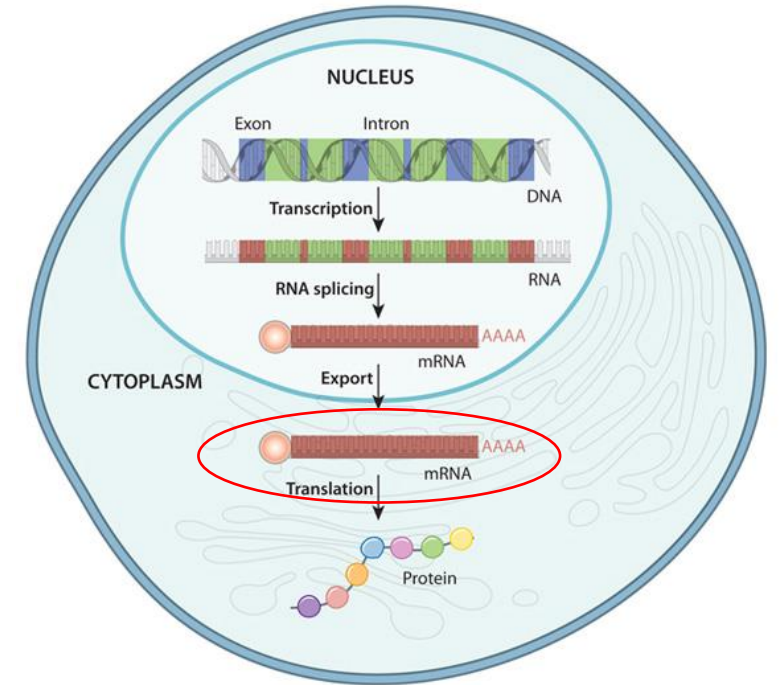
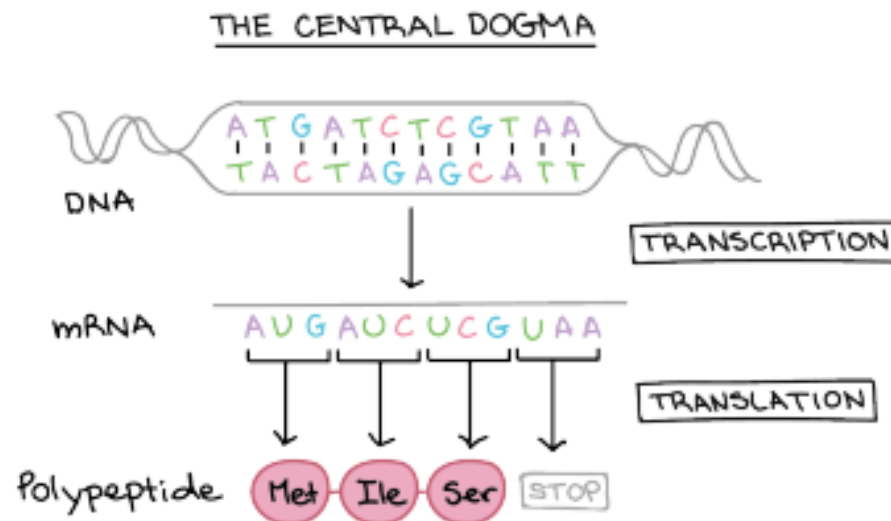
Transcriptomics

- Focusses on RNA
 - Gene expression
 - miRNA



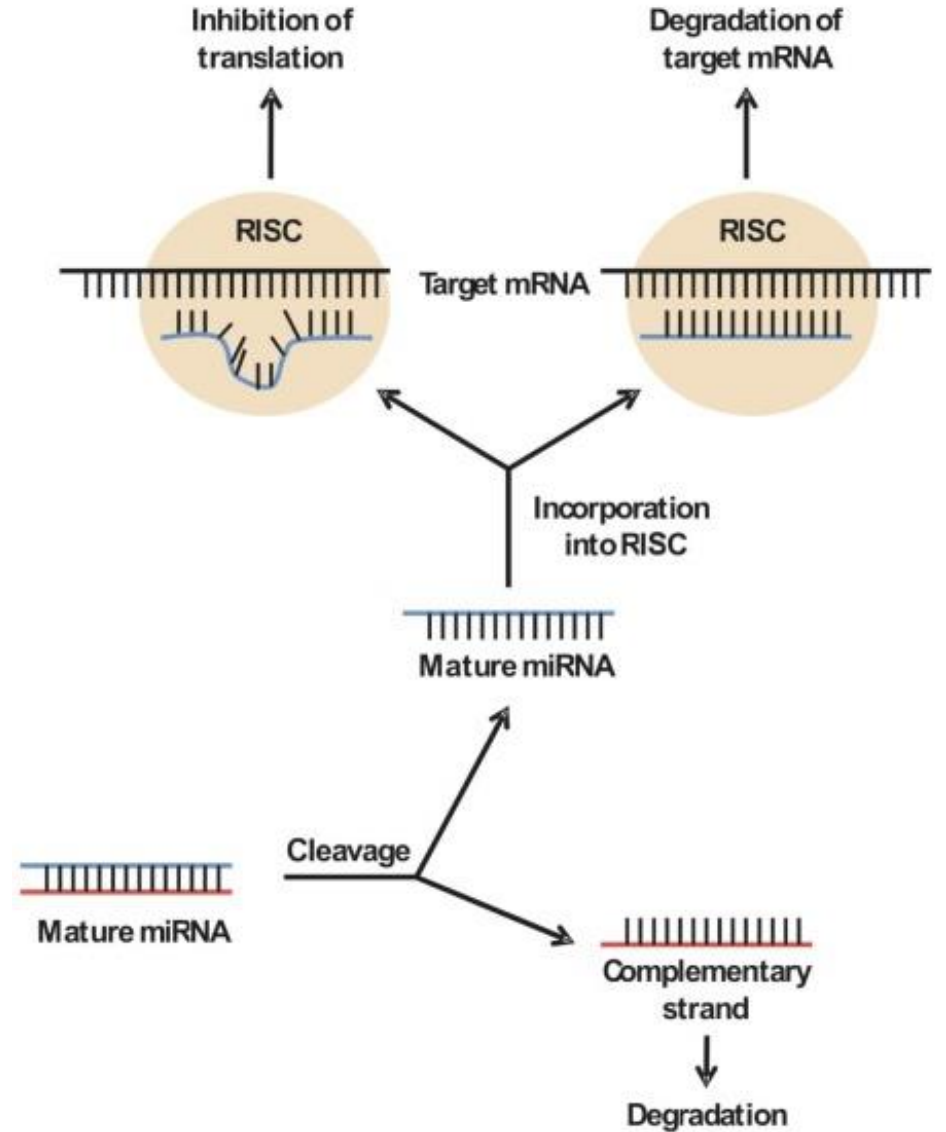
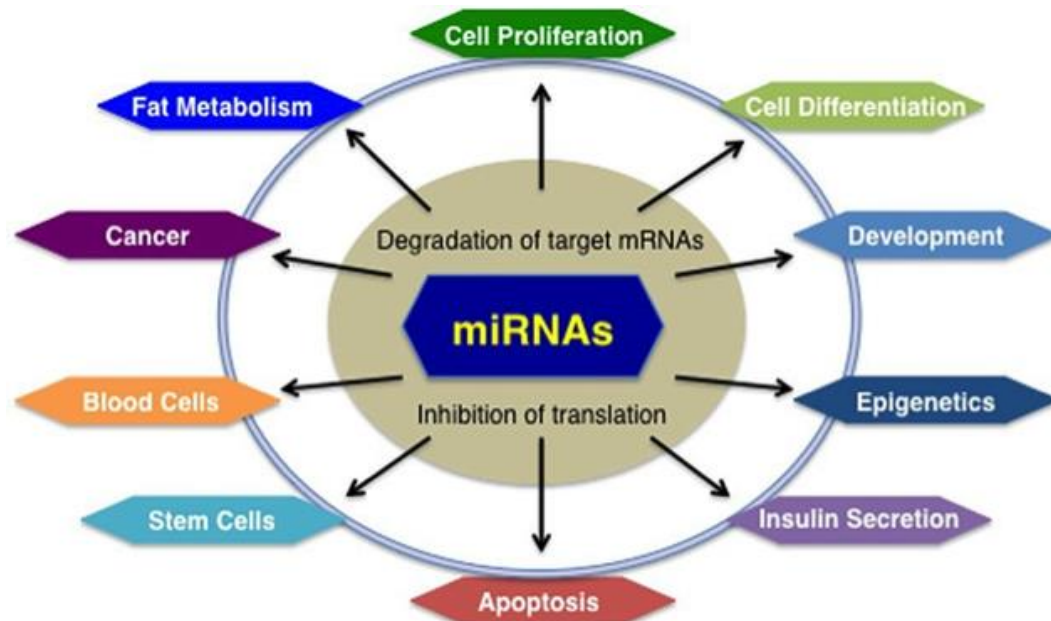
Transcriptomics – Gene Expression

- DNA get copied in RNA
 - Gene Expression looks at mRNA
 - Type of RNA that is copied from the genes
 - Quantification of the processes happening in the cell



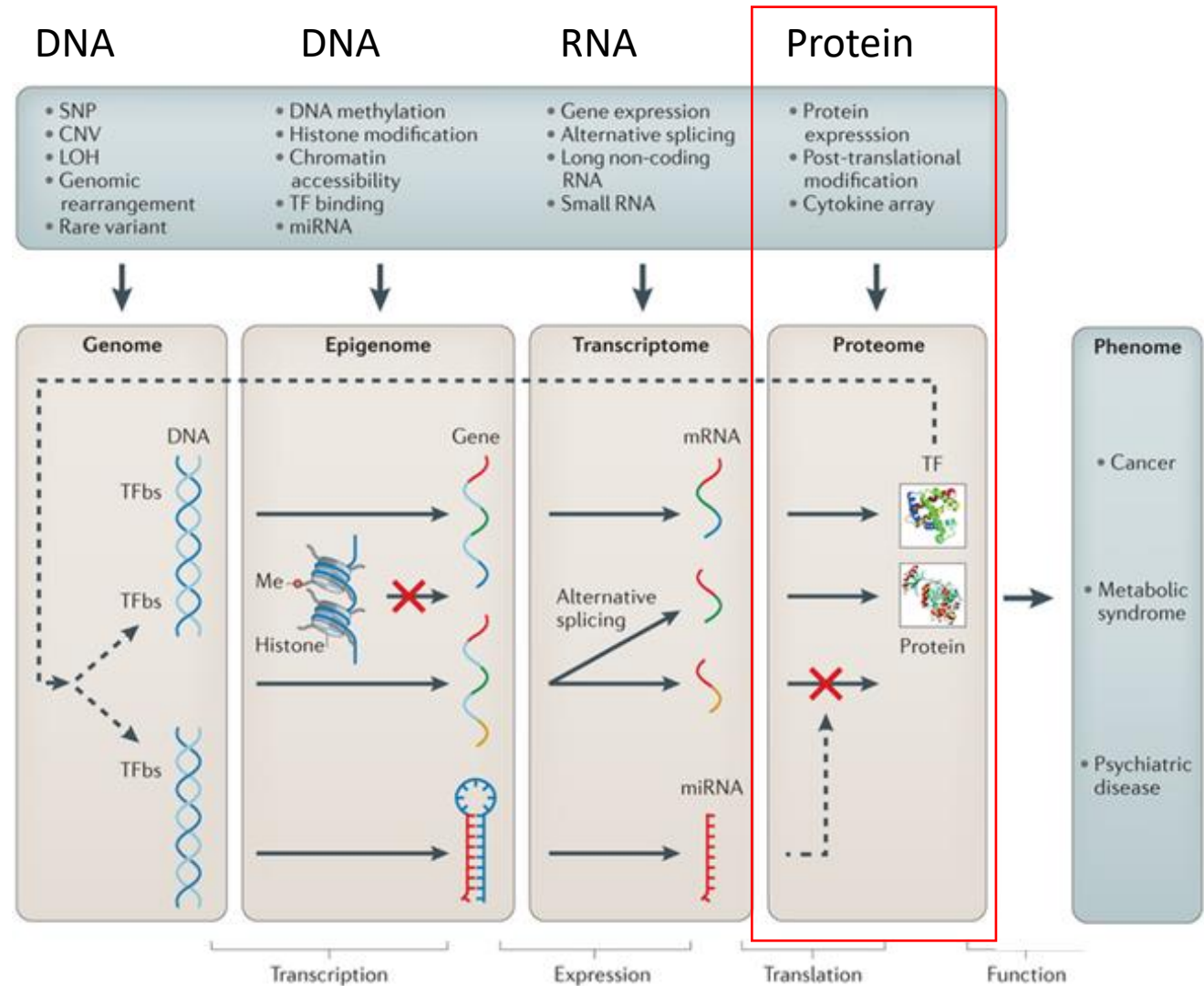
Transcriptomics – miRNA

- Another RNA is miRNA
 - Regulation of processes
 - Especially regulates mRNA
 - Degradation of mRNA
 - Stabilization of mRNA



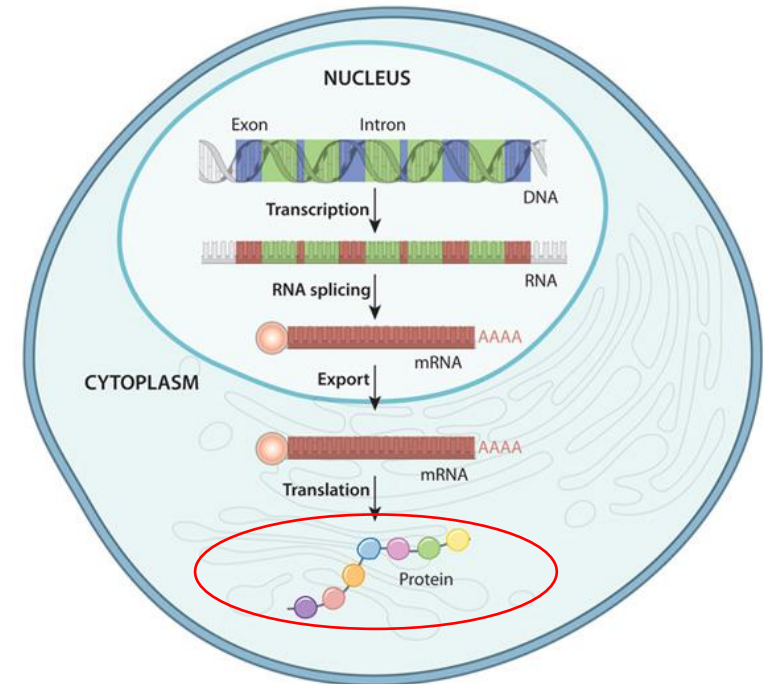
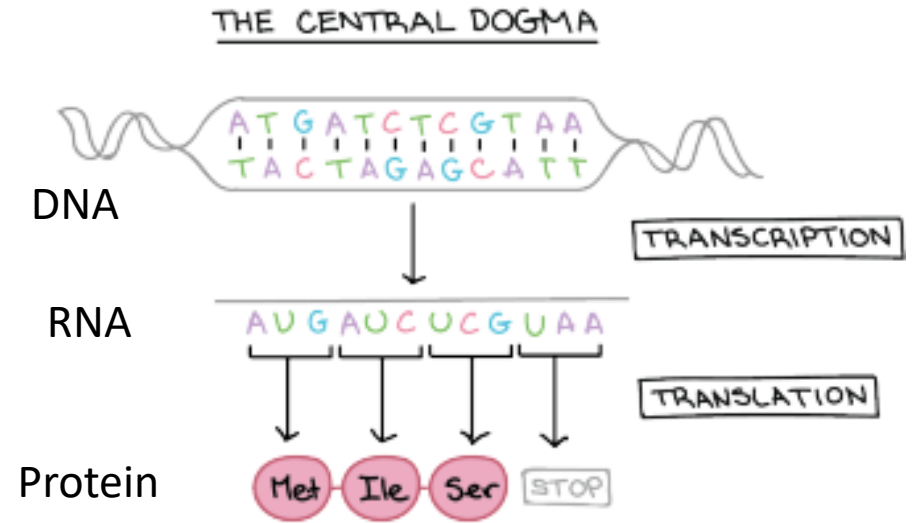
Proteomics

- Focusses on proteins



Proteomics

- Protein expression
 - Processes in a cell
 - Most complex
- Technically not possible to measure all proteins

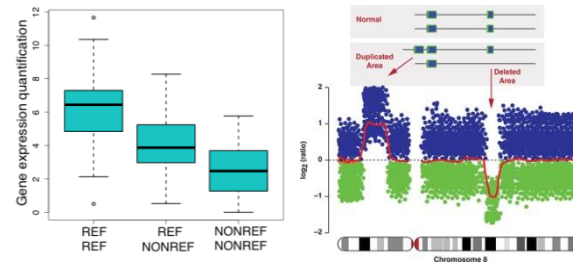


Relationship of the Omics

- Gene Expression Regulation

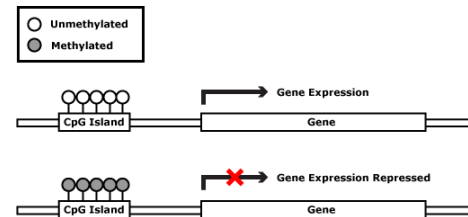
- Genomics

- SNPs/Mutations
 - Copy Number



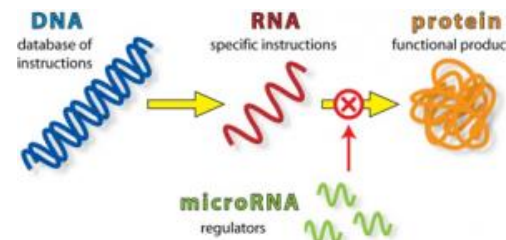
- Epigenomics

- Methylation



- Transcriptomics

- miRNA



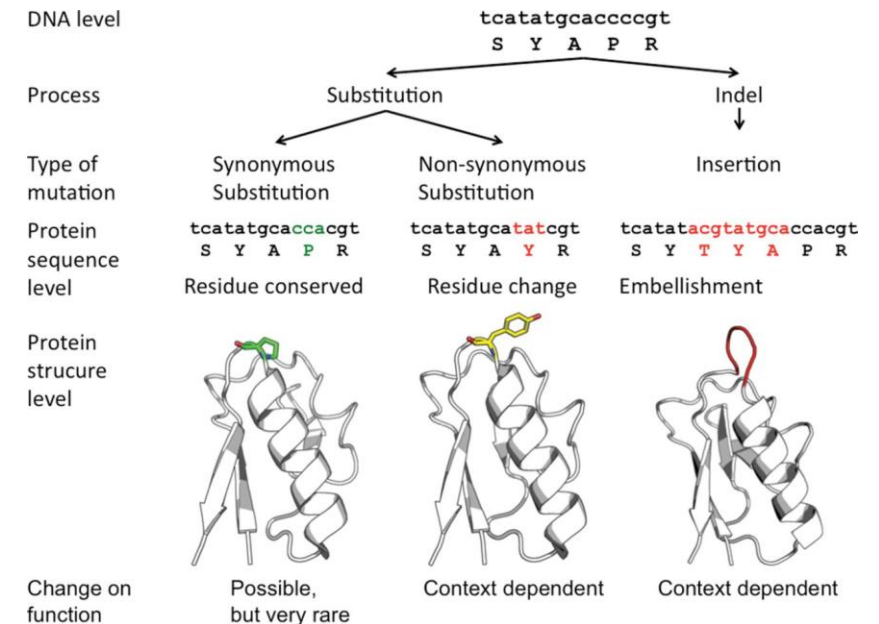
- Proteomics

- Proteins

- Protein Function

- Genomics

- Mutations



Omic Integration Necessary

