

BACK TO SCHOOL: **MOLECULAR BIOLOGY**

Evolution and the Natural World

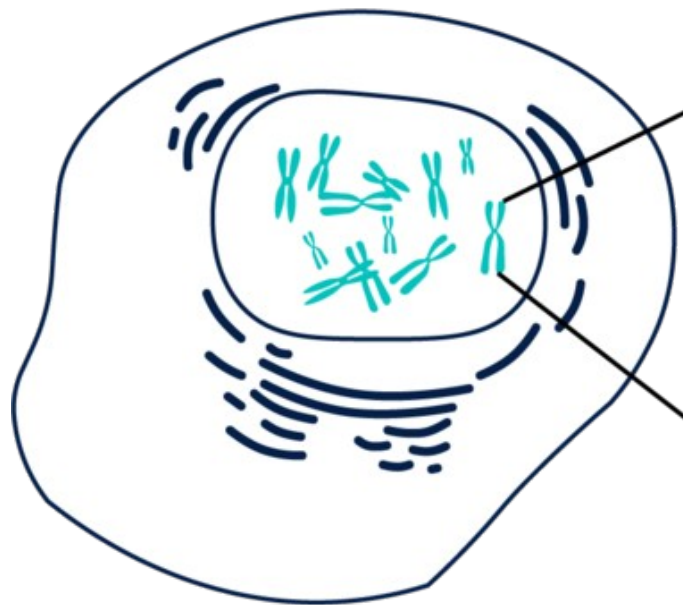
Lecture 2

21/09/2021

Vasili Pankratov

QUICK RECAP

What are genes?



Cell



Chromosome



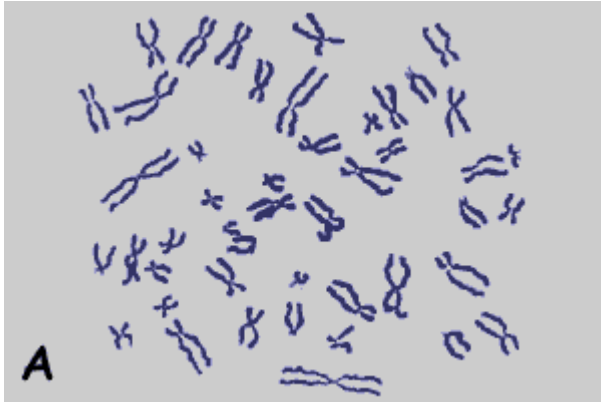
DNA

Gene

Can one see chromosomes and DNA?

Can one see chromosomes and DNA?

Light
microscopy

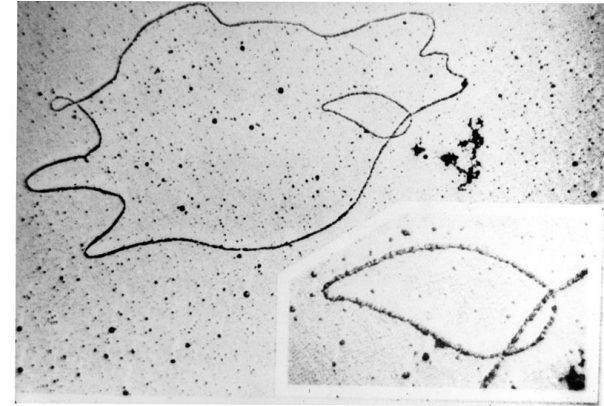


Electron
microscopy



<https://docwithpen.org/2015/07/28/science-marvels-1/>

Electron
microscopy



Wikimedia:
DNA Under electron microscope Image 3576B-PH.jpg

Can one see nucleotides and genes?

Can one see nucleotides and genes?

- To know the nucleotide sequence of a DNA we run some chemical reaction to discriminate between nucleotides – this is **DNA sequencing**

- Genes are information units:
fhfdhsgenesdshareyknlik
ervbkcwordsqadsfintersp
ersedpermwithiuertrando
merfgsequencesfhgpoofl
etterskiyvwwithxcnvpnof
spacesgherthnds fhsdqr

Can one see nucleotides and genes?

- To know the nucleotide sequence of a DNA we run some chemical reaction to discriminate between nucleotides – this is **DNA sequencing**

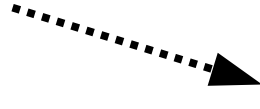
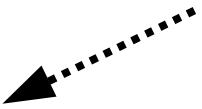
- Genes are information units:

fhfdhsgenesdshareyknlik
ervbkcwordsqadsfintersp
ersedpermwithiuertrando
merfgsequencesfhgpoofl
etterskiyvwwithxcnvpnof
spacesgherthnds fhsdqr

AABB x aabb



AaBb x aabb



25% AaBb

25% aabb

25% Aabb

25% aaBb

No linkage

50% AaBb

50% aabb

Complete linkage

x% AaBb

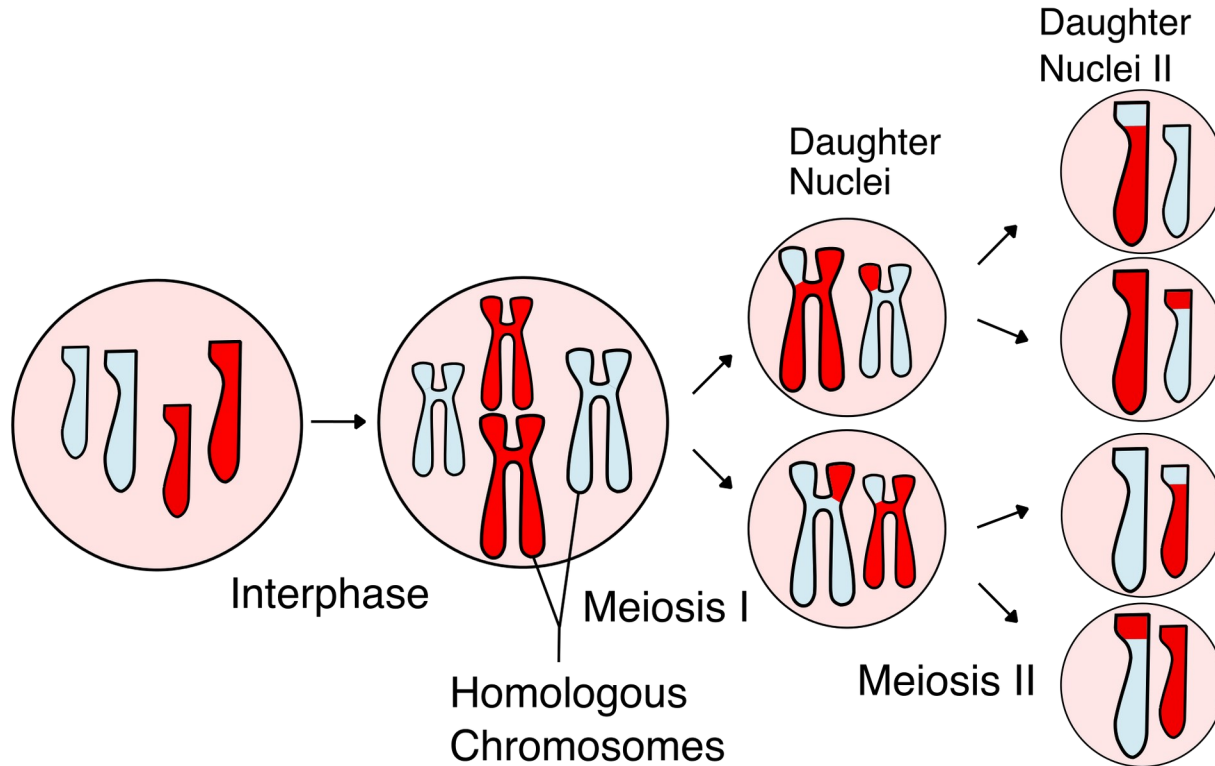
x% aabb

y% Aabb

y% aaBb

Incomplete linkage

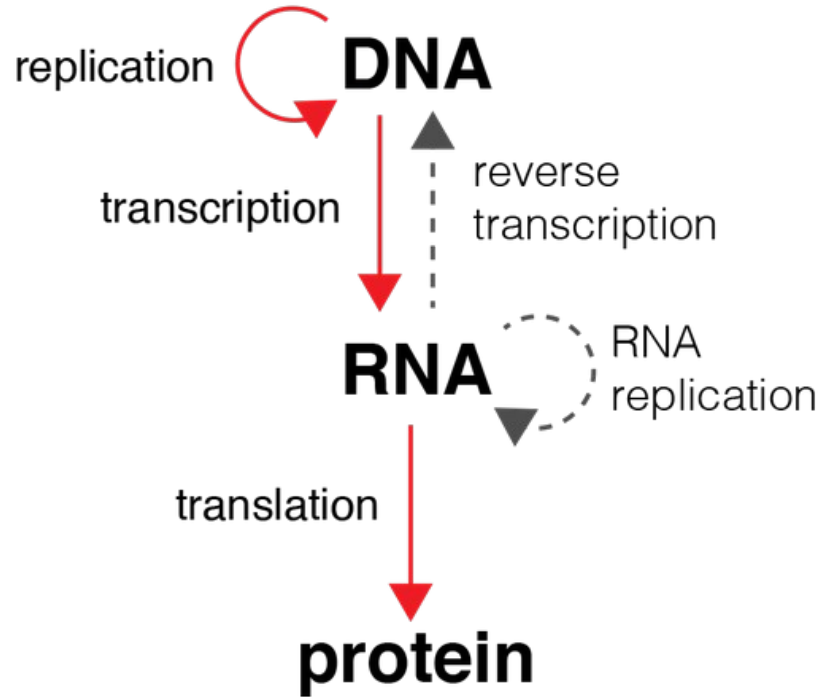
Recombination (crossing over)



MOLECULAR BIOLOGY (MB)

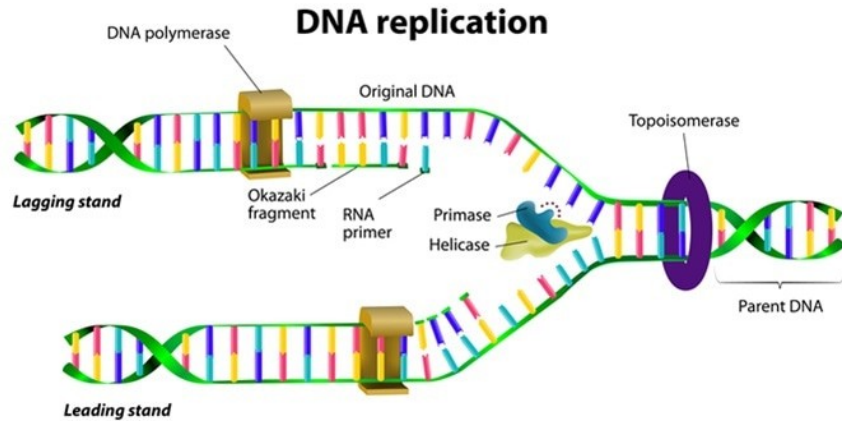
Molecular mechanisms of inheritance

The central dogma of MB



- **Replication** – DNA copying, ensures that daughter cells (including gametes) get the same DNA
- **Transcription + translation** – gene expression. These are the two steps needed to synthesize a protein encoded by a gene.

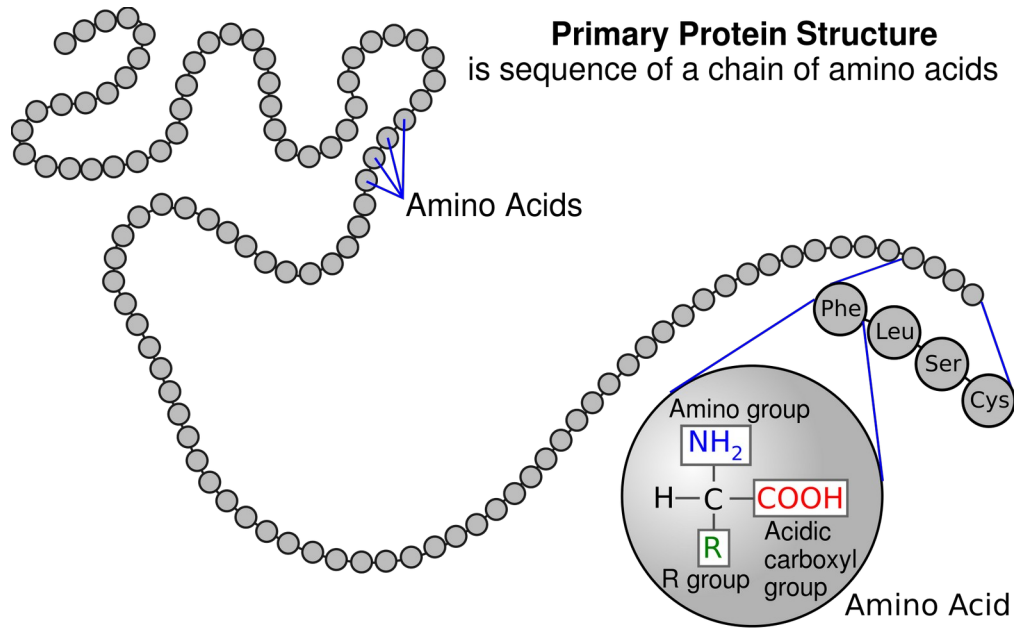
DNA replication – the basis of inheritance



<https://www.news-medical.net/life-sciences/Mechanism-of-DNA-Synthesis.aspx>

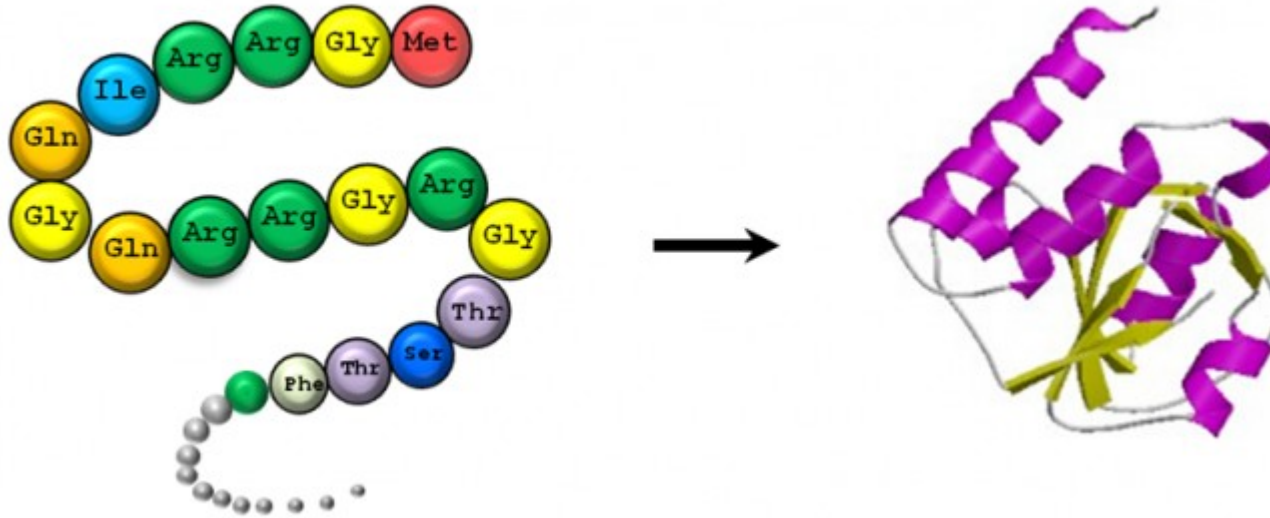
- Happens via a semi-**conservative** mechanism
- The main enzyme is DNA-**polymerase**
- Is very precise but not perfect – **mutations** may happen

Genes code for proteins



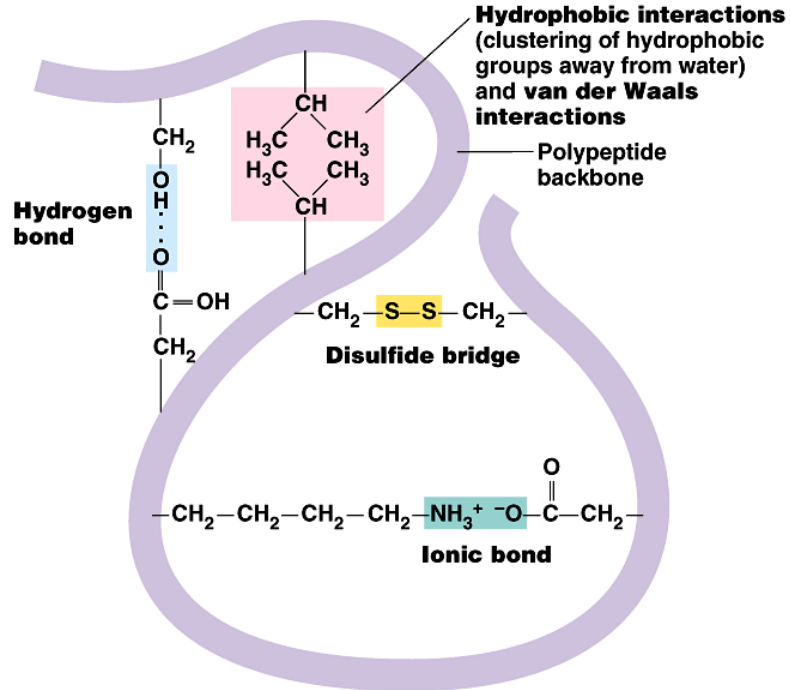
- Proteins are polymers of amino acids
- Proteins do most of the work in the body, most importantly, **enzymes** are proteins

Why can proteins do different stuff?



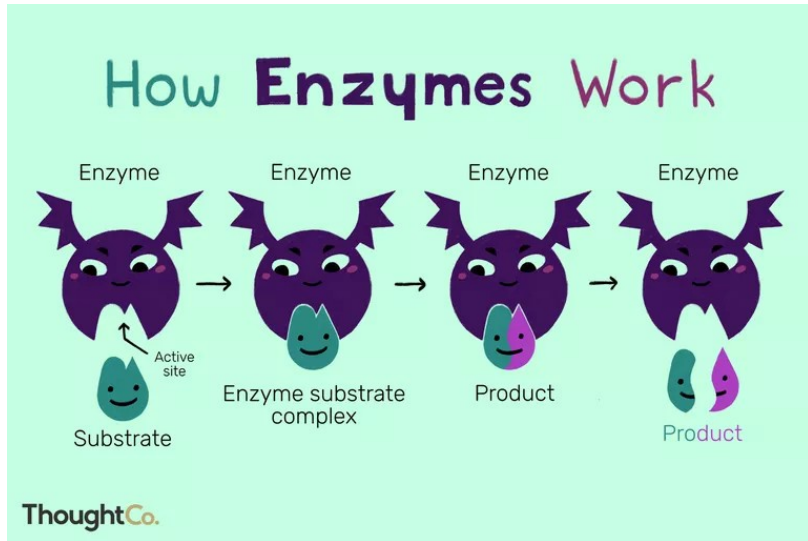
- Each protein has a specific **3D structure**, defined by its' AA sequence, which determines protein's properties

Protein 3D structure



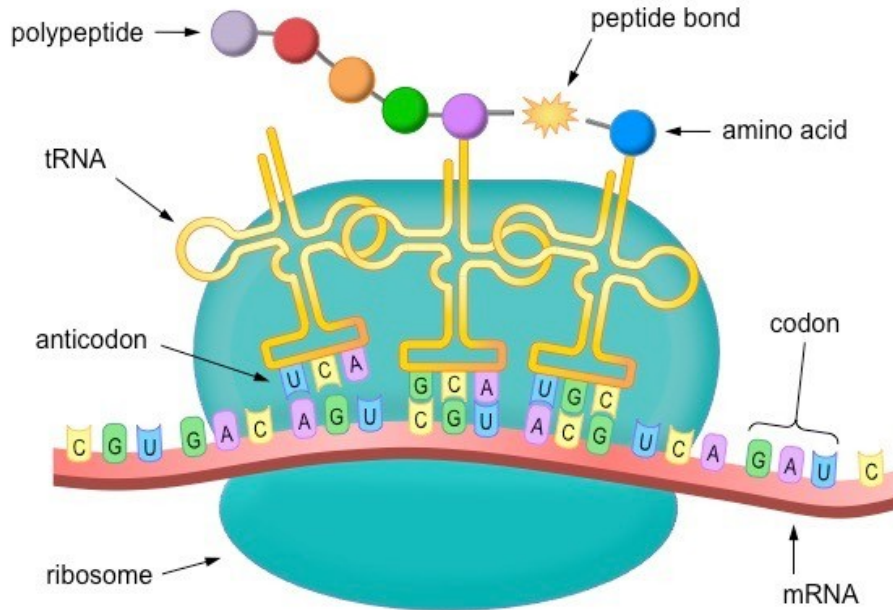
- **Proteins' 3D structure** is the key to their functions
- The 3D structure depends on the amino acid sequence
- But it also depends on conditions like pH and temperature and it may change as a result of chemical modifications

Enzymes



- Every type of compound (sugars, lipids, nucleotides etc.) are synthesized with the help of enzymes (each reaction needs its enzyme)
- The chemical composition of a cell depends on the enzymes it contains

Protein synthesis (Translation)



- **Ribosome** – the place and the enzyme
- **Messenger RNA** – the source of info about the amino acid sequence
- **Codon** – information unit
- **Transport RNA** – adapter between mRNA and each amino acid

mRNA to protein decoding

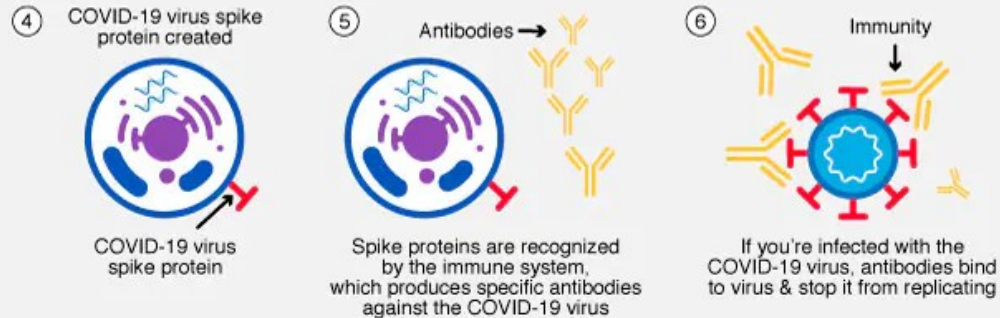
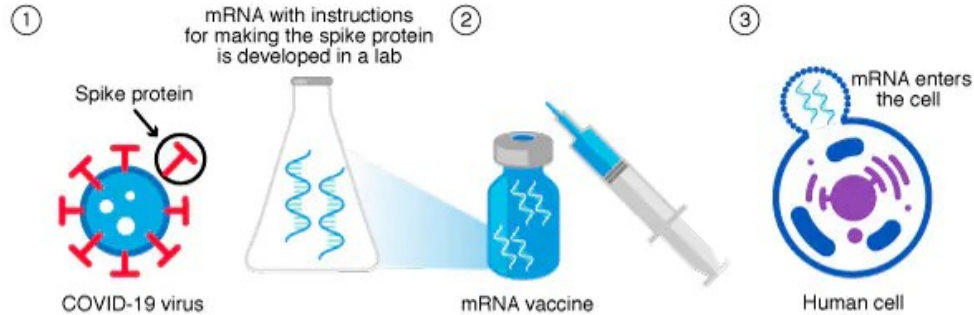
		Second letter				
		U	C	A	G	
First letter	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA STOP UAG STOP	UGU } Cys UGC } UGA STOP UGG Trp	U C A G
	C	CUU } CUC } Leu CUA } CUG }	CCU } CCC } Pro CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } Arg CGA } CGG }	U C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

Key:

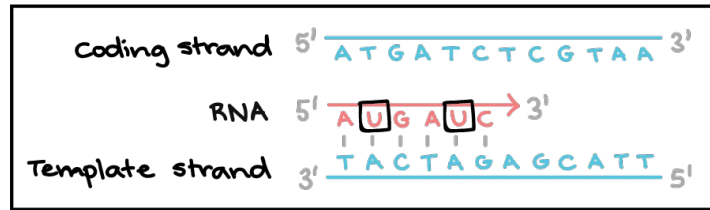
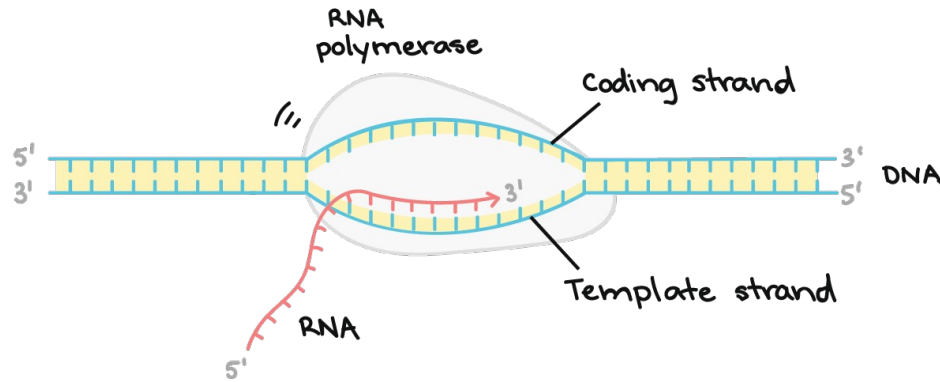
Ala = Alanine (**A**)
 Arg = Arginine (**R**)
 Asn = Asparagine (**N**)
 Asp = Aspartate (**D**)
 Cys = Cysteine (**C**)
 Gln = Glutamine (**Q**)
 Glu = Glutamate (**E**)
 Gly = Glycine (**G**)
 His = Histidine (**H**)
 Ile = Isoleucine (**I**)
 Leu = Leucine (**L**)
 Lys = Lysine (**K**)
 Met = Methionine (**M**)
 Phe = Phenylalanine (**F**)
 Pro = Proline (**P**)
 Ser = Serine (**S**)
 Thr = Threonine (**T**)
 Trp = Tryptophan (**W**)
 Tyr = Tyrosine (**Y**)
 Val = Valine (**V**)

- **Genetic code** is a “dictionary” to translate RNA nucleotide sequence into protein amino acid sequence
- It is **redundant** and (almost) **universal**

MRNA vaccines



RNA synthesis (Transcription)



- **RNA polymerase** – the enzyme
- **Complementarity** – the rule for going from DNA to RNA
- **DNA template strand** – the source of info about the nucleotide sequence

Controlling gene expression

Types of Cells in the Body



Stem Cells



Bone Cells



Blood Cells



Muscle Cells



Fat Cells



Skin Cells



Nerve Cells



Endothelial Cells



Sex Cells



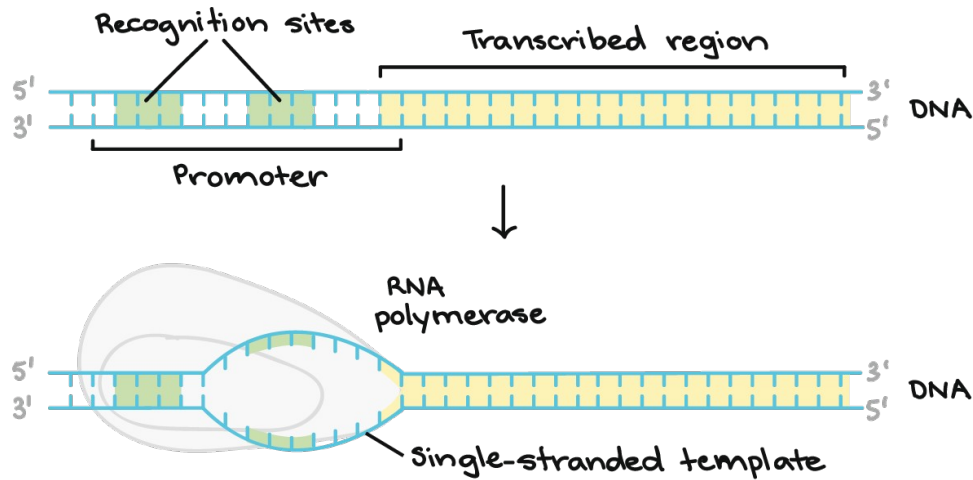
Pancreatic Cells



Cancer Cells

Gene expression differs between cell types, stages of the cell cycle, organismal life stage and depending on various conditions

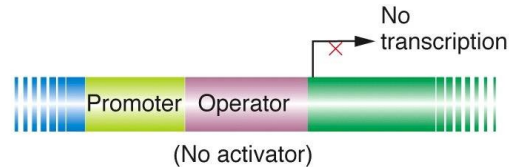
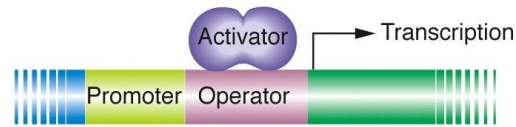
Controlling transcription



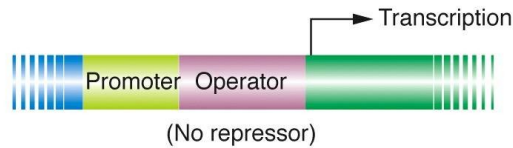
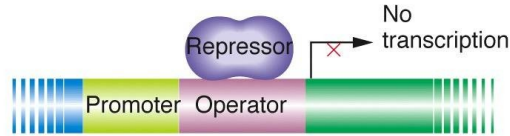
- **Promoter** is a DNA sequence where RNA polymerase binds – it «marks» the start of the gene
- **Promoters** control transcription initiation

Controlling transcription

Positive regulation

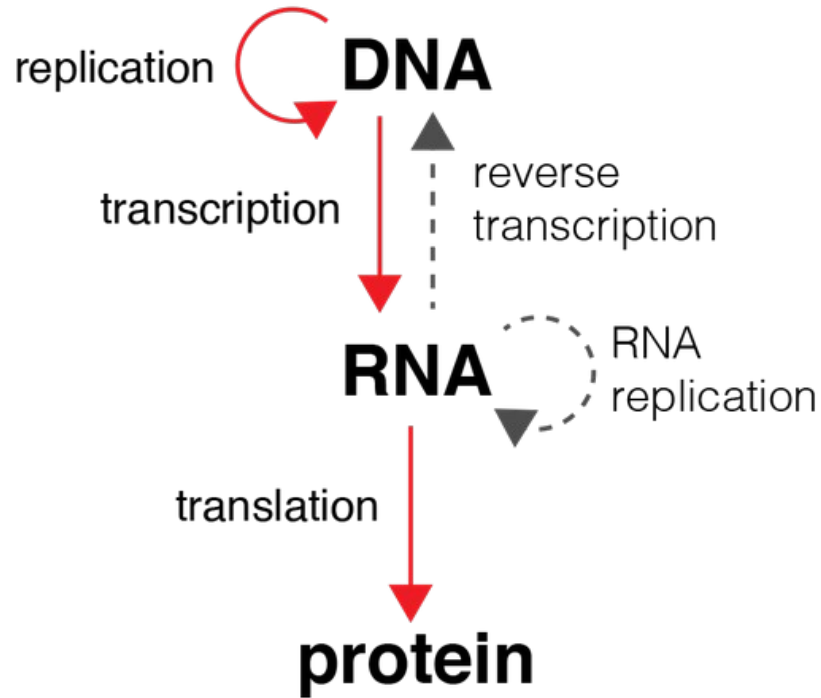


Negative regulation



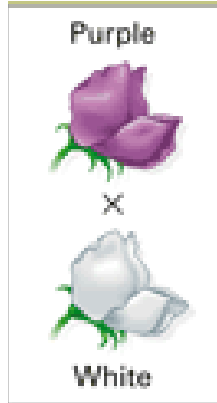
- **Regulatory proteins (RPs)** that bind to promoters can either activate or repress transcription of a given gene
- Transcription is mostly regulated by synthesizing / destroying / modifying RPs

Summary: the central dogma



- **Genes** are chromosomal regions that **code** for **proteins** (“one gene – one protein”)
- Some DNA sequences provide instructions on when, where and how much of a protein to produce – **regulatory sequences (like promoters)**

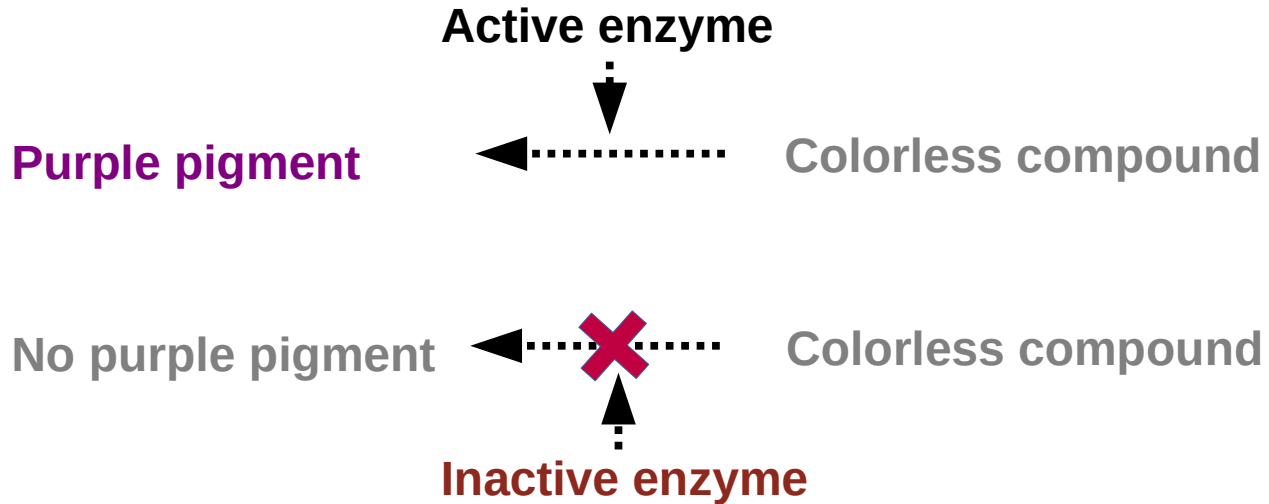
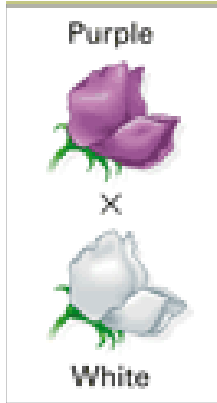
Genes to phenotype: simple case



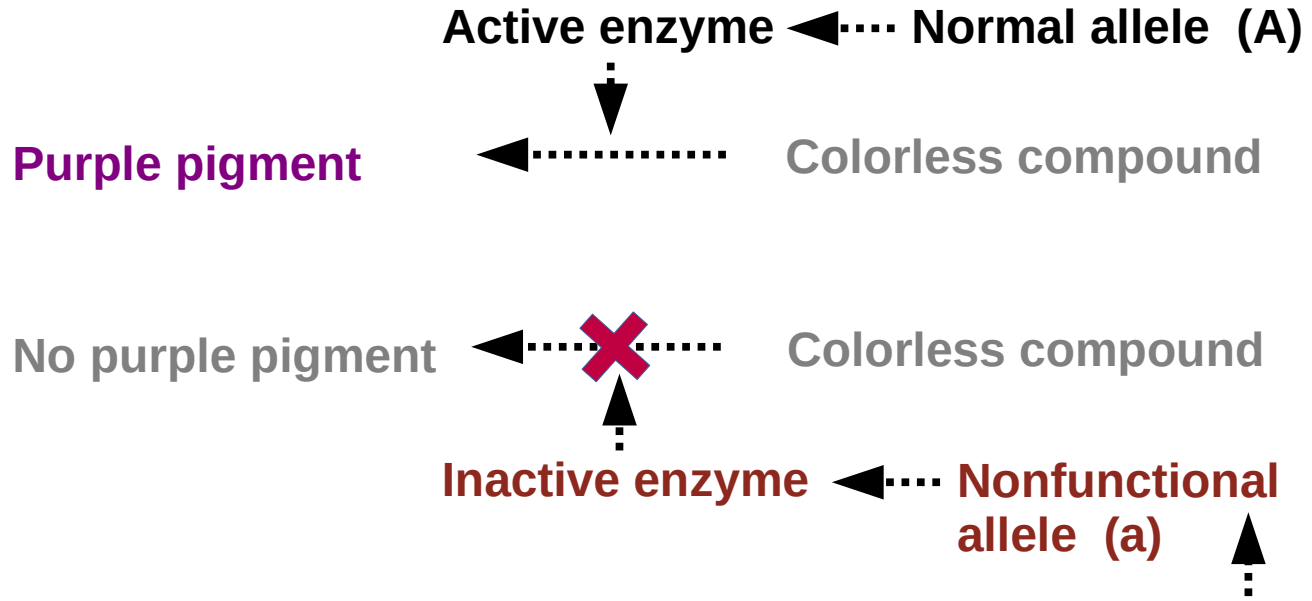
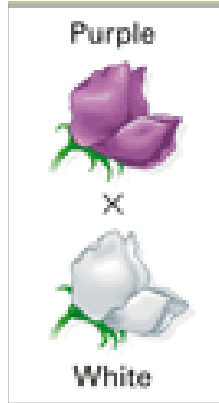
Purple pigment

No purple pigment

Genes to phenotype: simple case

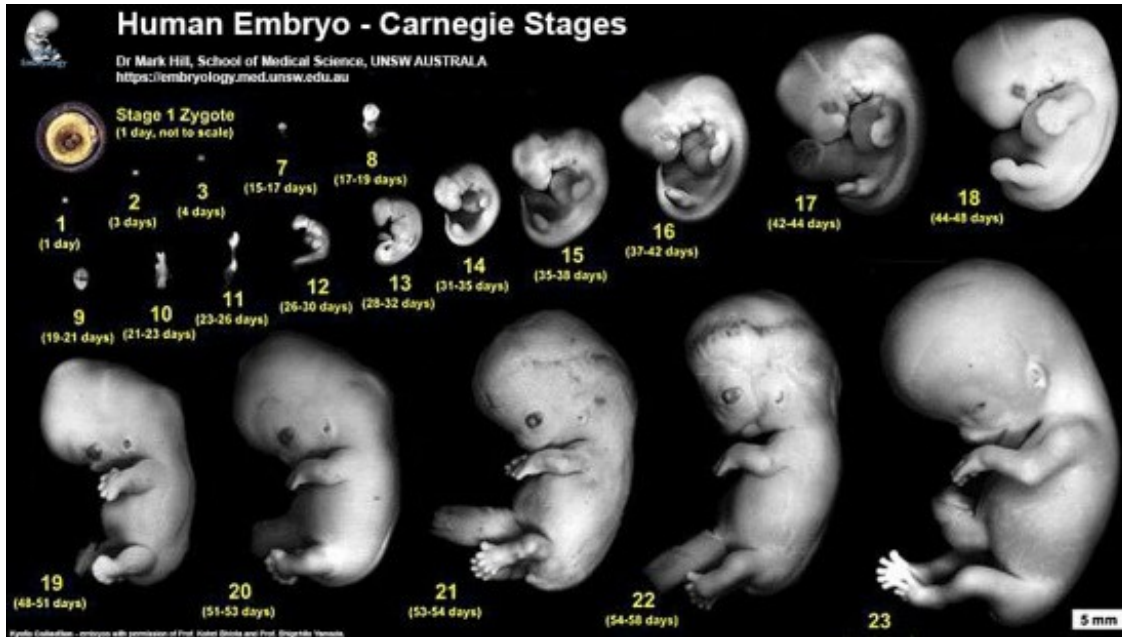


Genes to phenotype: simple case



Mutation in the protein-coding part: incorrect AA sequence
Mutation in the promoter – no transcription happening

Genotype to phenotype



https://embryology.med.unsw.edu.au/embryology/index.php/Embryonic_Development

- **Development** is the link between genotype and phenotype
- RPs control the **time, place and levels** of other proteins' expression
- This controls the cellular and organismal processes incl. development

Summary

- Proteins do most of the work in the cell/organism including being enzymes
- The function of a protein depends on its amino acid sequence
- This sequence is defined by the nucleotide sequence of a gene and is decoded during transcription and translation
- The genetic code is a rule how to convert nucleotide sequence into amino acid sequence

Summary

- Interaction between regulatory sequences and regulatory proteins controls most of the processes in the cells and organisms by controlling the concentration of other proteins through time and space