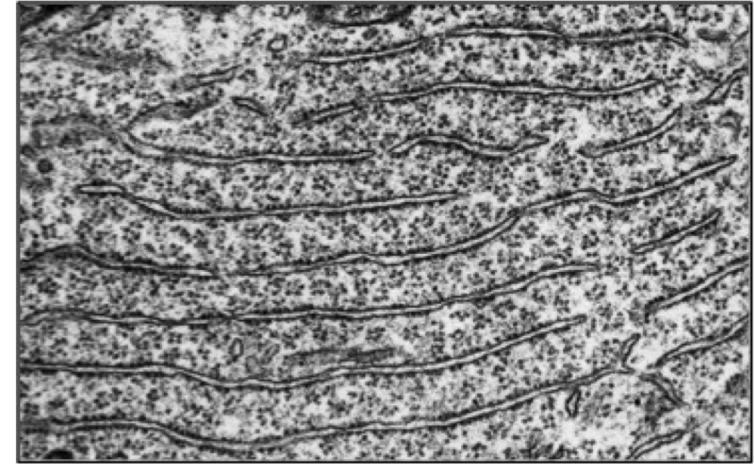
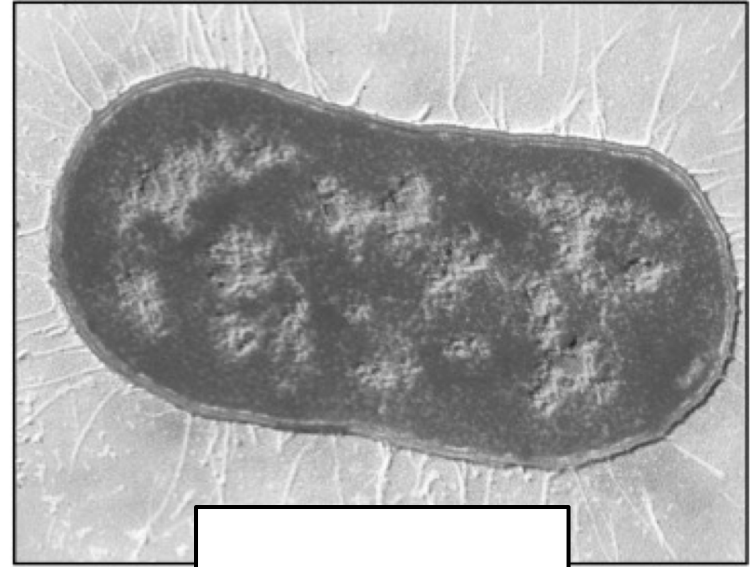
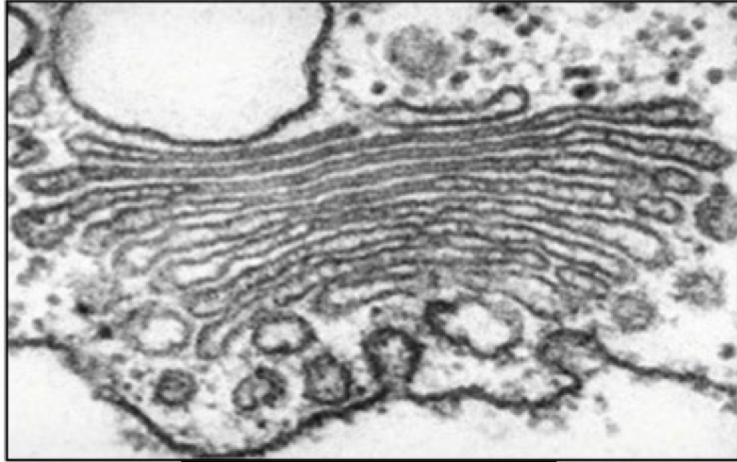
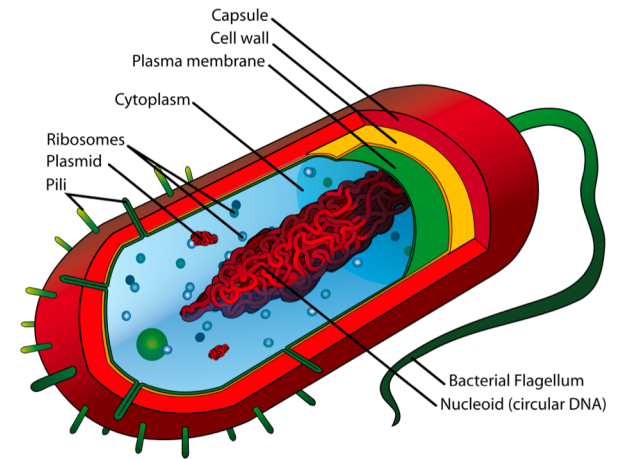
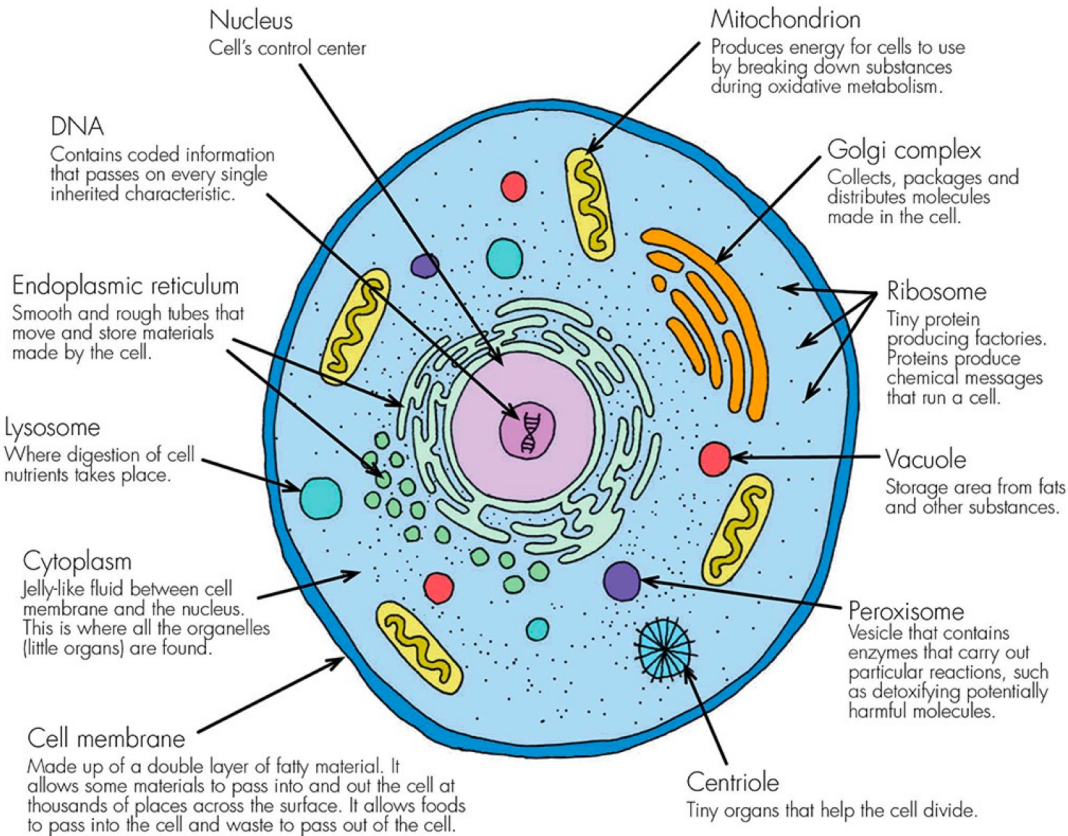


How many organelles can you name?

Image borrowed from Columbia College of Physicians and Surgeons Histology Laboratory Lab Manual
http://www.columbia.edu/itc/hs/medical/sbpm_histology_old/index.html



Cells!



Prokaryotes:
~1-2 um in diameter

Eukaryotes:
~10-40 um in diameter

TRANSCRIPTION AND TRANSLATION; GENETICS AND EPIGENETICS

How does one set of genetic instructions generate so many different outcomes?

Biological Macromolecules

- The “chemical building blocks of life”

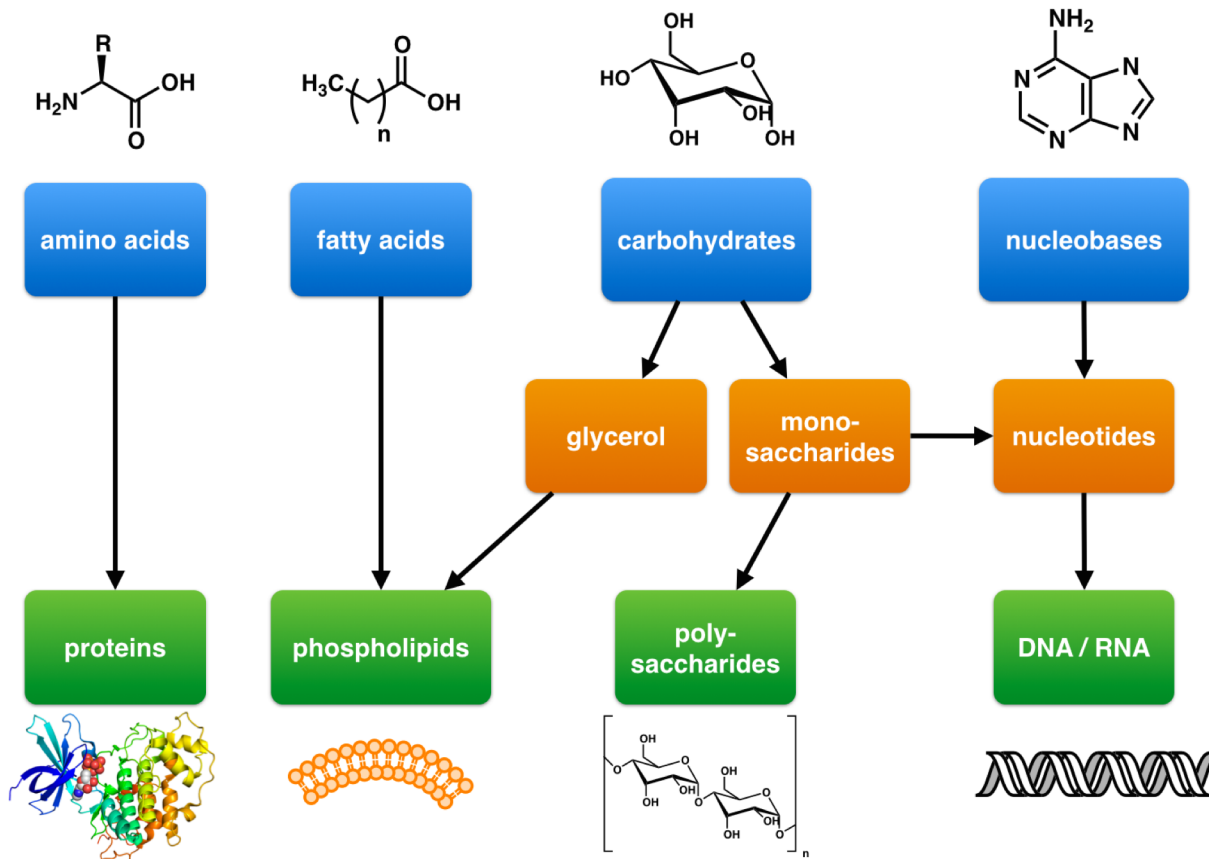
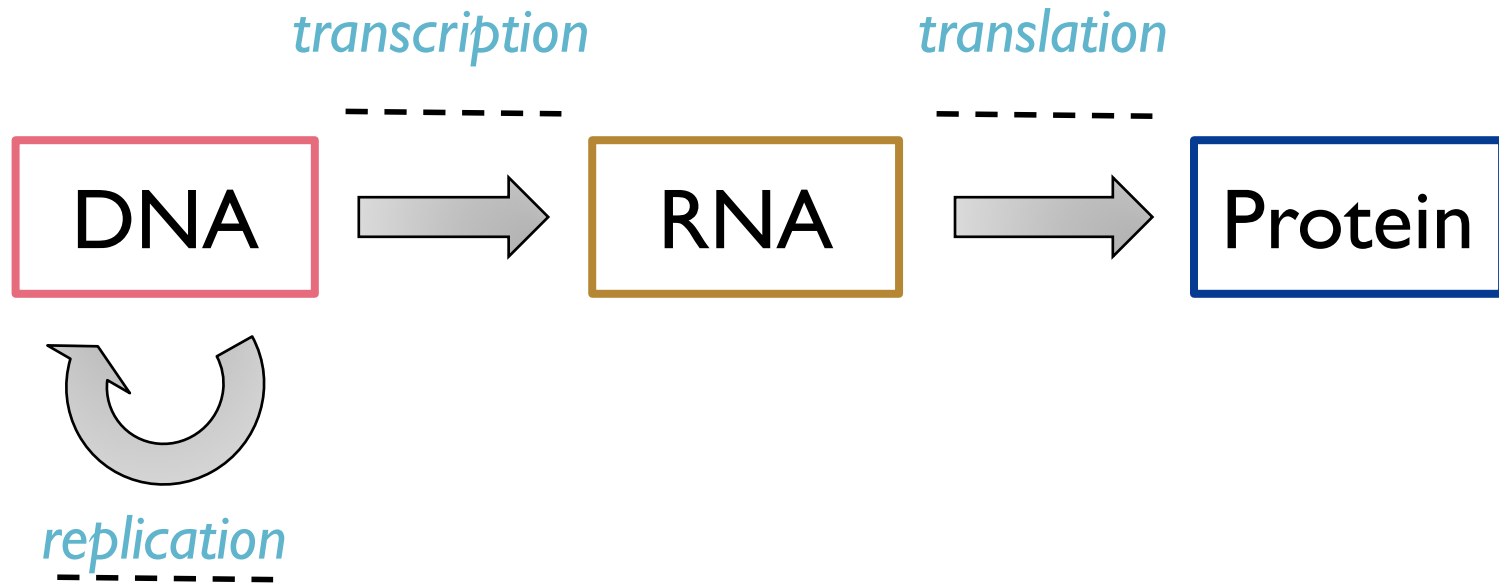


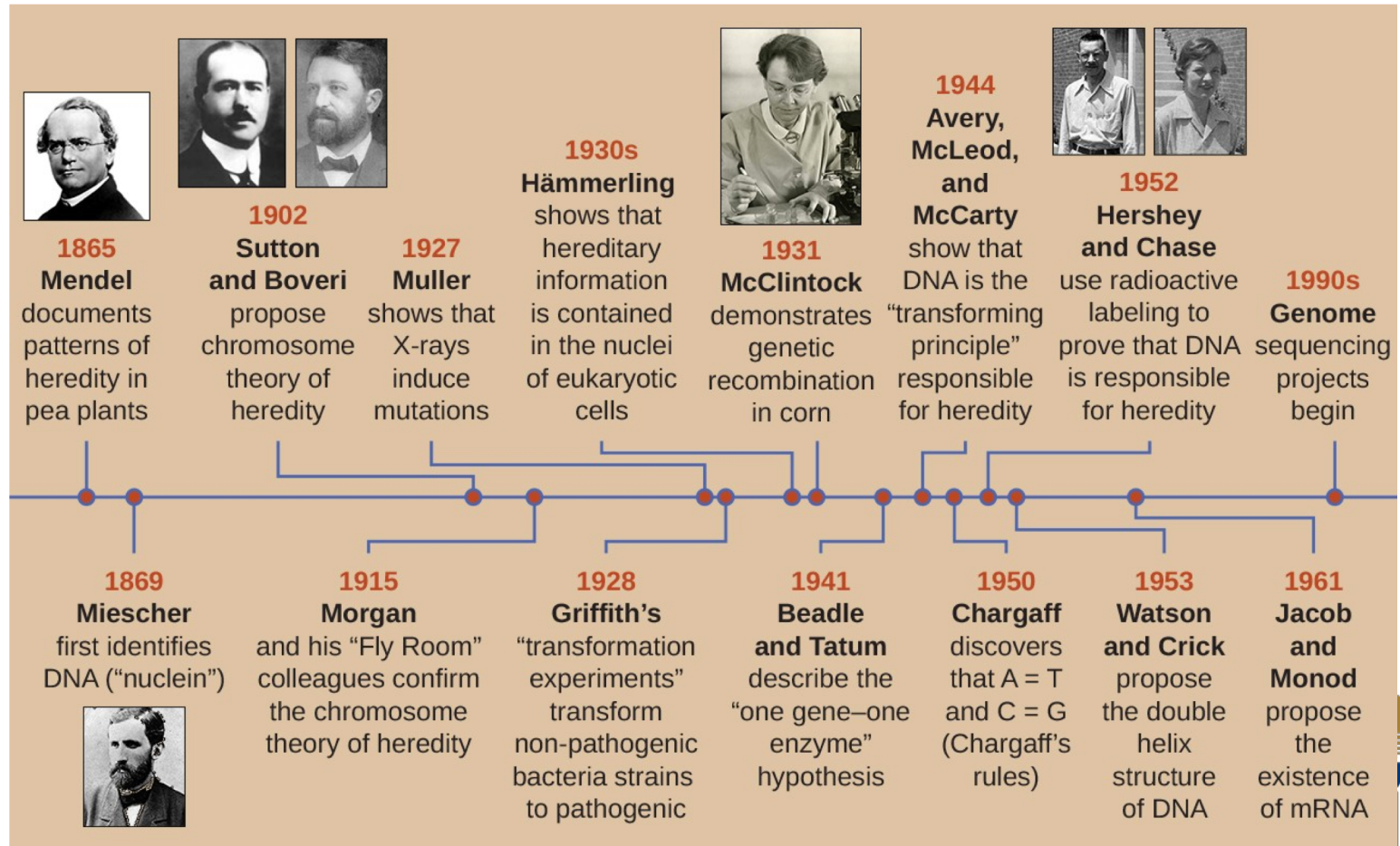
Image from Wikipedia, by BogHog
https://commons.wikimedia.org/wiki/File:Building_blocks_of_life.png

The Central Dogma



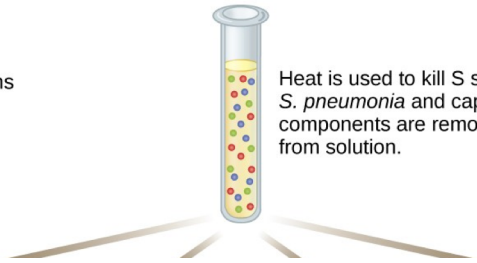
Let's go way back – before we knew what was what in a cell...

1830's
Discovery
of proteins



Determining the identity of the hereditary material

green = proteins
blue = DNA
red = RNA



Heat is used to kill S strain of *S. pneumoniae* and capsule components are removed from solution.

Avery-McLeod-McCarty experiment

Bacteria:

S strain – smooth surface, deadly

R strain – rough surface, not deadly

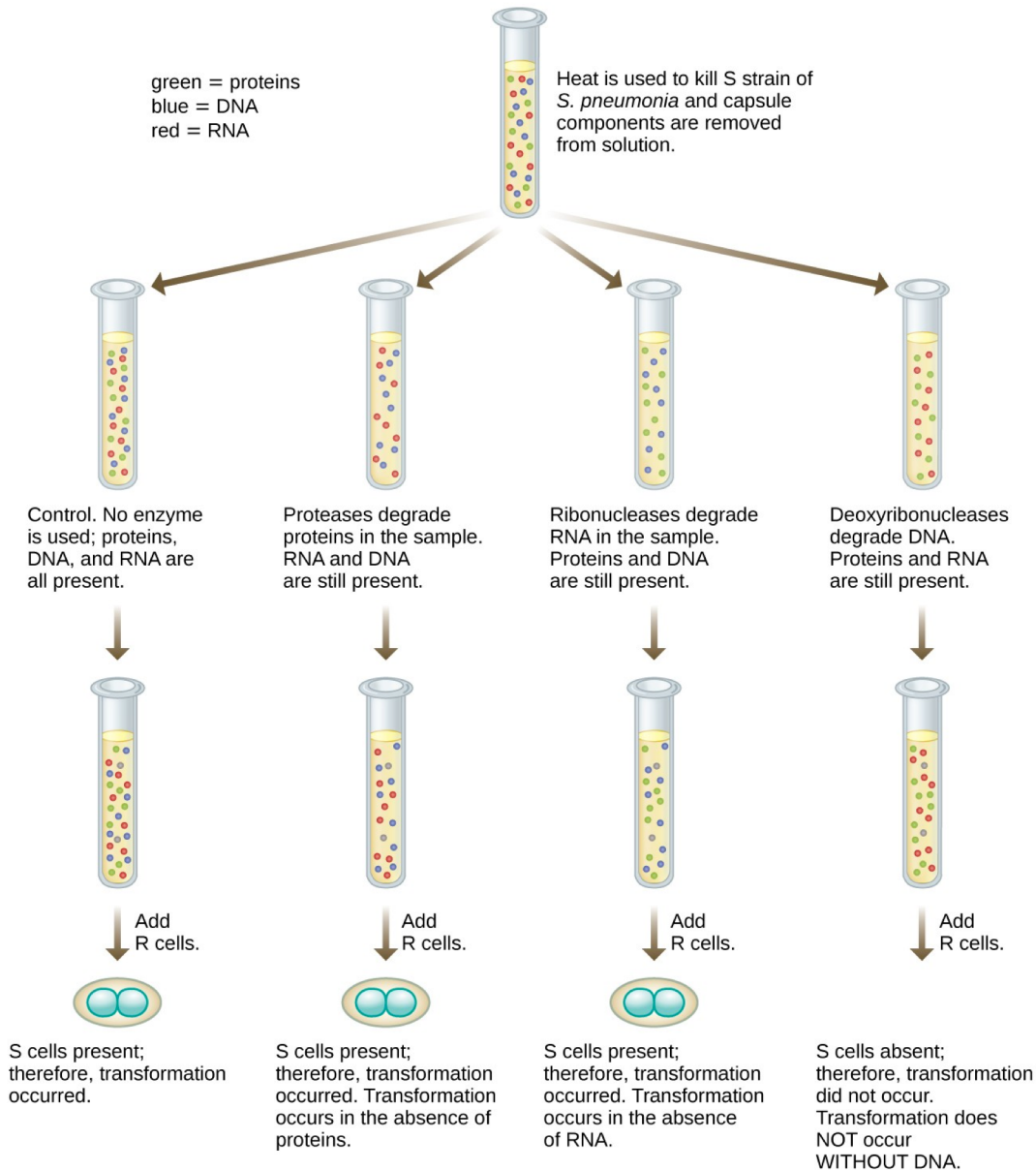


People knew the existence of proteins, RNA, and DNA

They had reagents/chemicals that could destroy each of those molecule types

How do you design the experiment to figure out what is the molecule of genetic material?

Determining the identity of the hereditary material



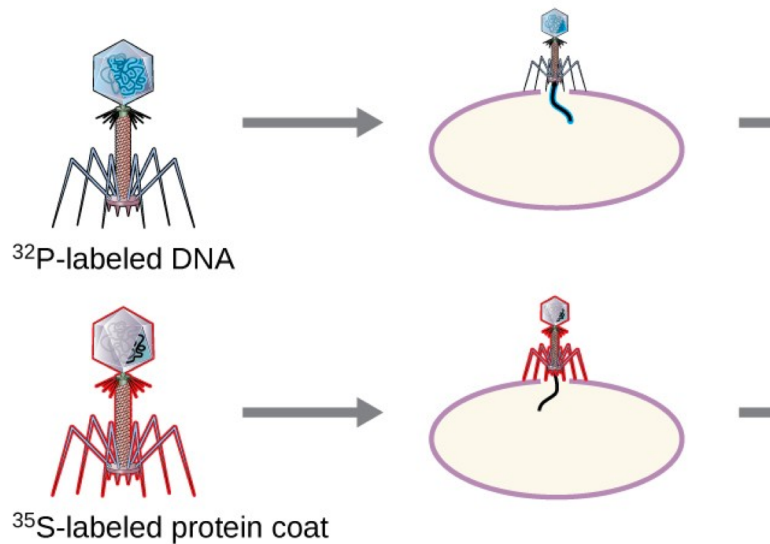
Avery-McLeod-McCarty experiment

Bacteria:

S strain – smooth surface, deadly

R strain – rough surface, not deadly

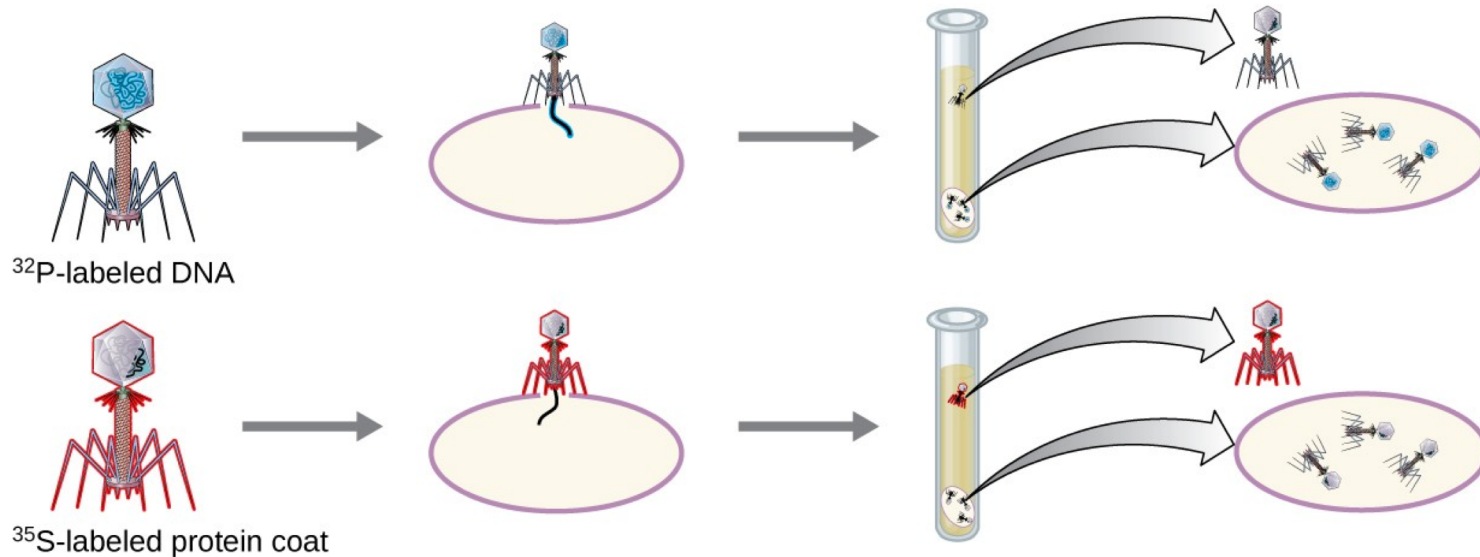
Hershey-Chase experiment: DNA (not protein) is the genetic material



?

- 1 One batch of phage was labeled with ^{32}P , which is incorporated into the DNA. Another batch of phage was labeled with ^{35}S , which is incorporated into the protein coat.
- 2 Bacteria were infected with the phage. The researchers were looking to identify if viral DNA or viral protein entered the host cell.
- 3

Hershey-Chase experiment: DNA (not protein) is the genetic material



1 One batch of phage was labeled with ^{32}P , which is incorporated into the DNA. Another batch of phage was labeled with ^{35}S , which is incorporated into the protein coat.

2 Bacteria were infected with the phage. The researchers were looking to identify if viral DNA or viral protein entered the host cell.

3 The cultures were blended and centrifuged to separate the phage from the bacteria. The centrifuge separated the lighter phage particles from the heavier bacterial cells.

4 Bacteria infected with phage containing ^{32}P -labeled DNA produced ^{32}P -labeled phage. Bacteria infected with ^{35}S -labeled phage produced unlabeled phage.

Chargaff's Rules

Table 3-2 Data Leading to the Formulation of Chargaff's Rules

Source	Adenine to Guanine	Thymine to Cytosine	Adenine to Thymine	Guanine to Cytosine	Purines to Pyrimidines
Ox	1.29	1.43	1.04	1.00	1.1
Human	1.56	1.75	1.00	1.00	1.0
Hen	1.45	1.29	1.06	0.91	0.99
Salmon	1.43	1.43	1.02	1.02	1.02
Wheat	1.22	1.18	1.00	0.97	0.99
Yeast	1.67	1.92	1.03	1.20	1.0
<i>Hemophilus influenzae</i>	1.74	1.54	1.07	0.91	1.0
<i>E-coli</i> K2	1.05	0.95	1.09	0.99	1.0
Avian tubercle bacillus	0.4	0.4	1.09	1.08	1.1
<i>Serratia marcescens</i>	0.7	0.7	0.95	0.86	0.9
<i>Bacillus schatz</i>	0.7	0.6	1.12	0.89	1.0

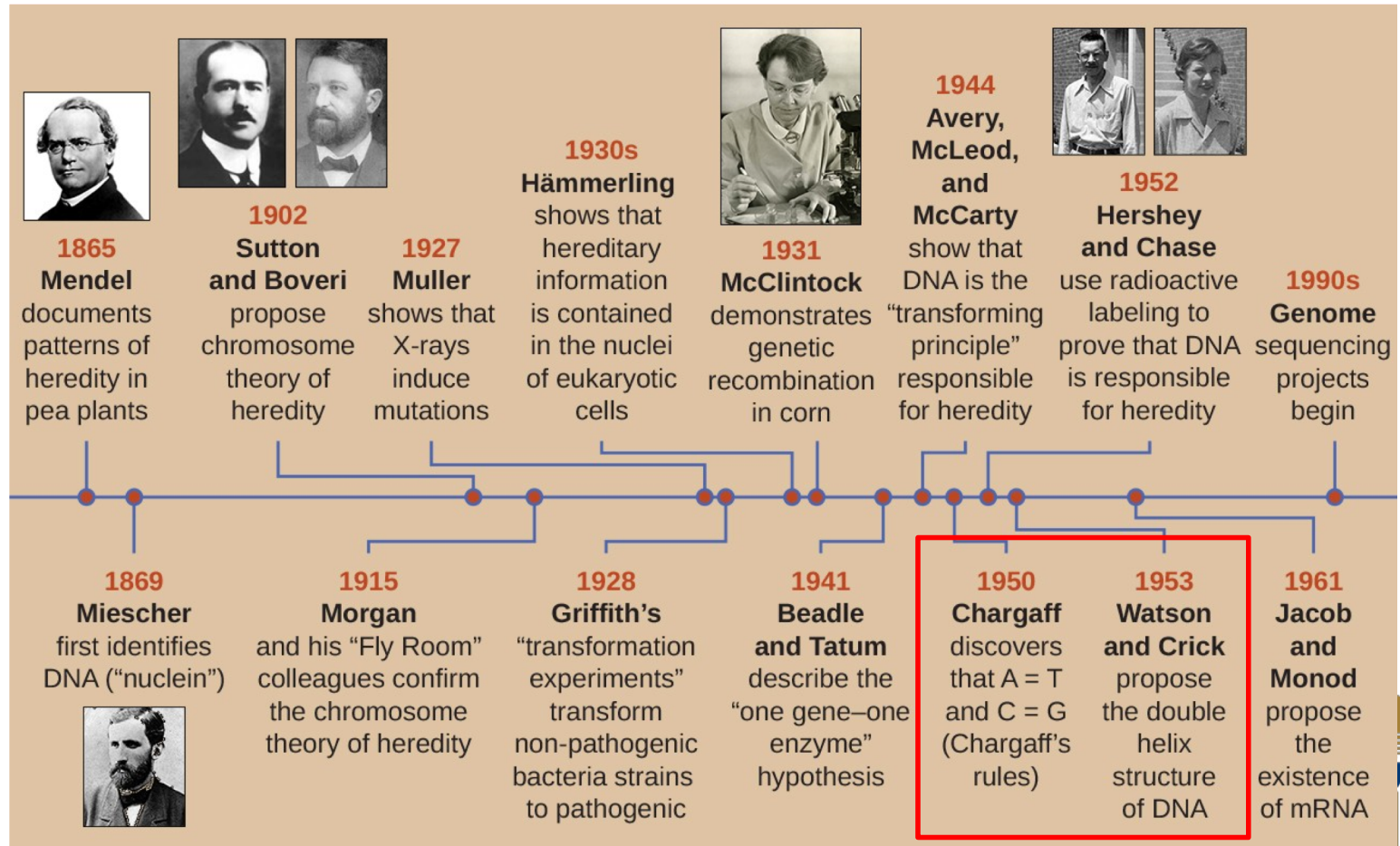
SOURCE: After E. Chargaff et al., *J. Biol. Chem.* 177 (1949).

1. The base composition of DNA varies between species
2. In any species the number of A and T bases are equal, and the number of G and C bases are equal

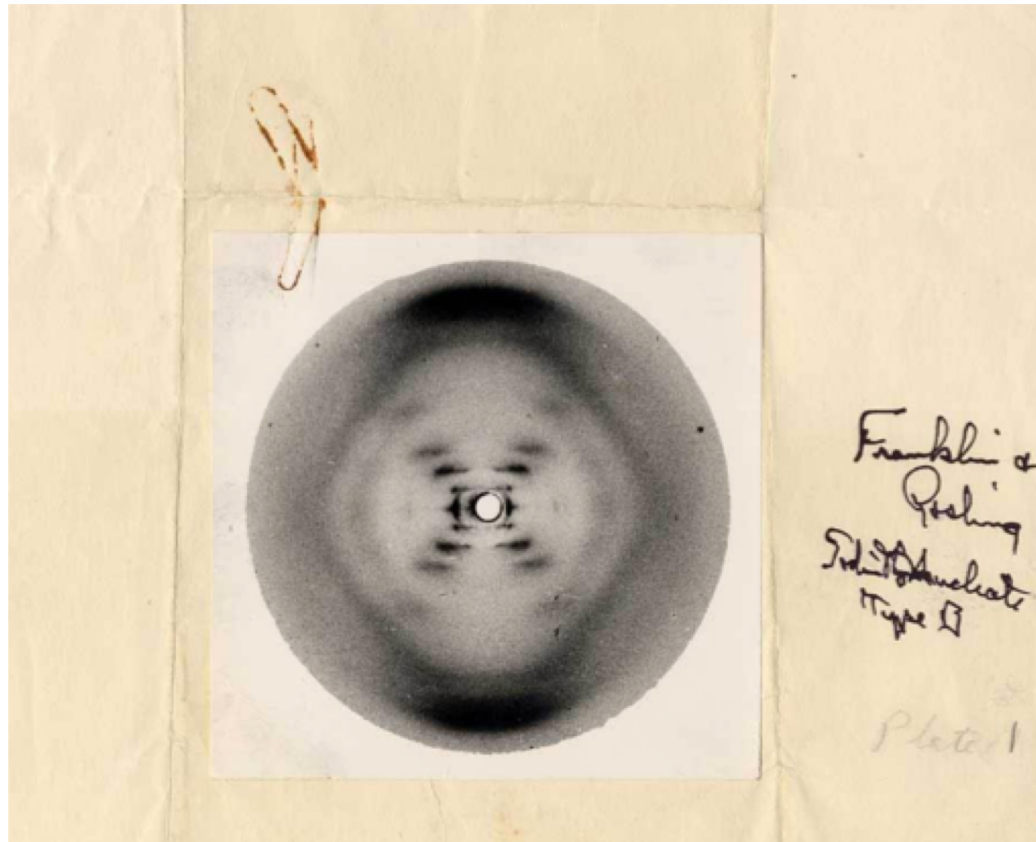
But why?

Let's go way back – before we knew what was what in a cell...

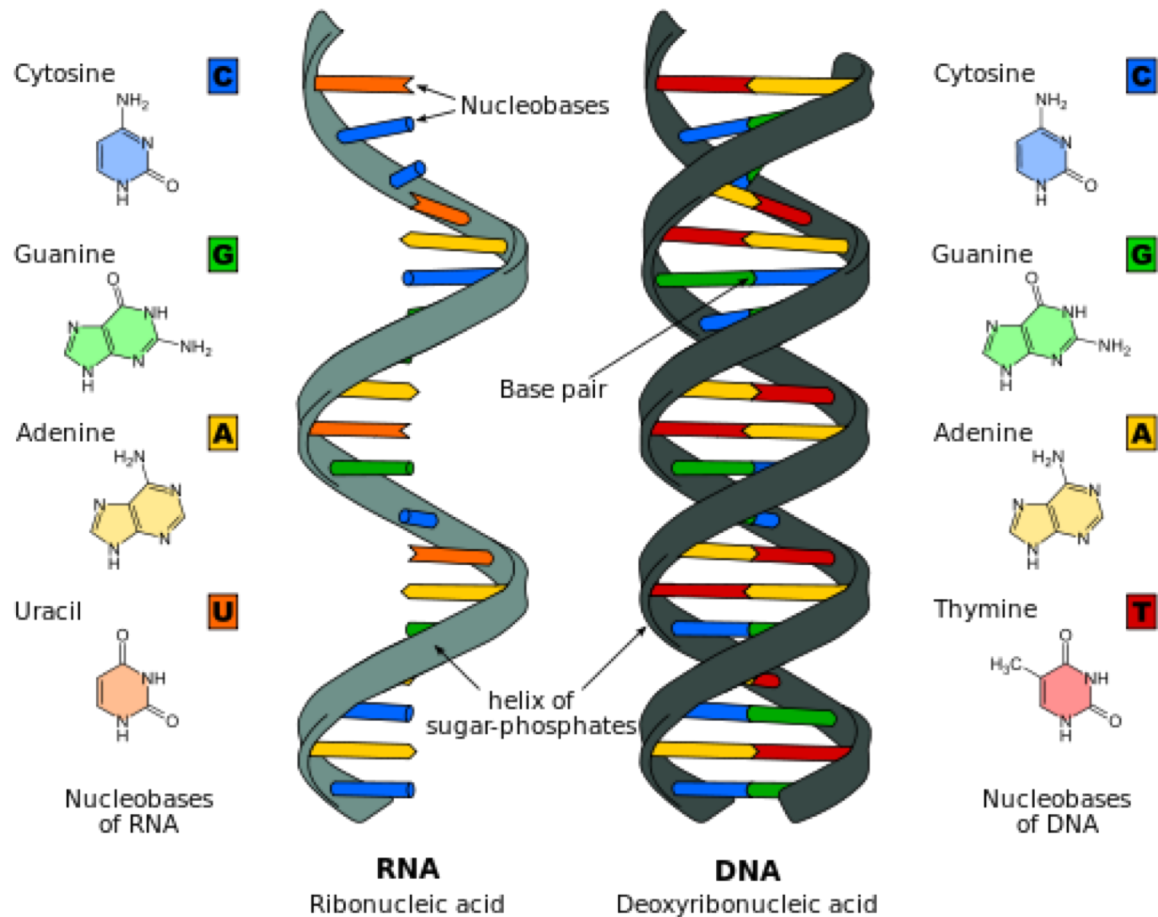
1830's
Discovery
of proteins



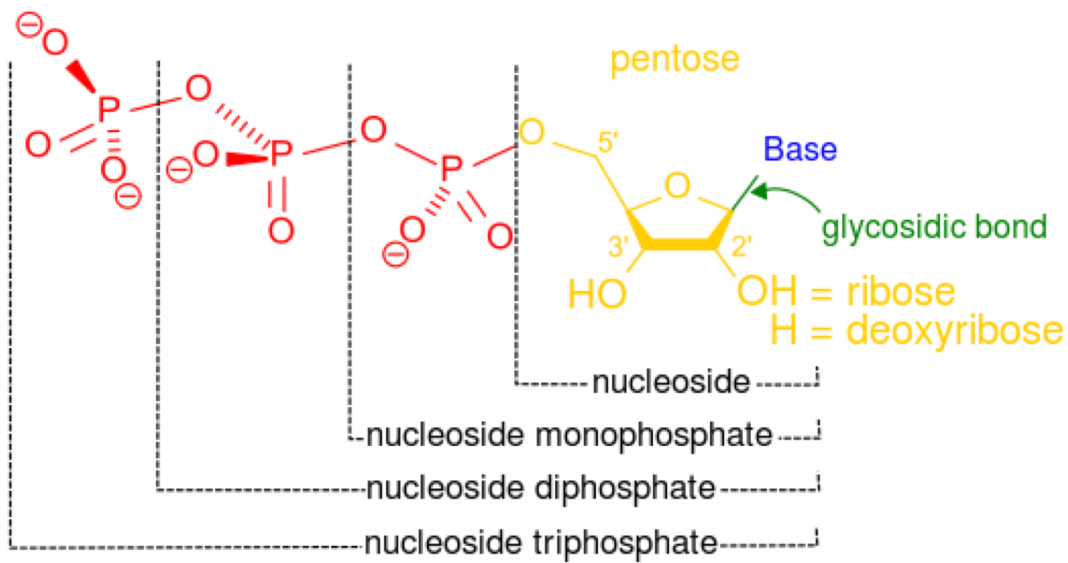
The discovery of the structure of DNA explains Chargaff's rules



DNA double helix



By Difference_DNA_RNA-DE.svg: Spunk (talk) translation: Spunk [CC BY-SA 3.0 (<http://creativecommons.org/licenses/by-sa/3.0>), via Wikimedia Commons



Purines

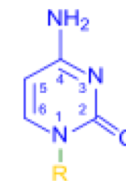


Adenine

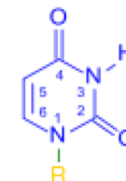


Guanine

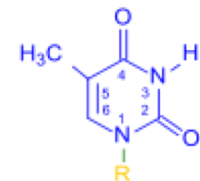
Pyrimidines



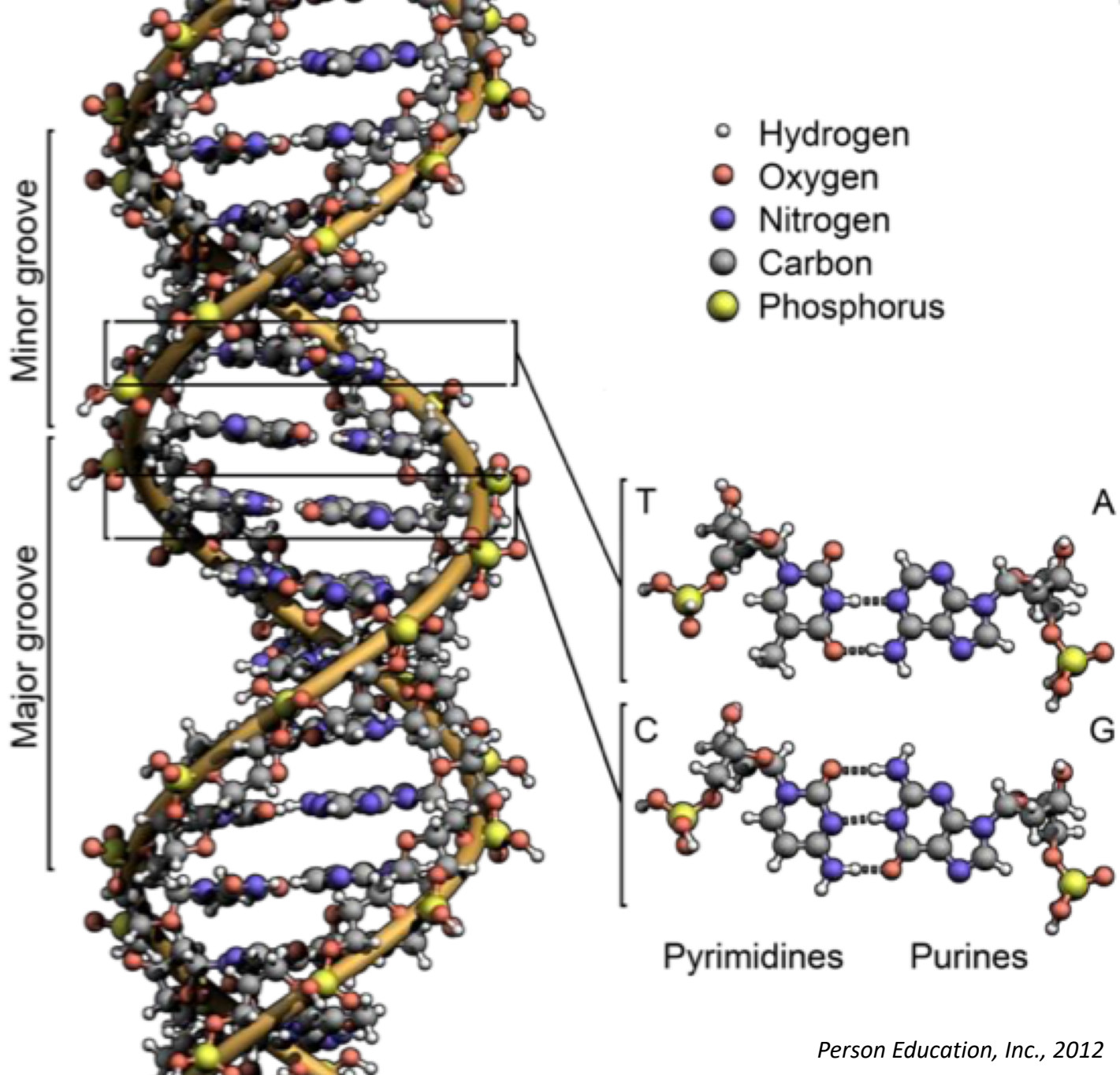
Cytosine



Uracil

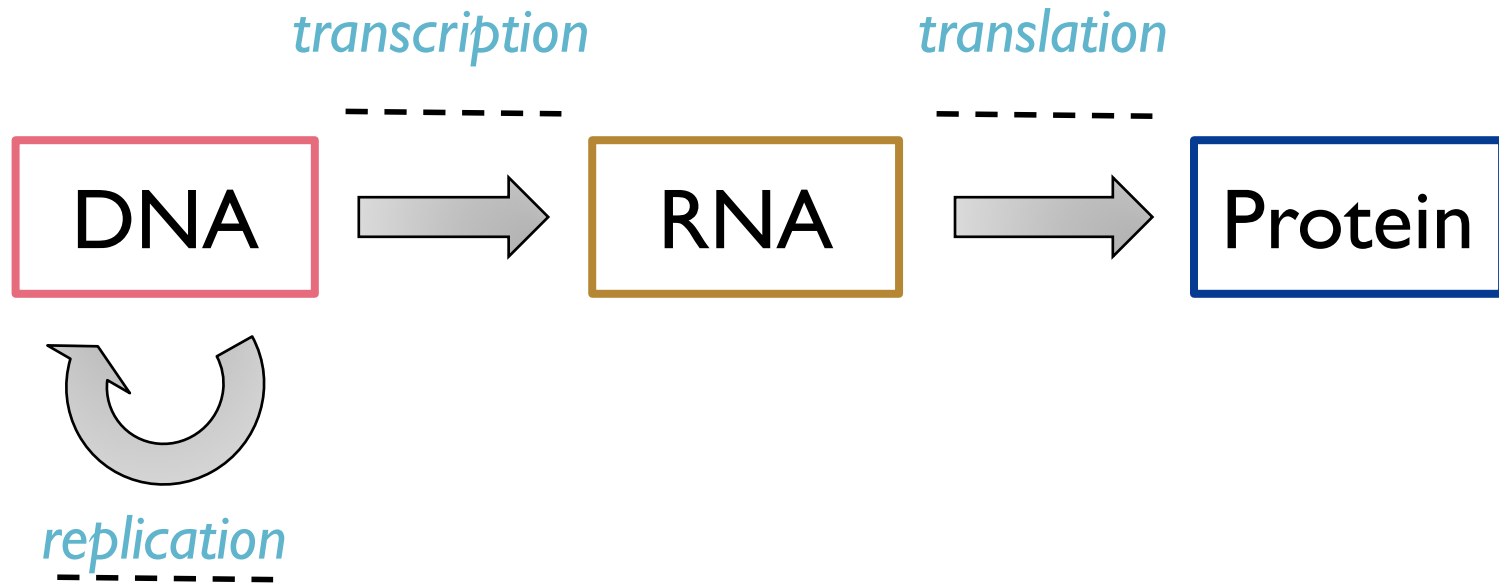


Thymine



Person Education, Inc., 2012

The Central Dogma



DNA replication

Three postulated methods of DNA Replication




Semi-Conservative



Conservative*



Dispersive*

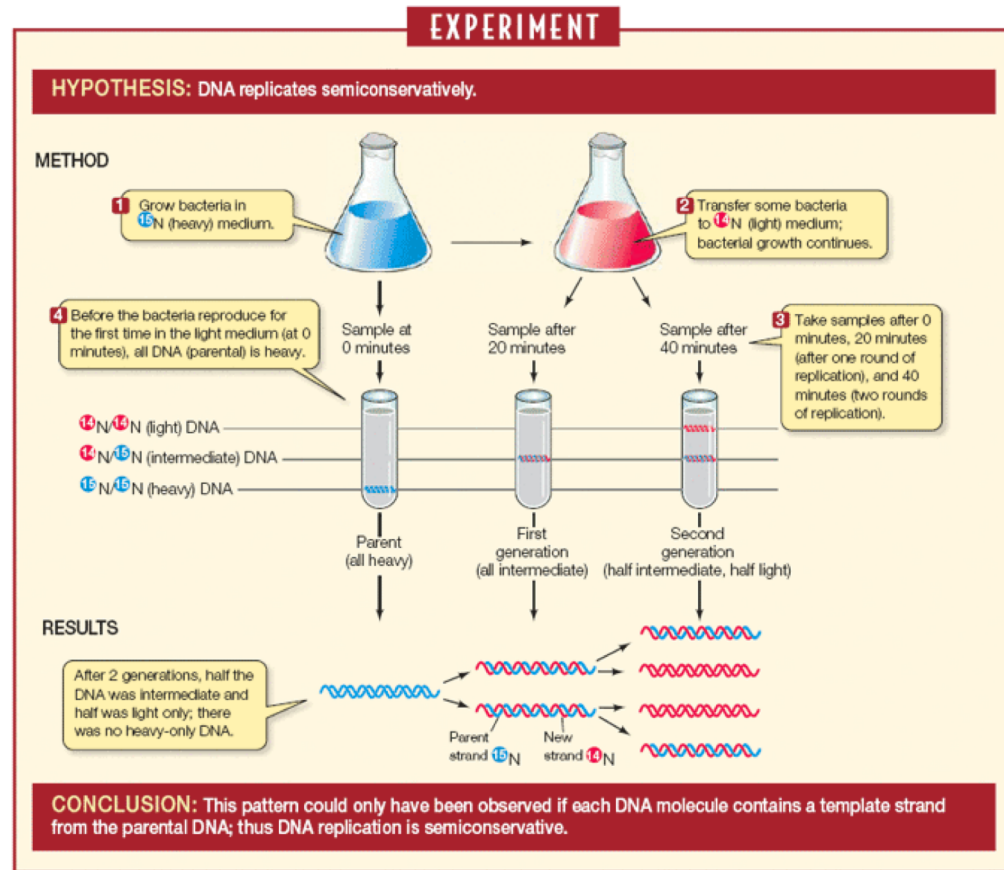
 Newly, synthesized strand

From: wikipedia

Discussion: Design an experiment to show which of these is the correct model

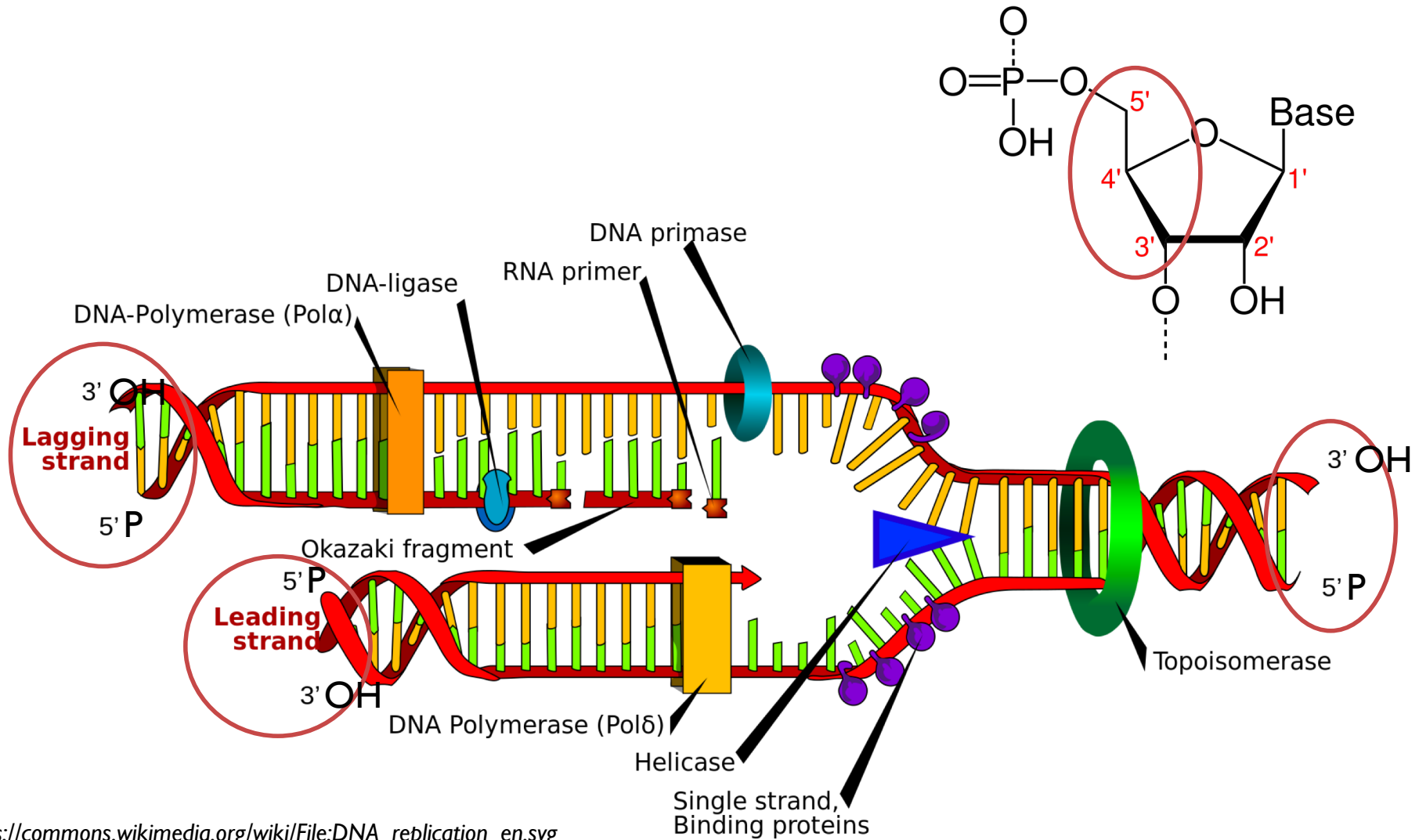
Meselson-Stahl demonstrated that DNA replication was semiconservative

Helpful video: <https://www.youtube.com/watch?v=4gdWOWjioBE>



<https://www.nature.com/scitable/content/the-meselson-stahl-experiment-18551>

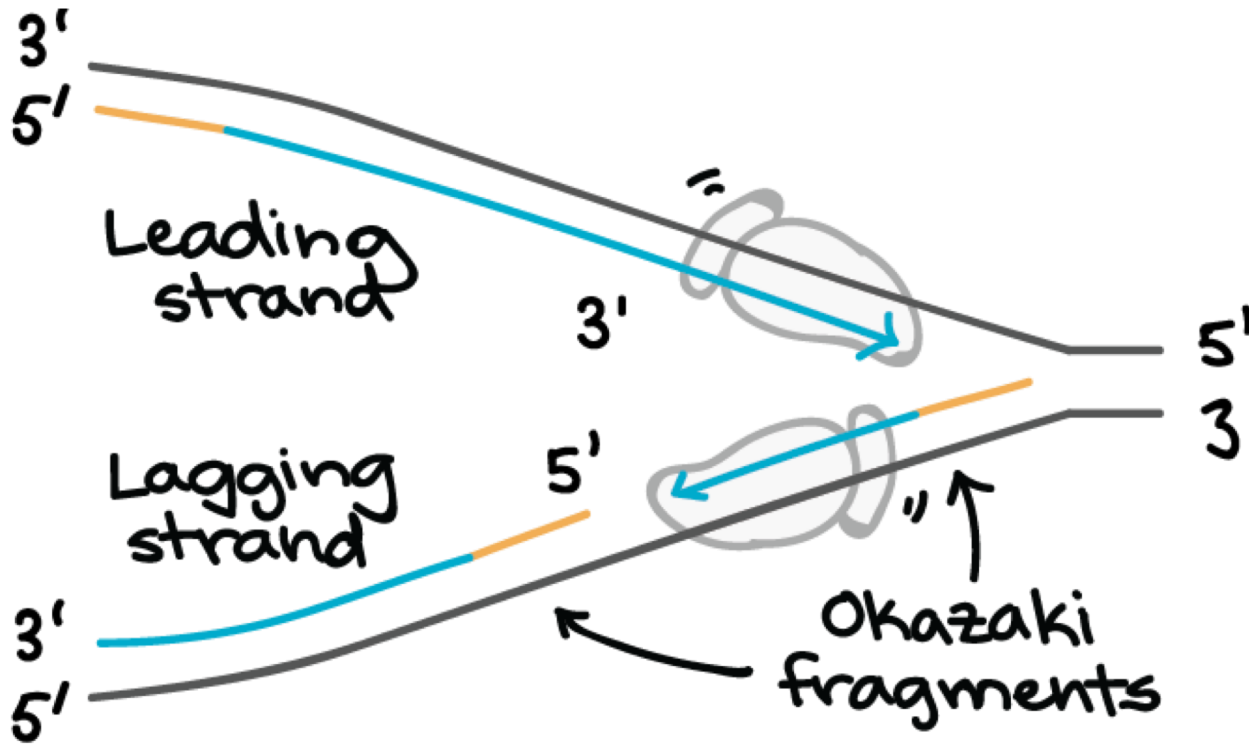
DNA replication machinery



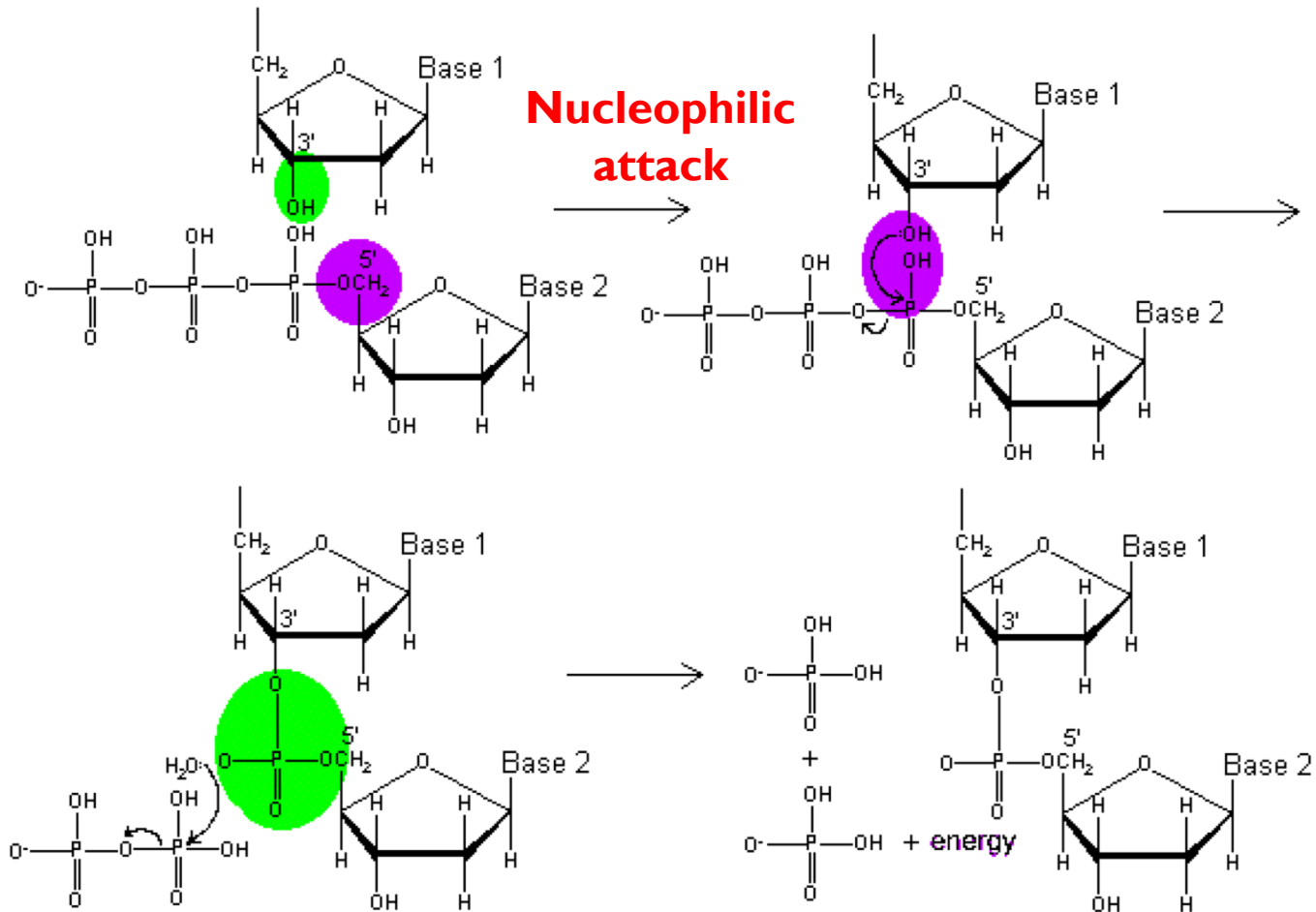
https://commons.wikimedia.org/wiki/File:DNA_replication_en.svg

<https://www.youtube.com/watch?v=TNKWgcFPHqw>

DNA replication machinery

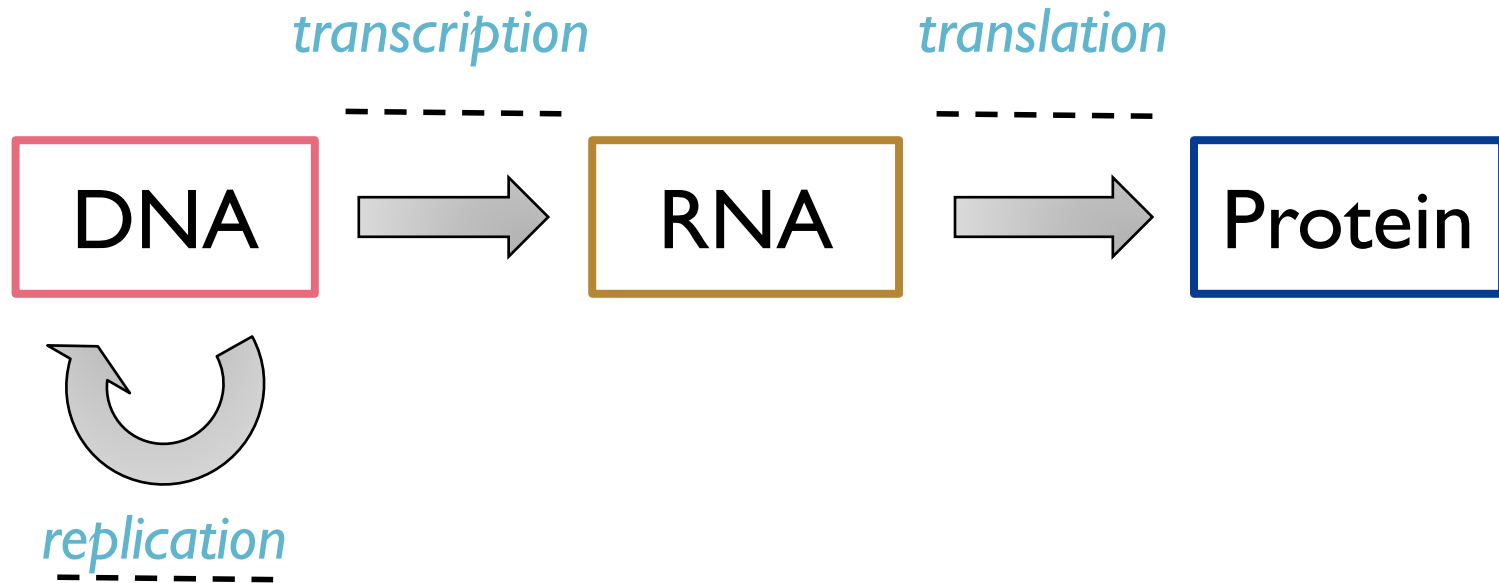


DNA replication chemistry

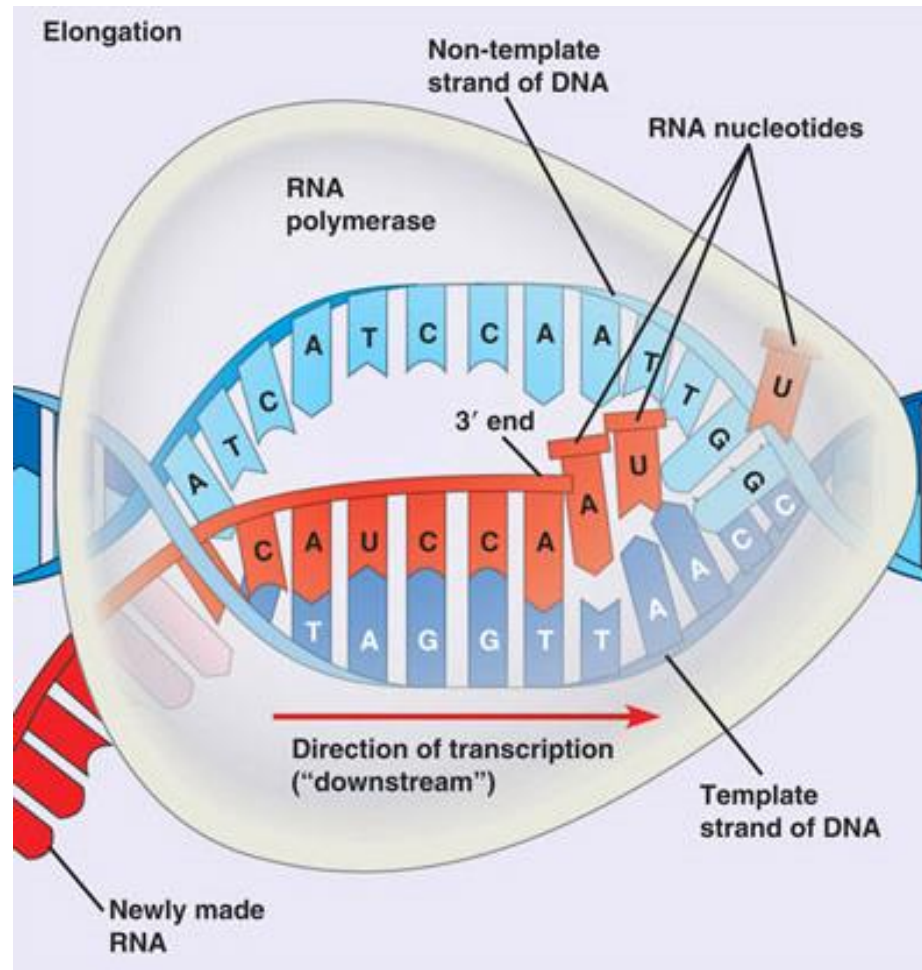


[https://chem.libretexts.org/Bookshelves/General_Chemistry/Book%3A_ChemPRIME_\(Moro_et_al.\)/20Molecules_in_Living_Systems/20.20%3A_DNA_Replication](https://chem.libretexts.org/Bookshelves/General_Chemistry/Book%3A_ChemPRIME_(Moro_et_al.)/20Molecules_in_Living_Systems/20.20%3A_DNA_Replication)

The Central Dogma



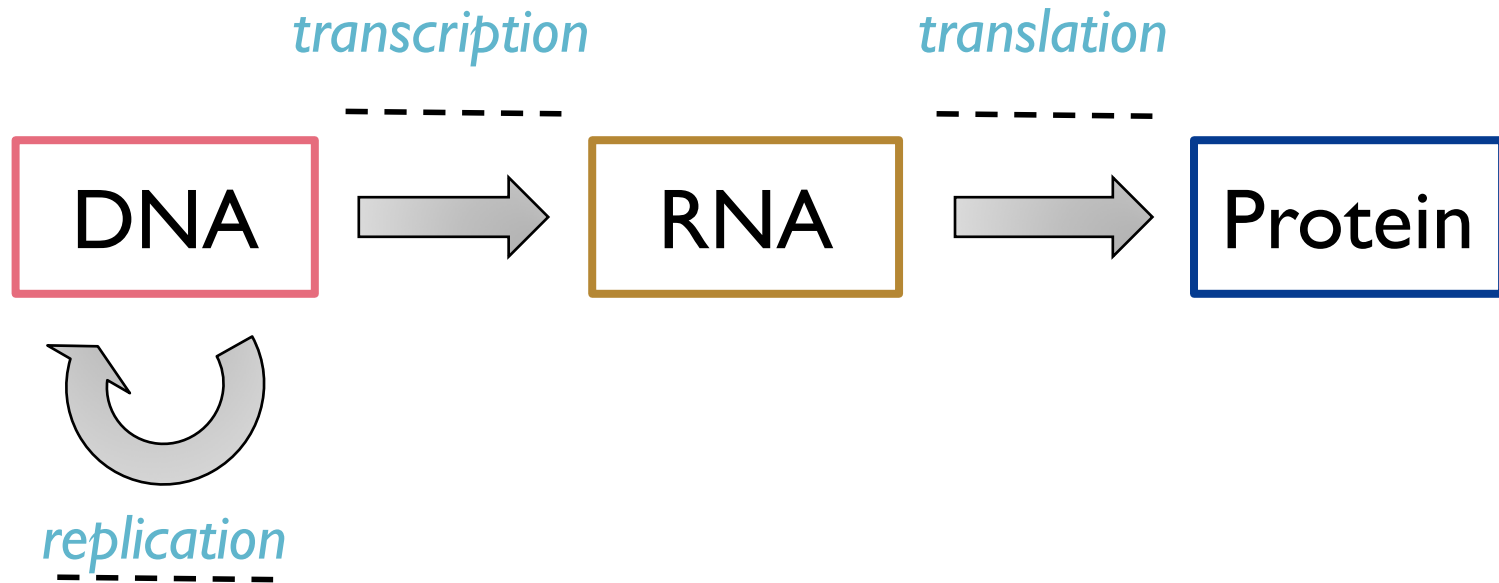
Transcription: Blueprint to Messages

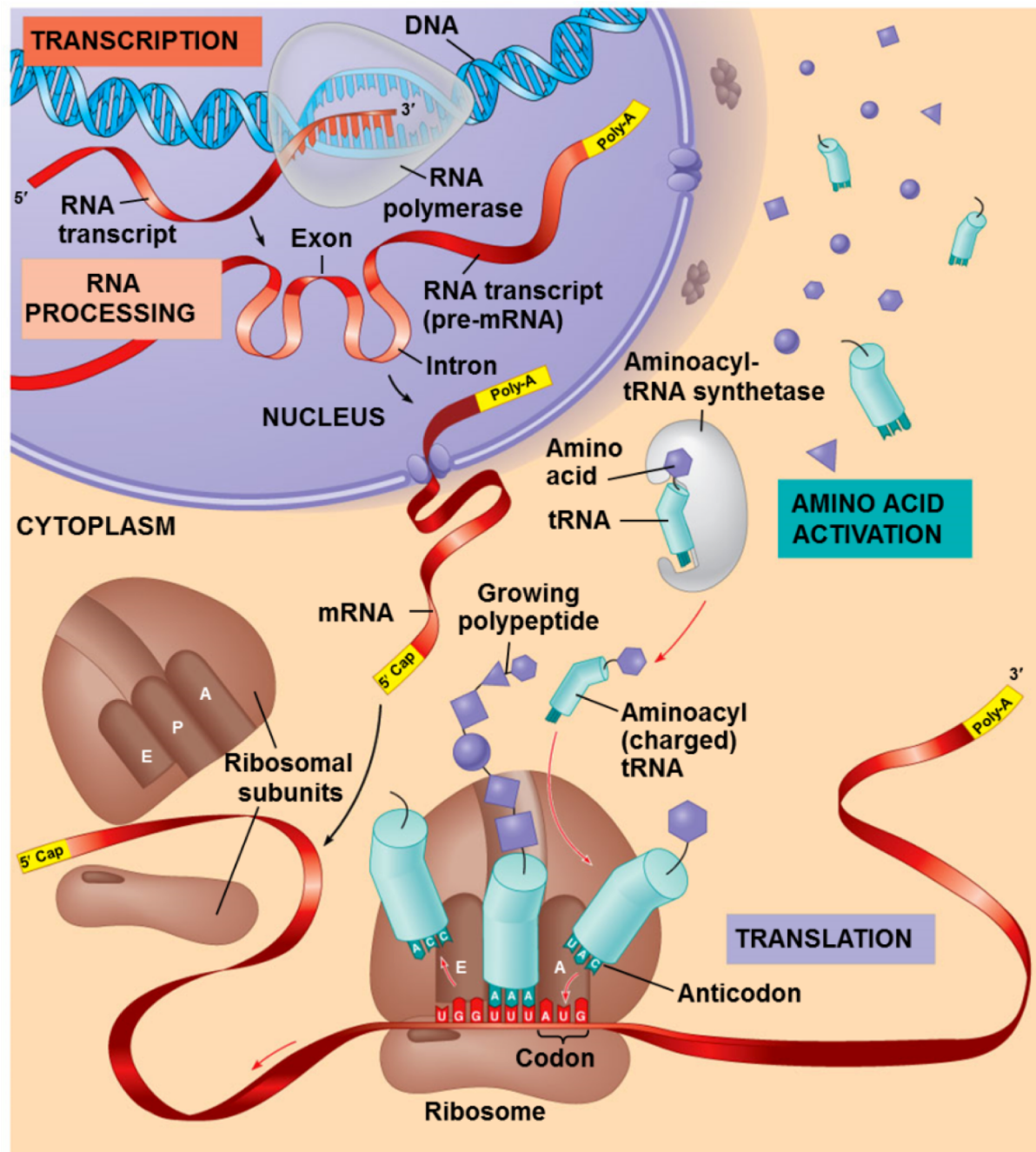
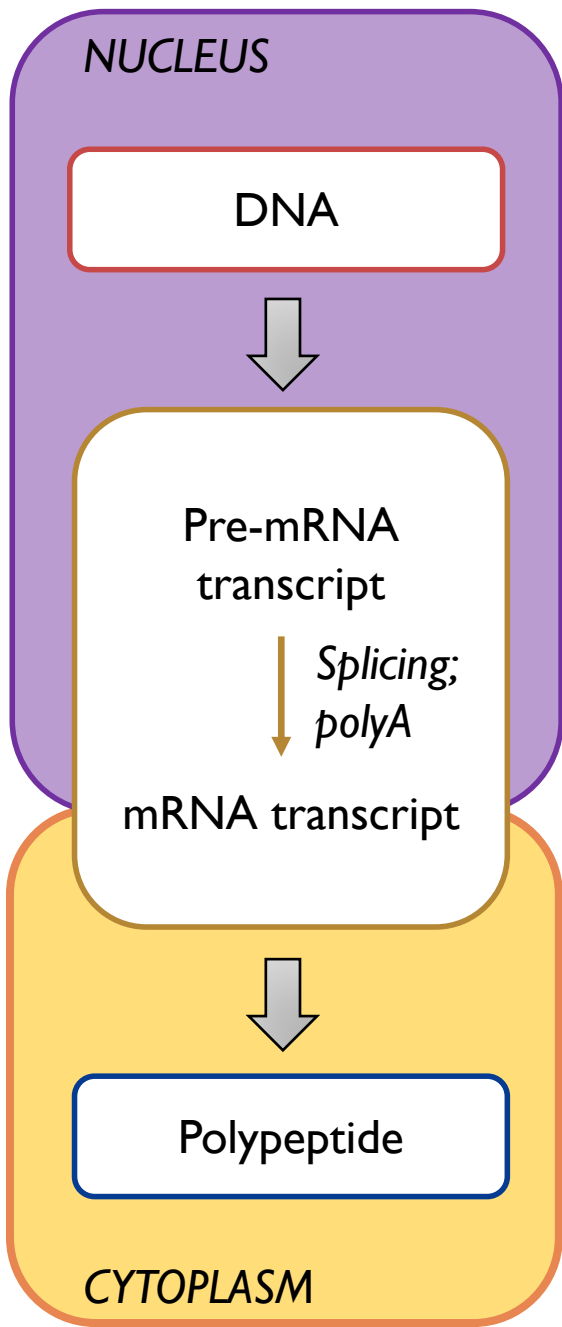


Molecular Biology of the Cell, 5th Edition Garland Science, 2008.

<https://youtu.be/vLz2A1cjPH8>

The Central Dogma

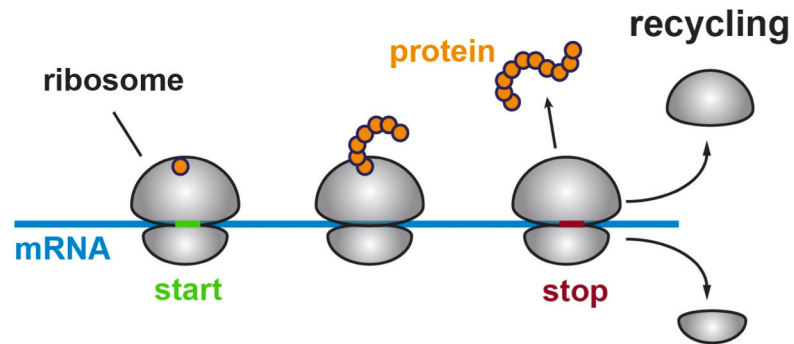
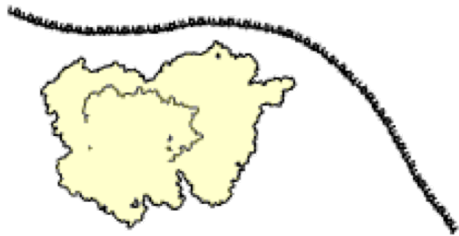
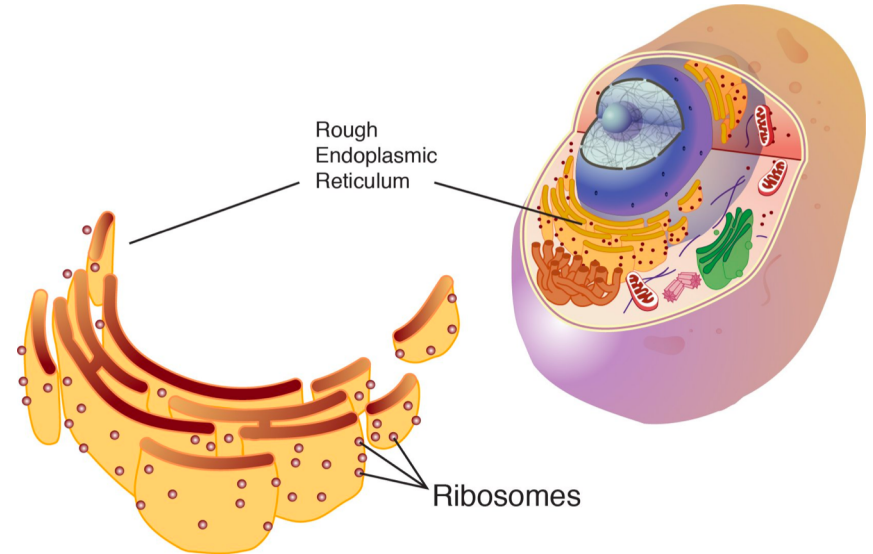




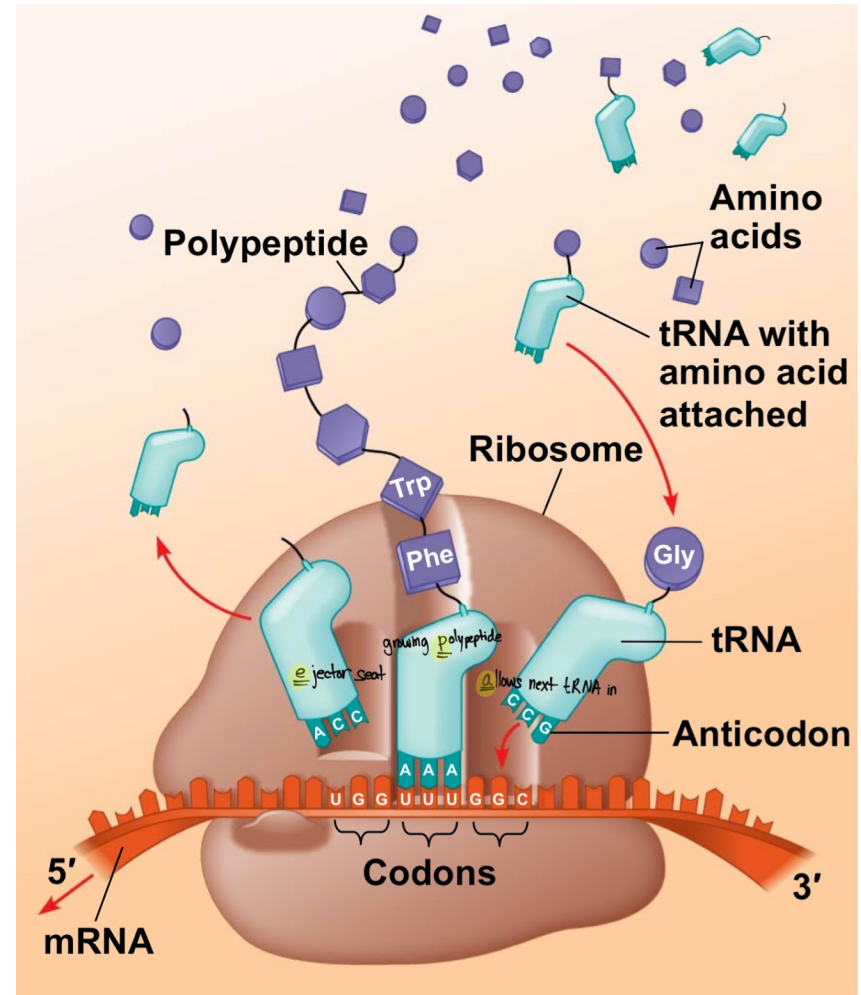
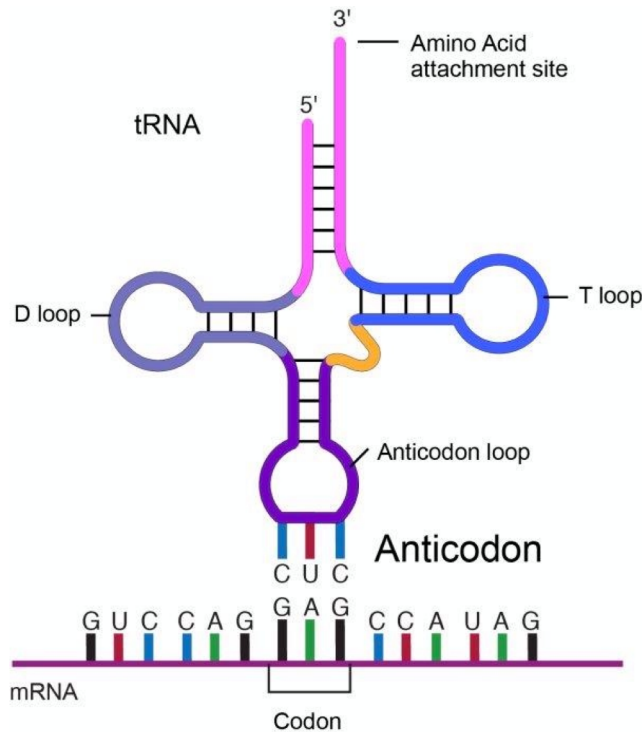
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Ribosome

- It makes proteins!
- Needs help from other things in the cell like tRNA

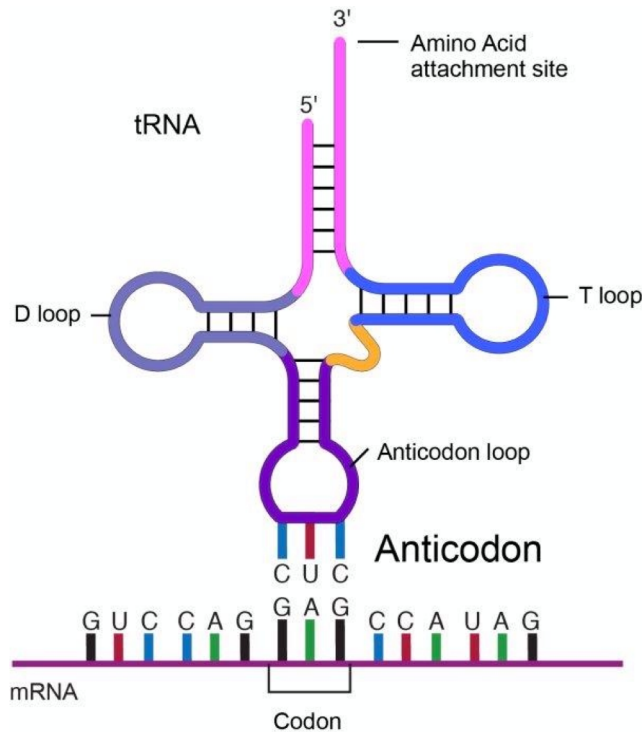


Translation: Messages to end products



Molecular Biology of the Cell, 5th Edition Garland Science, 2008.
Molecular Biology of the Cell, 7th Edition Garland Science, 2013.

Translation codon: The genetic code



		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 } Gin 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

Putting everything together

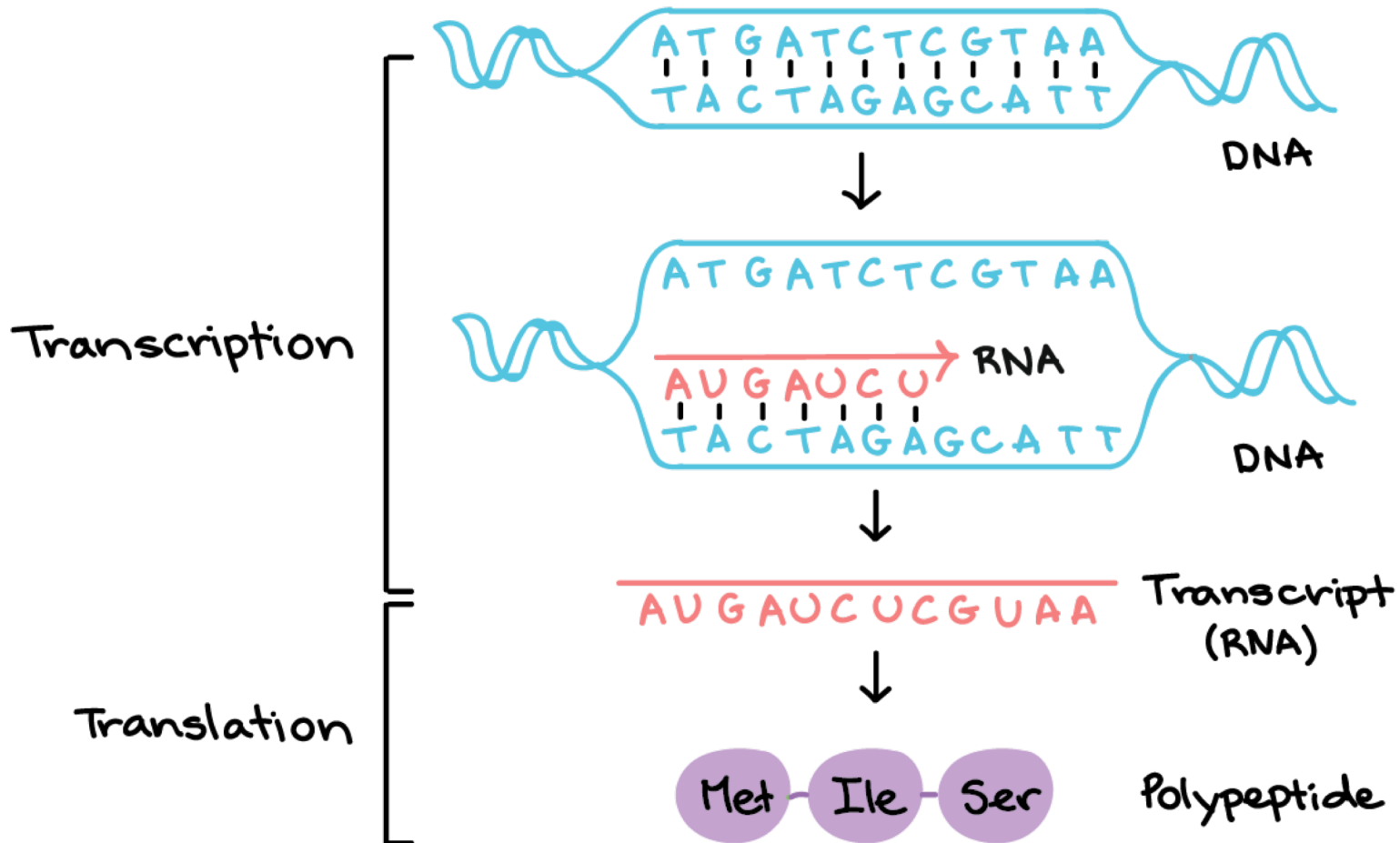
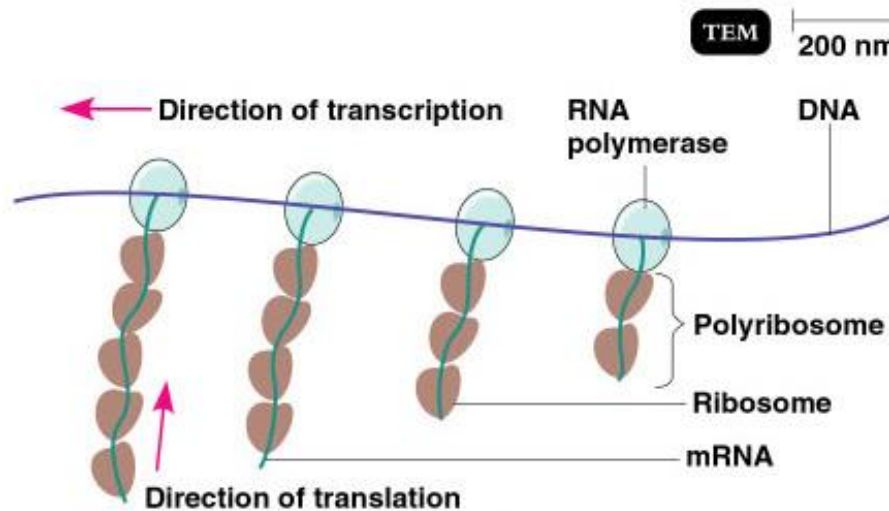
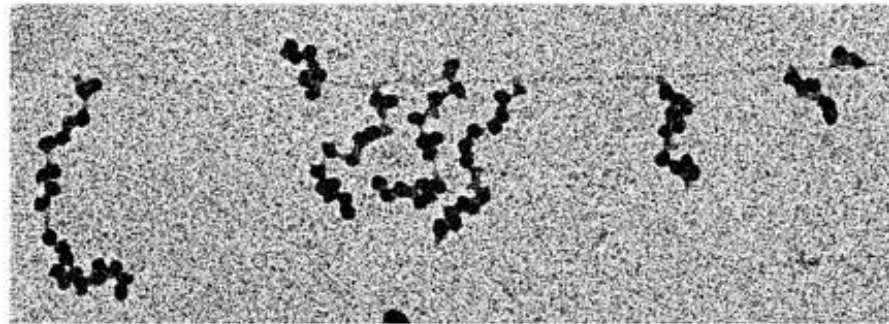


Image from Khan Academy

A review!

- Which main molecular components are needed for:
 - DNA replication
 - RNA transcription
 - Protein translation?
- How might these processes be different in prokaryotes compared to eukaryotes?

In prokaryotes, translation can begin before transcription is complete due to lack of compartmentalization



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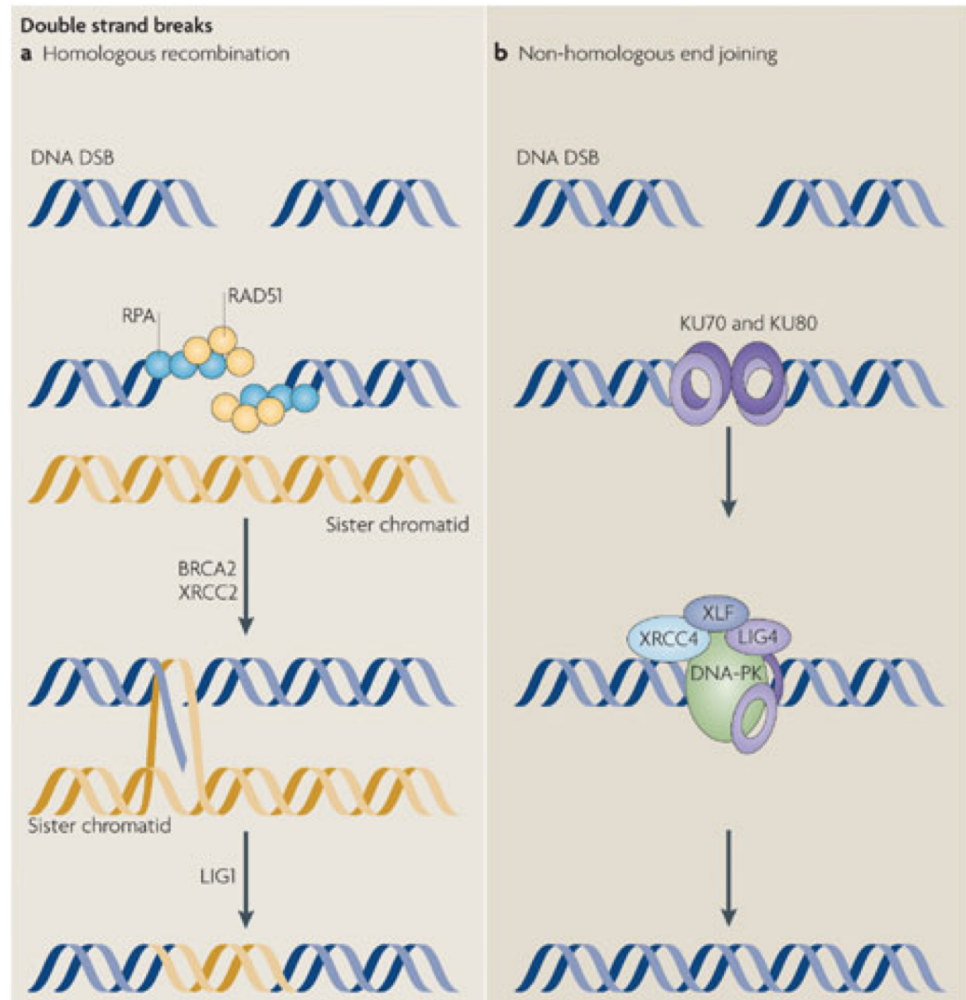


It's Time For A Break



Genetics - DNA repair

- Homology directed repair (HDR)
 - Requires homologous DNA to be present
 - <https://www.youtube.com/watch?v=86jCMM5kb2A>
- Non-homologous end joining (NHEJ)
 - <https://www.youtube.com/watch?v=3IstiofjjYw>

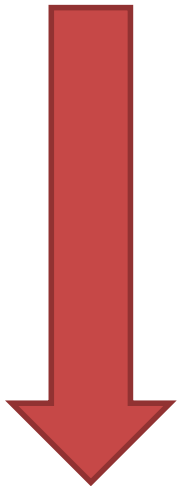


Genetics – DNA repair is a crap-shoot

- Mutations

- What kinds of mutations would affect gene function?

Large scale
changes

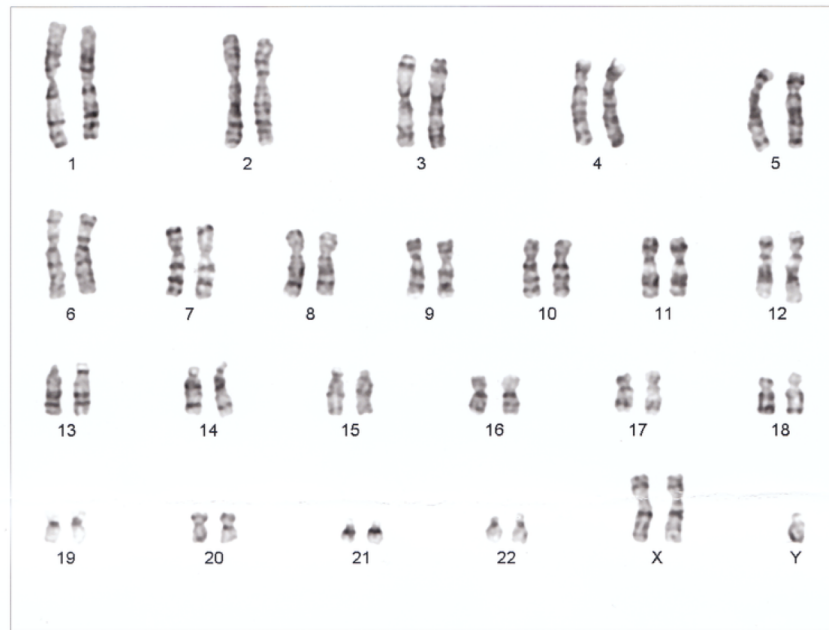


Small scale
changes

- Aneuploidy
- Large chromosomal translocations/truncations
- Other inversions, translocations
- Copy number variations (CNVs)
- Point mutations – non-sense, missense, frame-shift, silent...
- Single nucleotide variations/polymorphisms (SNVs/SNPs)

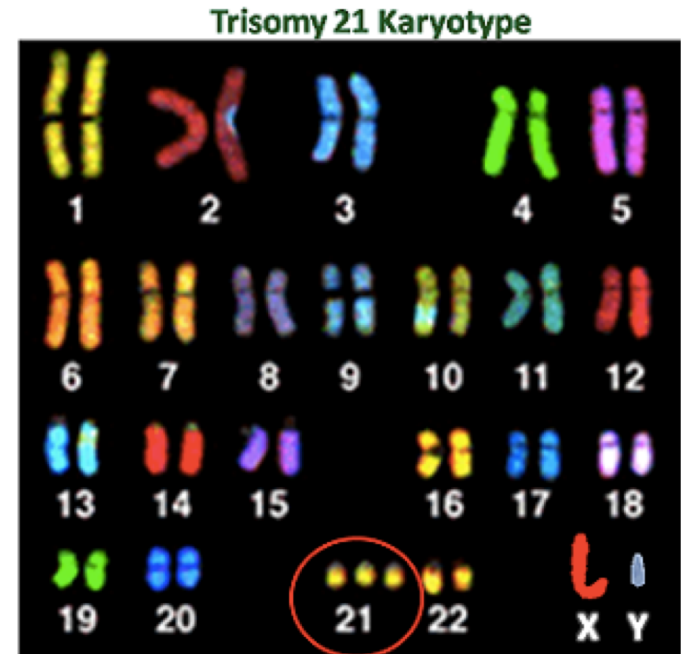
Genetics - Aneuploidy

- Down Syndrome
- XXY – Klinefelter Syndrome



核型 : 47, XXY

Cell No. : 003

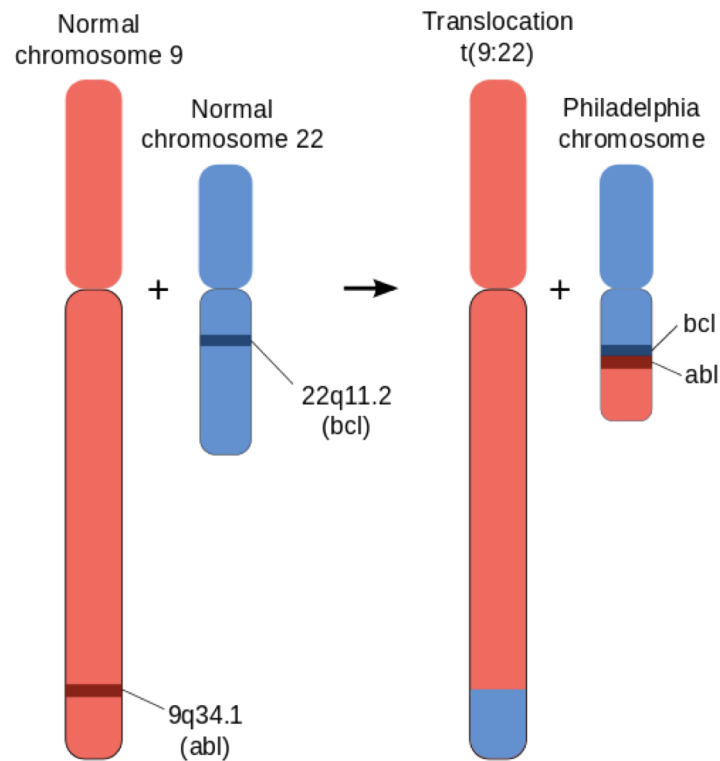


<http://study.com/academy/lesson/aneuploidy-definition-disorders-quiz.html>

By User:Nami-ja, via Wikimedia Commons

Genetics – Large chromosomal aberrations

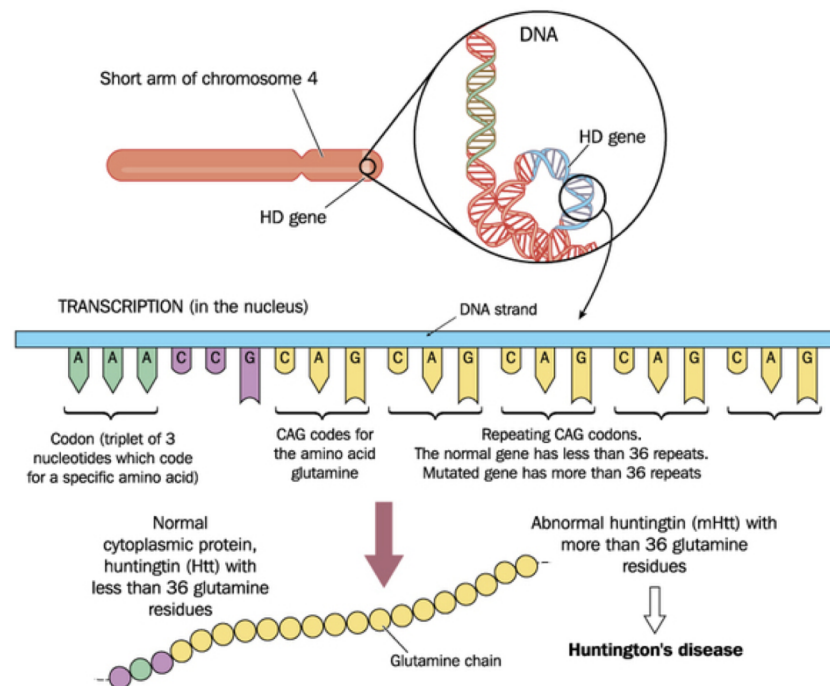
- Philadelphia chromosome and CML; BCR-ABL fusion



By Aryn89 (Own work) [CC BY-SA 4.0 (<http://creativecommons.org/licenses/by-sa/4.0>)], via Wikimedia Commons

Genetics - CNVs

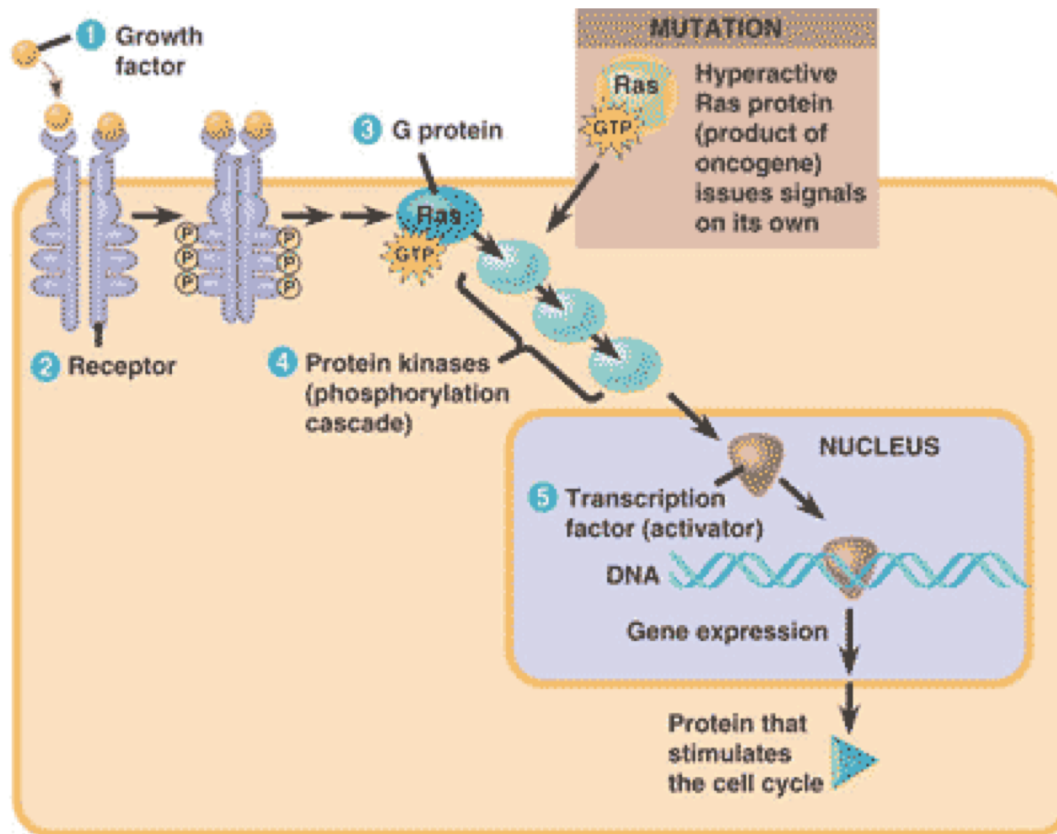
- Huntington's disease
 - CAG repeats, more than 44-46 times → likely to develop disease
- Breast cancer HER2/NEU/ERBB2 amplification



<https://ghr.nlm.nih.gov/condition/huntington-disease>

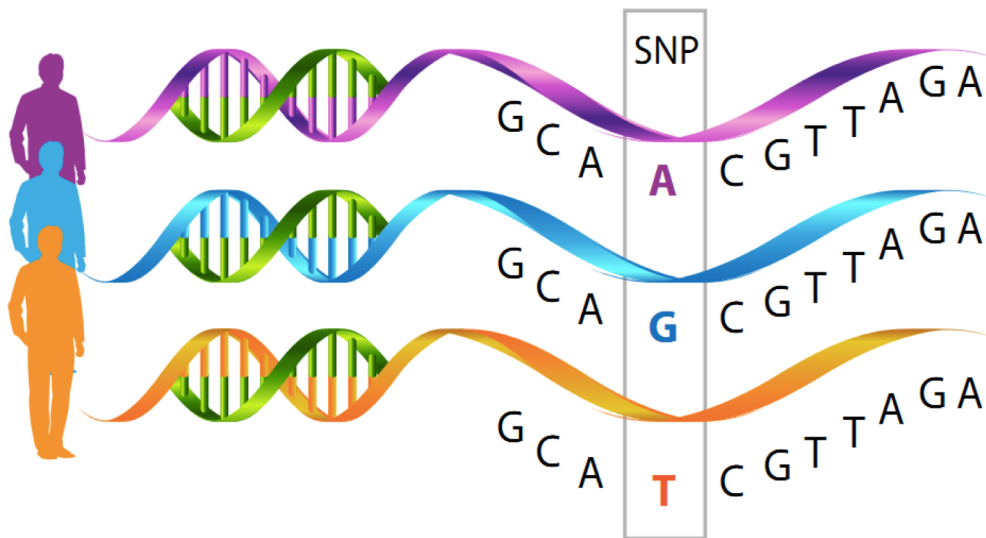
Genetics – Point mutations

- RAS mutations leading to cancer



Genetics - SNPs

- CCR5 receptor and immunity to HIV infection
- Difference between SNPs and ‘just a mutation’



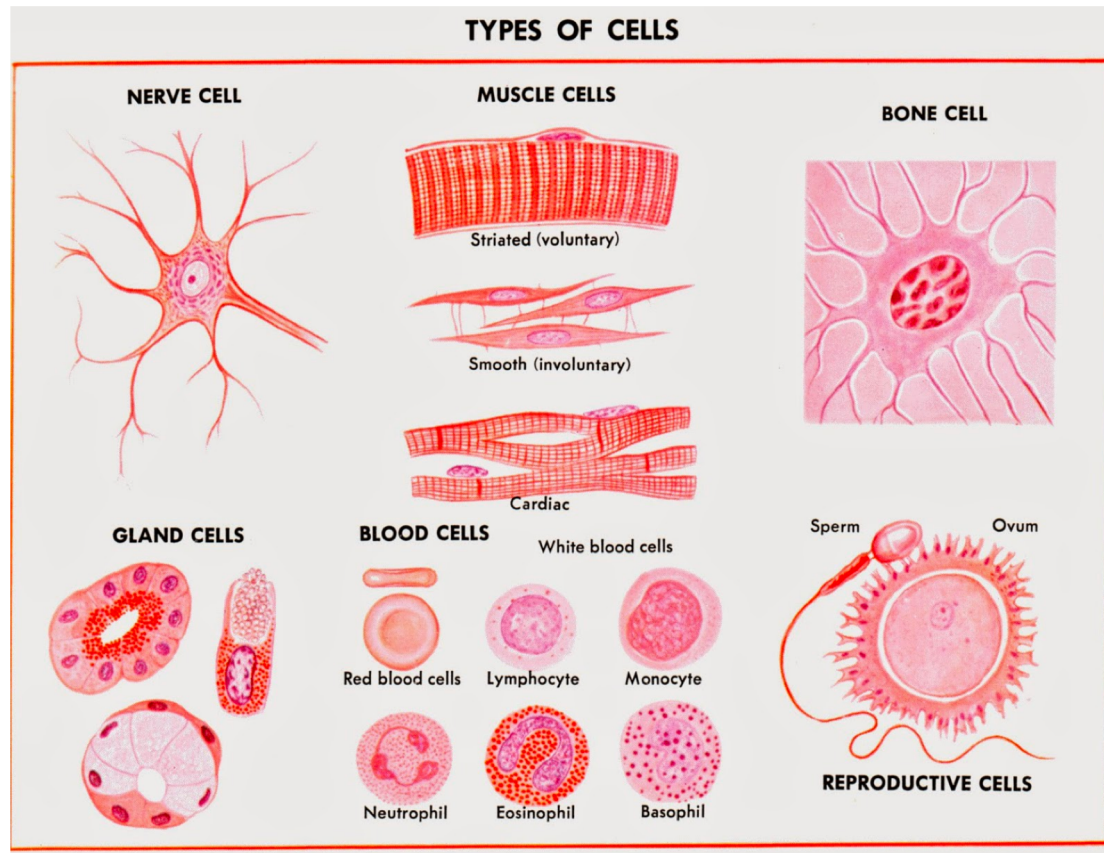
> 1% abundance in population

Humans have over 3 million recorded SNPs

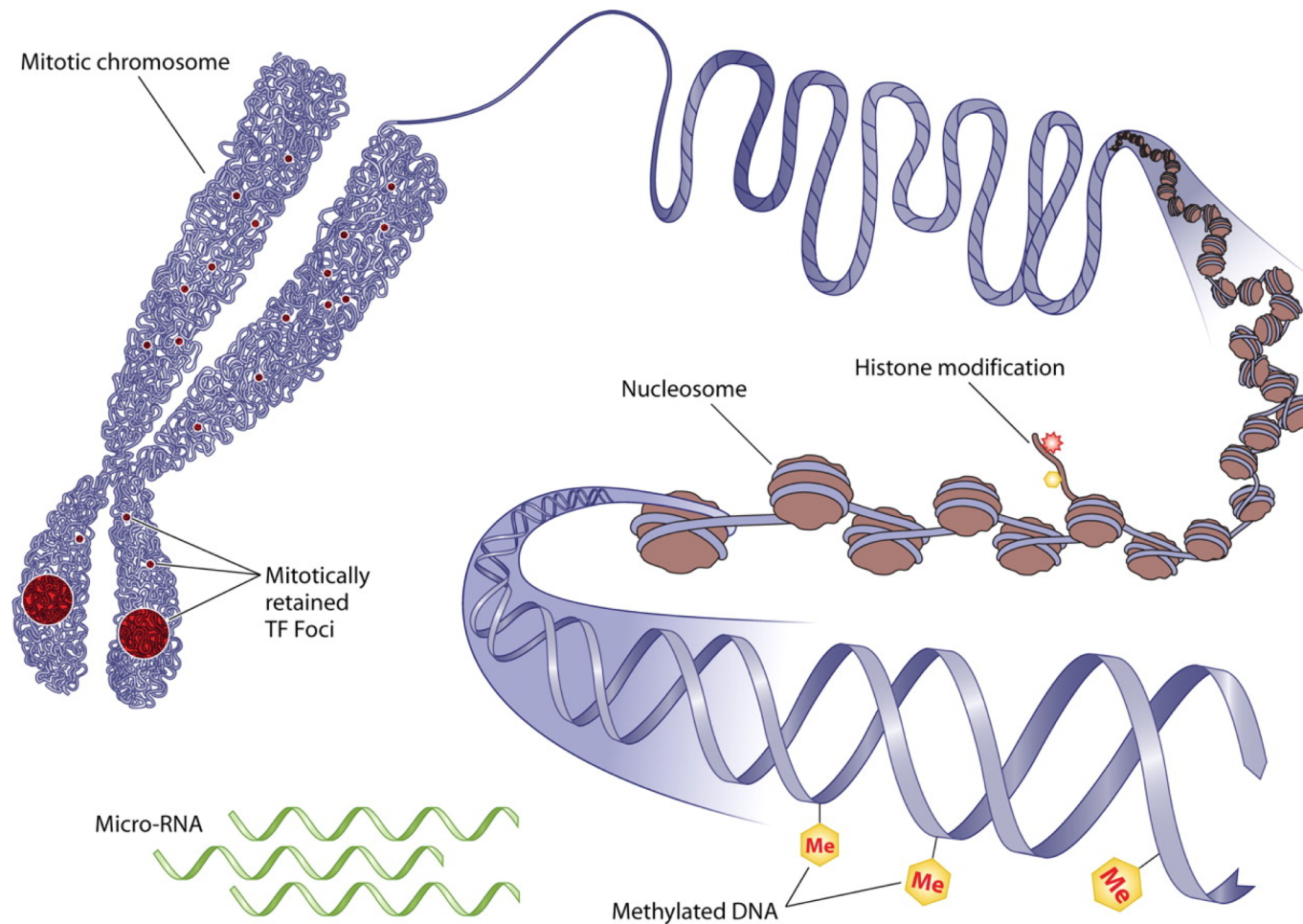
Link to personalized medicine

Question

- So many cell types, so few genomes...



Epigenetics – Layers upon layers of information



Epigenetics – controlling transcription

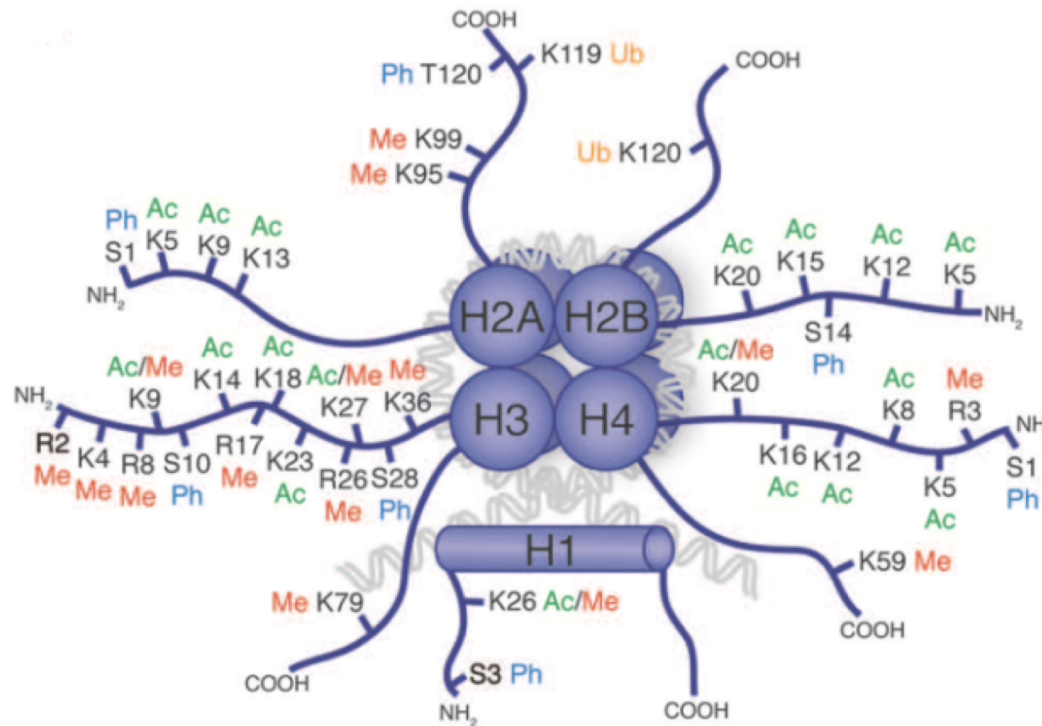
- Control of protein binding to DNA
- Control of DNA accessibility
 - Allele specific? X-inactivation?
- Control of coordinated expression of genes through 3D chromatin structure (Hi-C)
- Control of mRNA degradation

- Mis-regulation results in bad things:
 - Down syndrome
 - Many many many cancers

Epigenetics

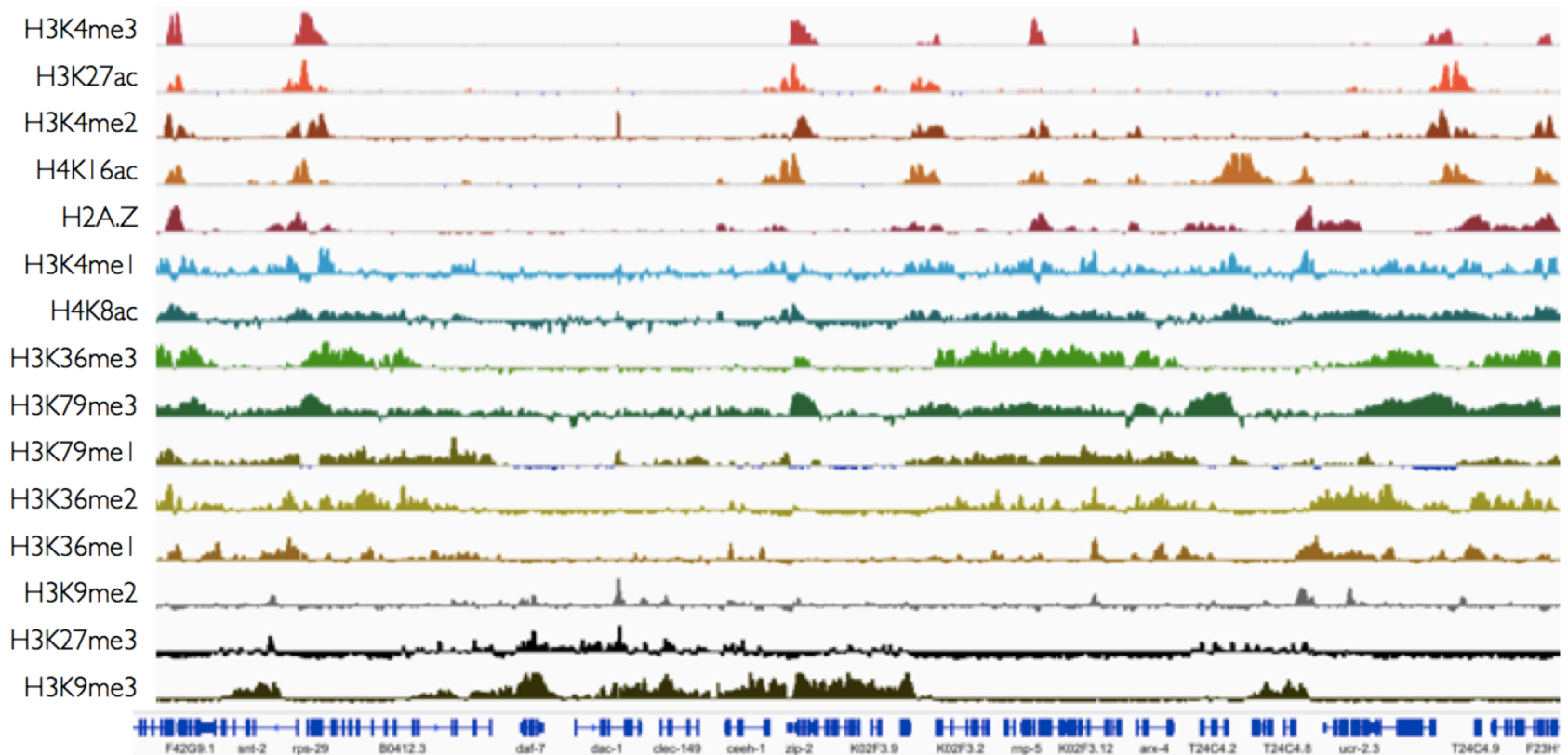
- Mechanisms of regulation:
 - DNA methylation
 - DNA hydroxymethylation
 - DNA XXX-ylation...
 - Histone modifications
 - miRNA silencing
 - lncRNA
 - Enhancers, repressors, ERVs,

Epigenetics – The histone code



Perla Cota, Mehdi Shafa and Derrick E. Rancourt (2013). *Stem Cells and Epigenetic Reprogramming, Pluripotent Stem Cells*, Dr. Deepa Bhartiya (Ed.), InTech, DOI: 10.5772/55983. Available from: <http://www.intechopen.com/books/pluripotent-stem-cells/stem-cells-and-epigenetic-reprogramming>

Epigenetics – The Roadmap/ENCODE project

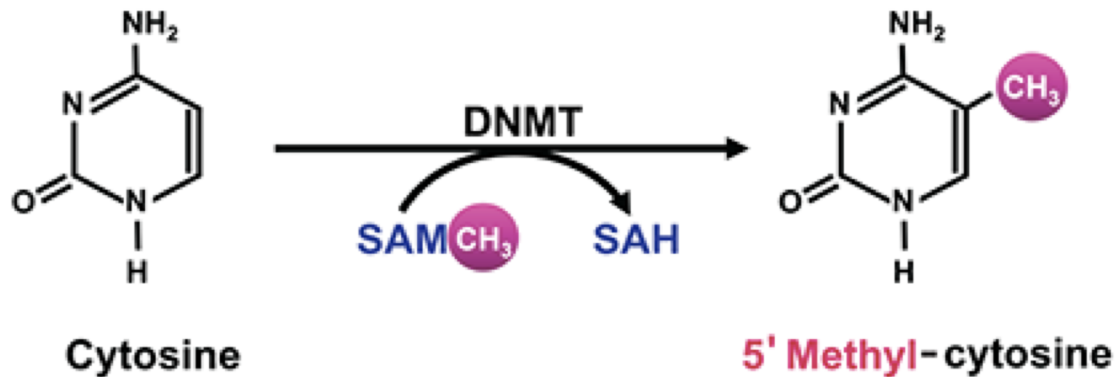
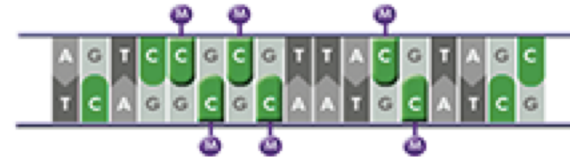


<http://www2.gurdon.cam.ac.uk/~ahringerlab/research-3.html>

Epigenetics – DNA methylation

DNA Methylation

Methylating the cytosine of a CpG motif silences genes



<http://pubs.niaaa.nih.gov/publications/arcr351/6-16.htm>