DNA, Genes and Aging (S1030)

Daniel Richardson, Professor of Physiology, Univ of Kentucky (retired)

1056 West Johnson Blvd
Tonto Village
Payson, AZ 85541
Email – danrichardson0510@gmail.com

Class dates: Thursdays, Mar 29 April 5, April 12: 10:00-11:30

DNA, Genes and Aging

Three unequally divided sections:

Basic genetics

Genetic expression and the genetic code

DNA damage and aging

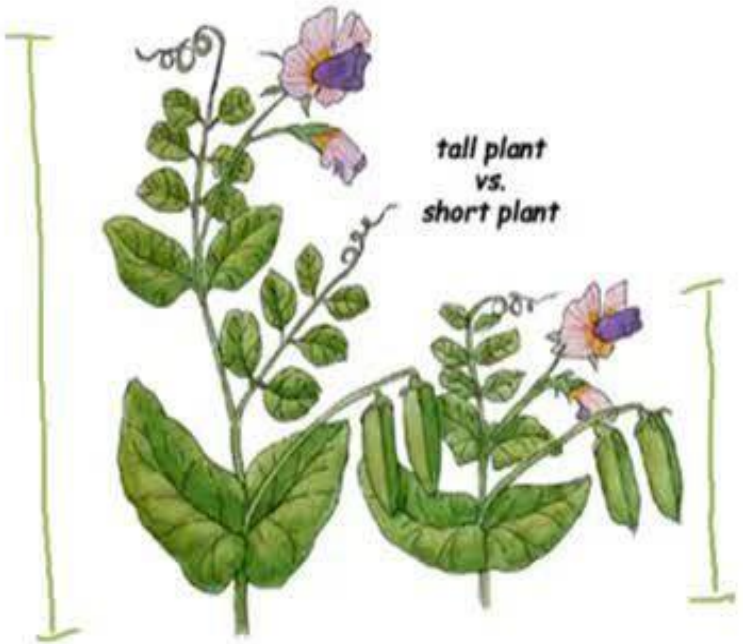
Gregor Johann Mendel, Augustinian friar, 1822-1884
Father of genetics

Mendel’s garden
St. Thomas Abbey, Czech Republic
(then part of the Austrian Empire)

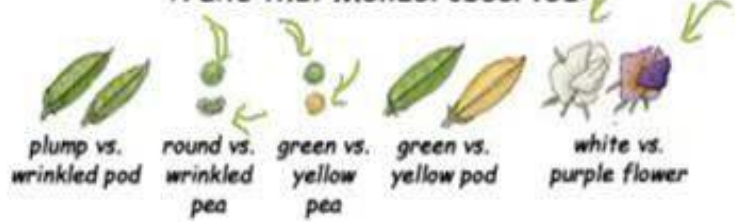
① dominance
② segr.

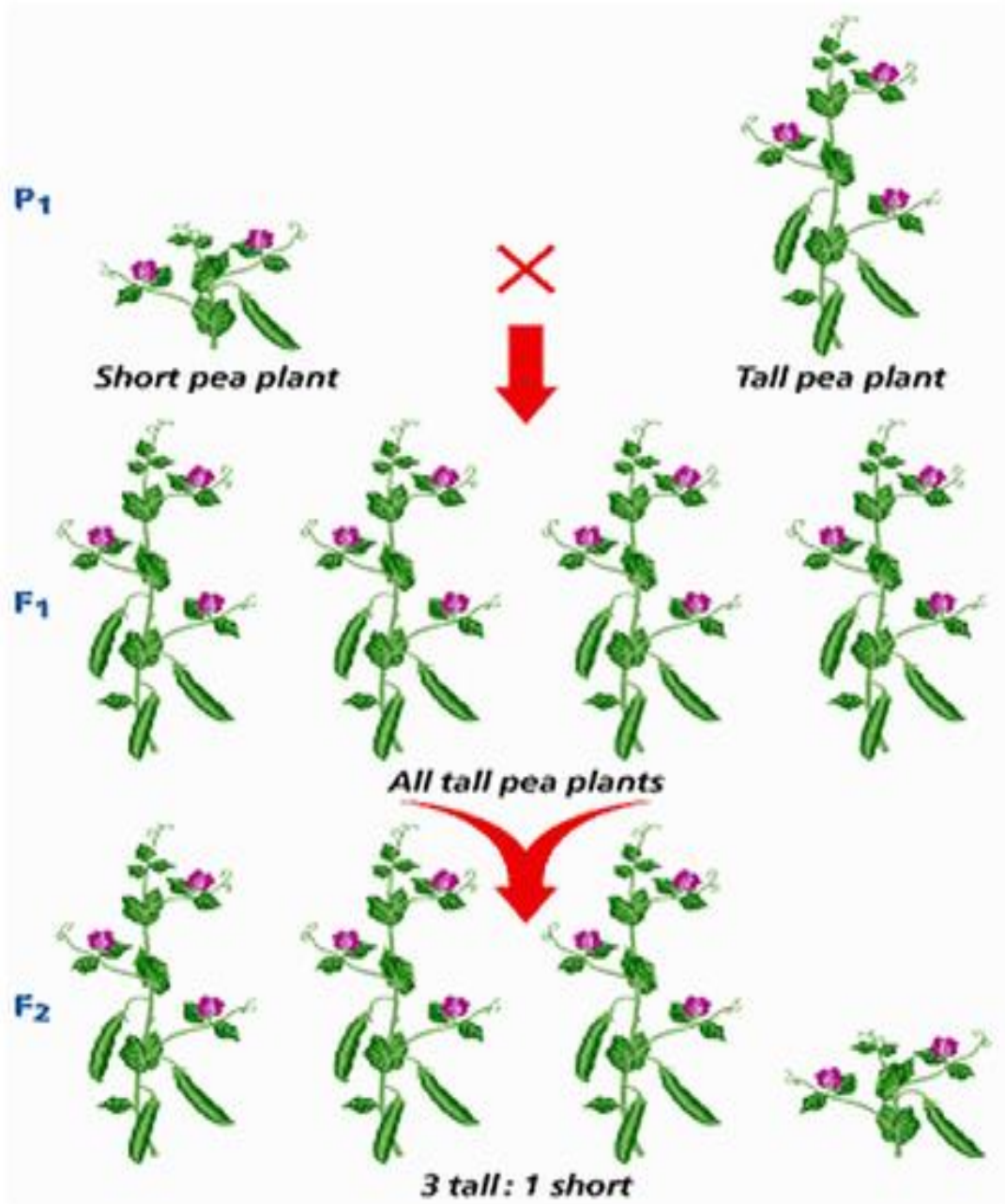
Mendel and His Peas

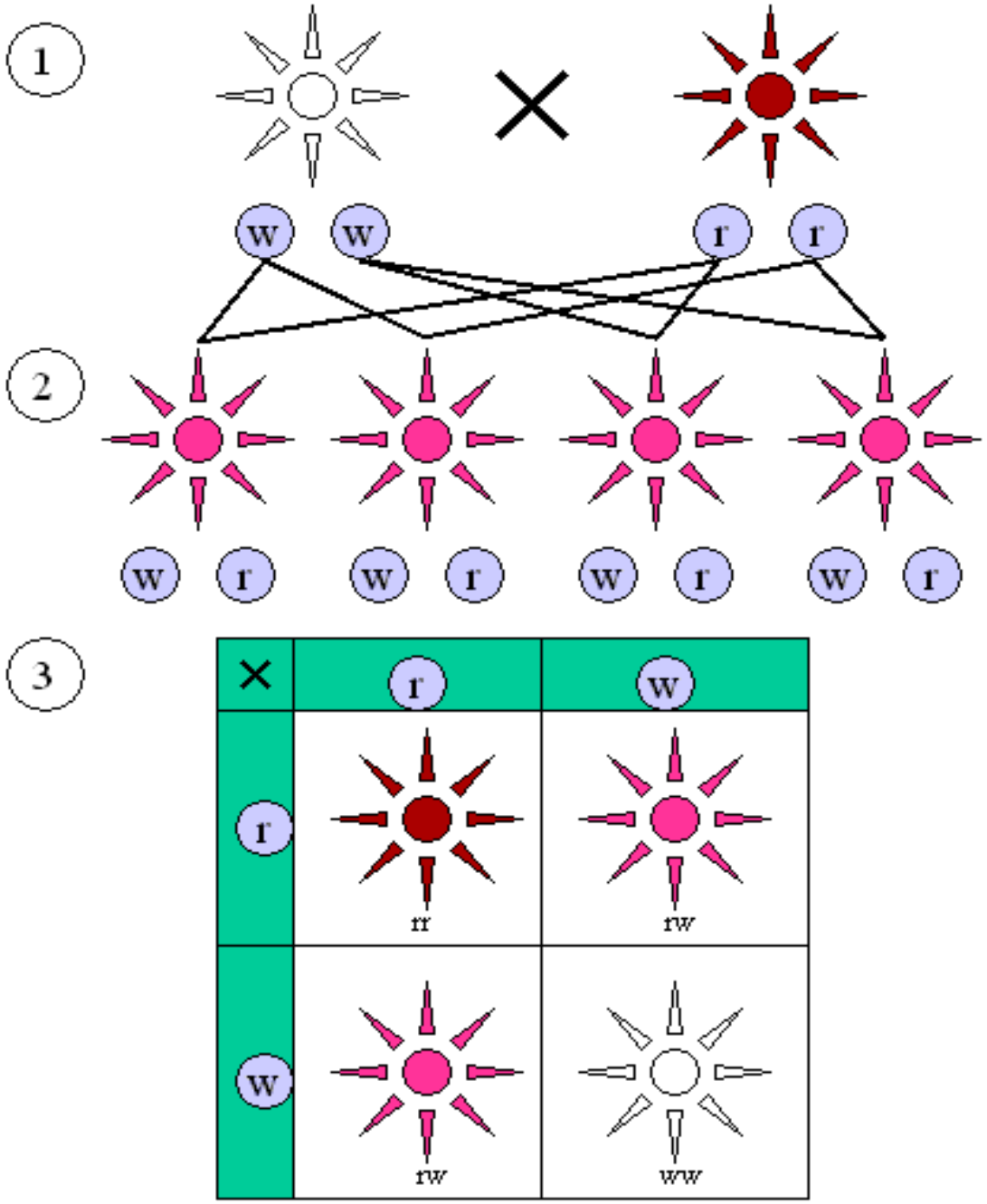
1865



Traits that Mendel observed:



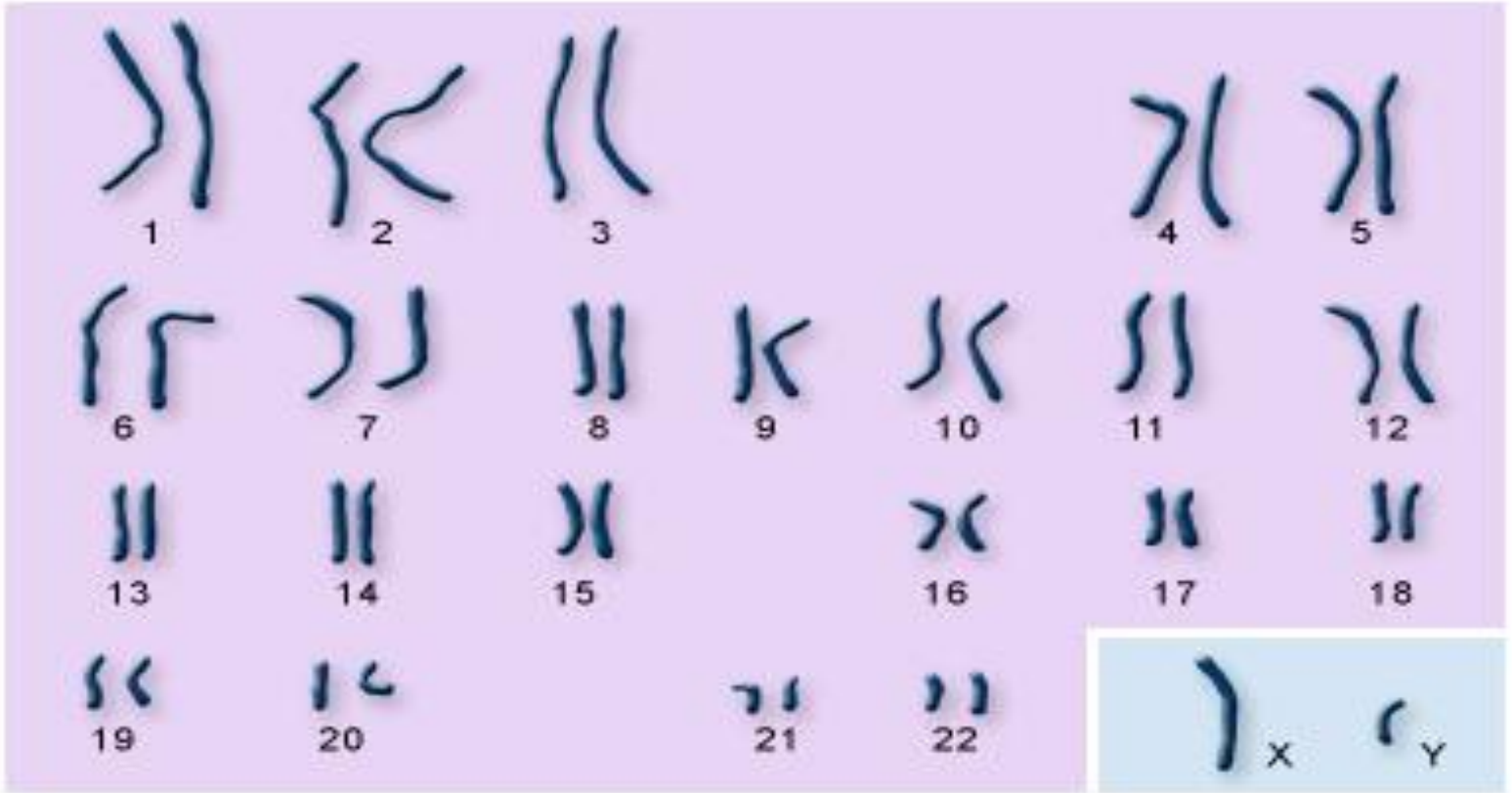

P1
Short pea plant
Tall pea plant
F1
All tall pea plants
F2
3 tall : 1 short



Heredity units, such as color, Mendel called “factors”, what we now know as genes.

An individual organism (plant) carries two factors (genes) for each trait.

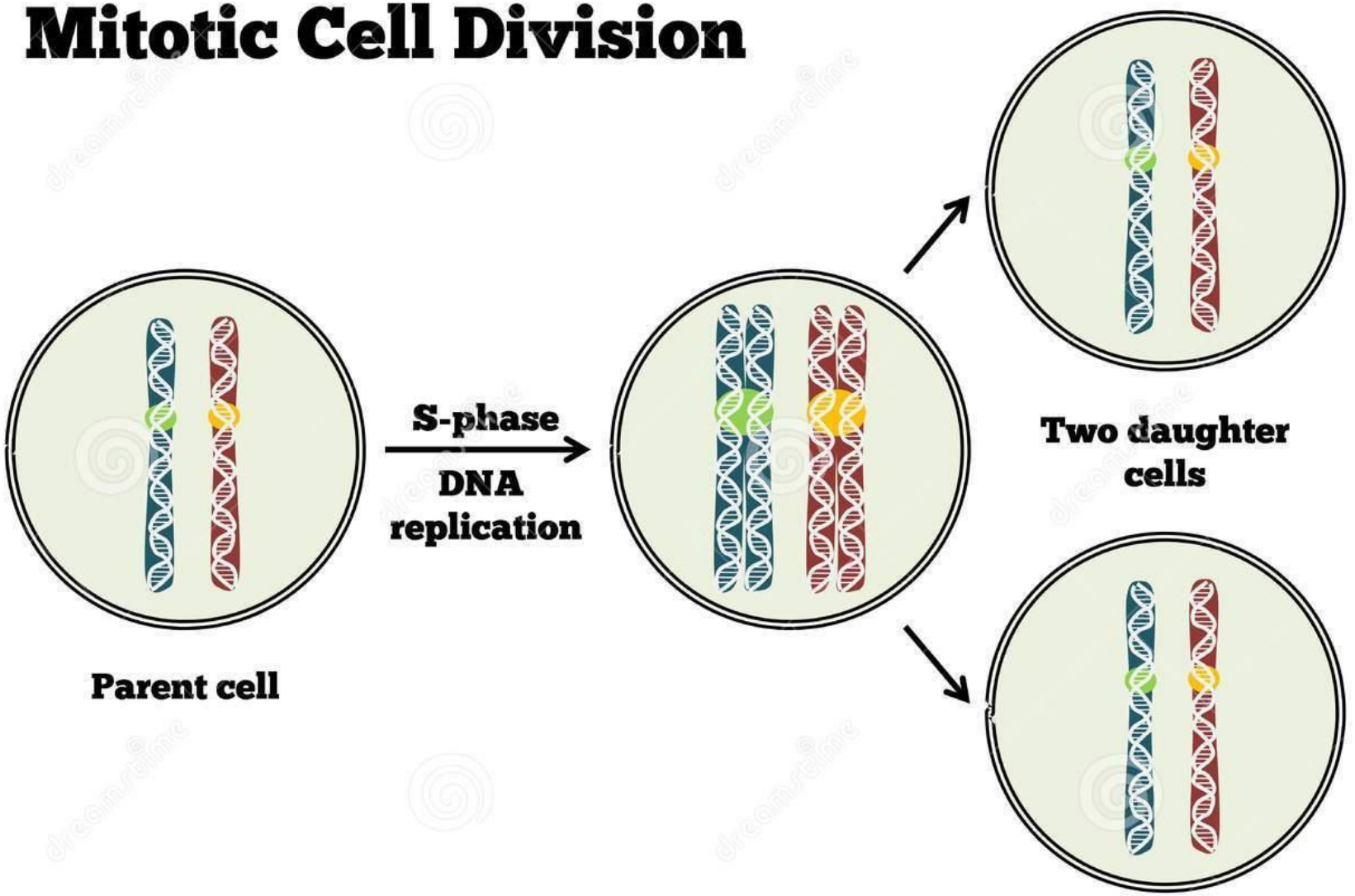
Genes (Mendel's factors) are small sections of chromosomes
Each nucleus of each cell in our body contains 23 pairs of chromosomes
One of the two in a pair is maternal in origin; the other is paternal
Each chromosome contains hundreds to over a thousand genes



discovered: 1903

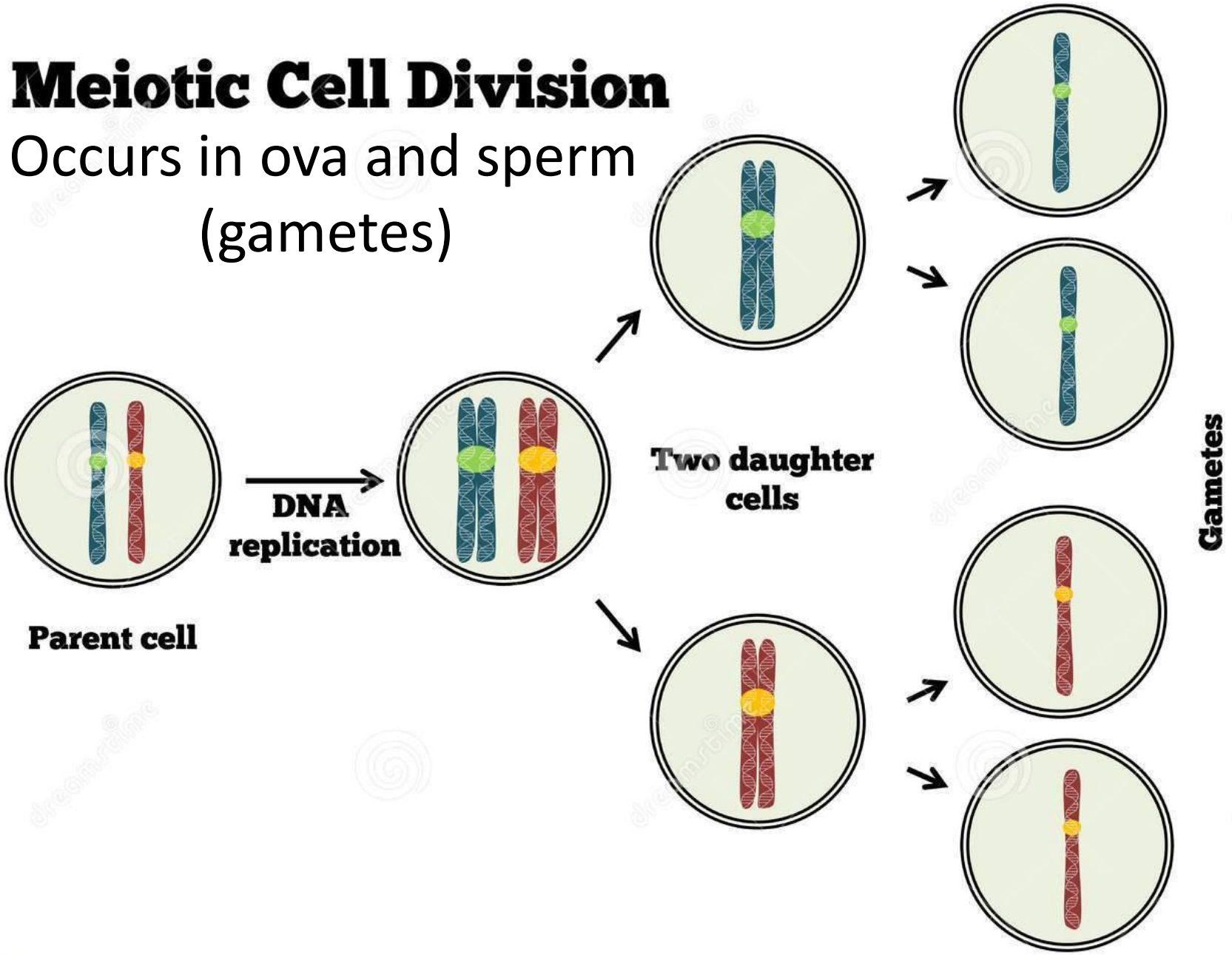
XX = female
XY = male

Mitotic Cell Division

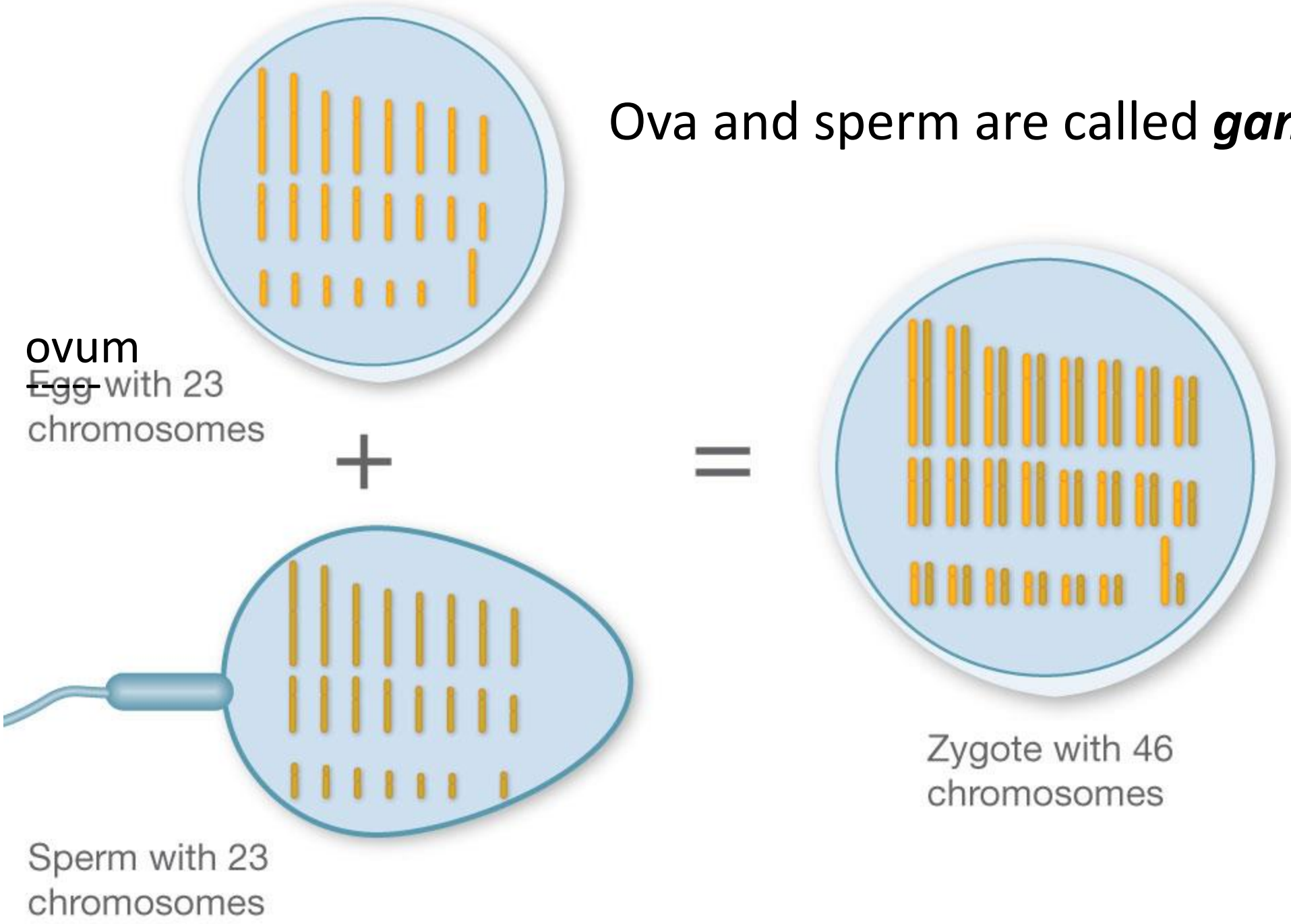


Meiotic Cell Division

Occurs in ova and sperm (gametes)



Ova and sperm are called ***gametes***



A bit of terminology

Paired genes, one of maternal and one of paternal origin, are ***alleles***

Identical alleles (red and red) are ***homozygotes***

Non identical alleles (red and white) are ***heterozygotes***

Mendel's Laws of Inheritance

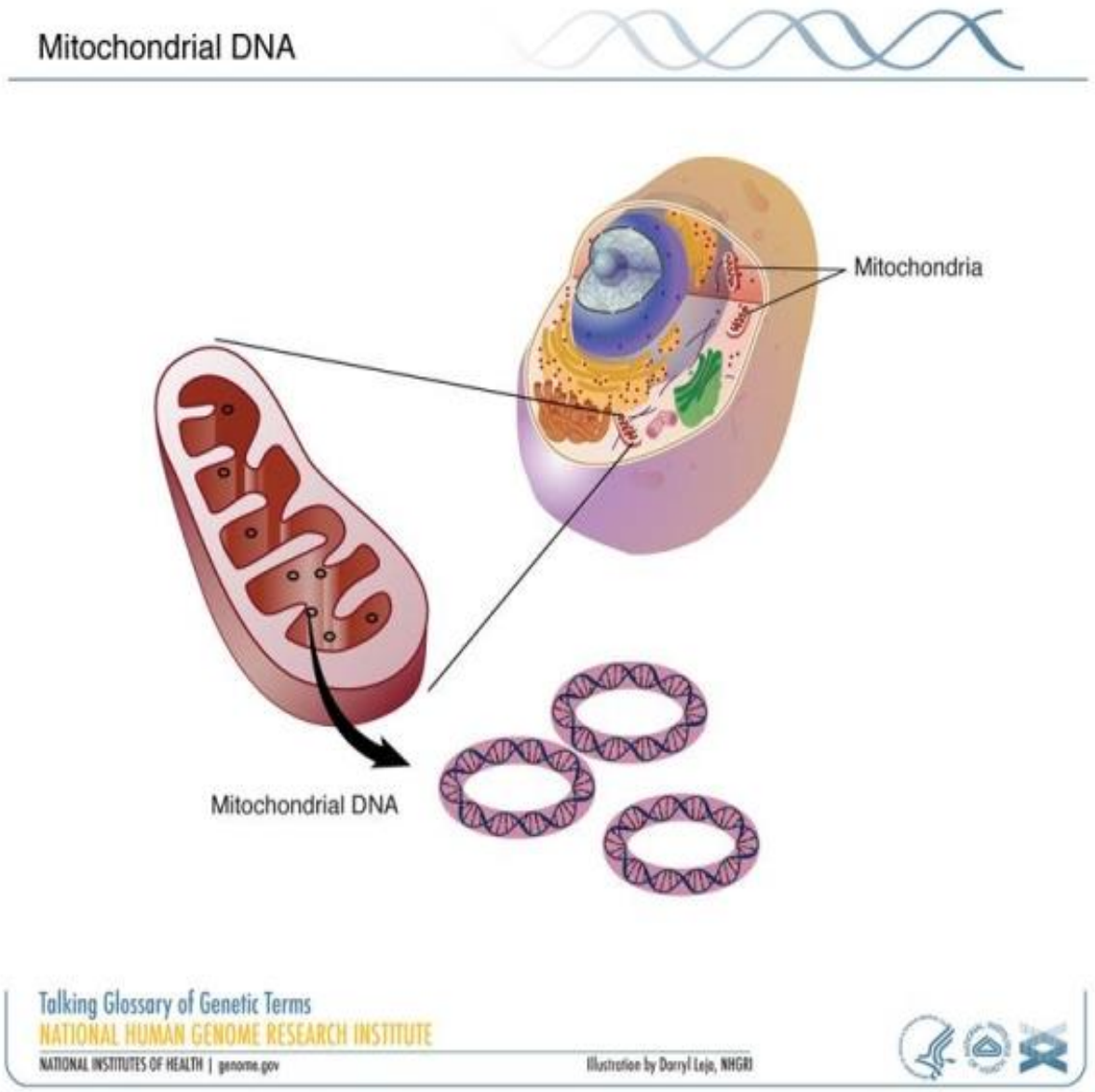
Segregation – each gamete carries only one allele for each gene.

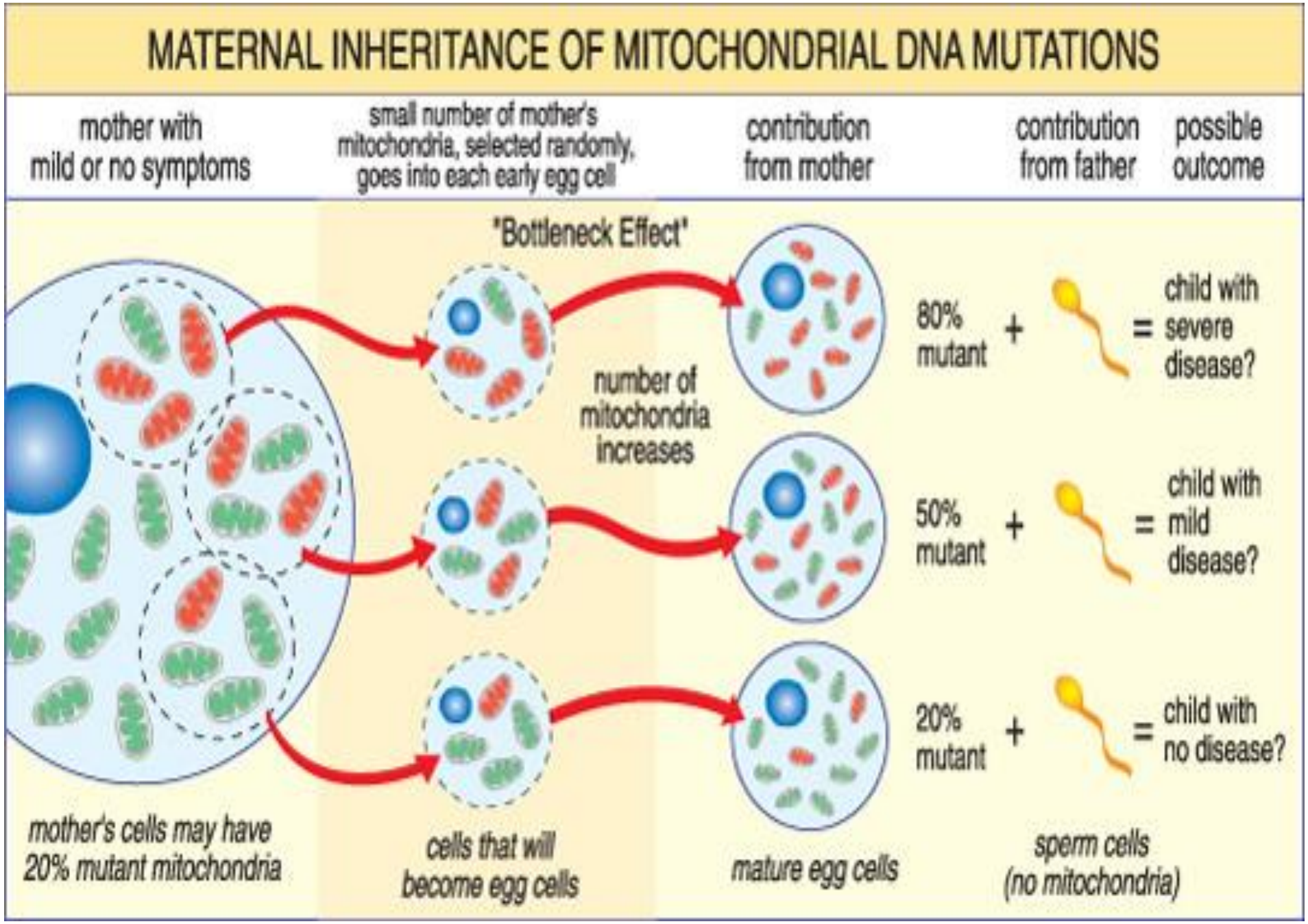
Independent assortment – genes for different traits segregate independently.

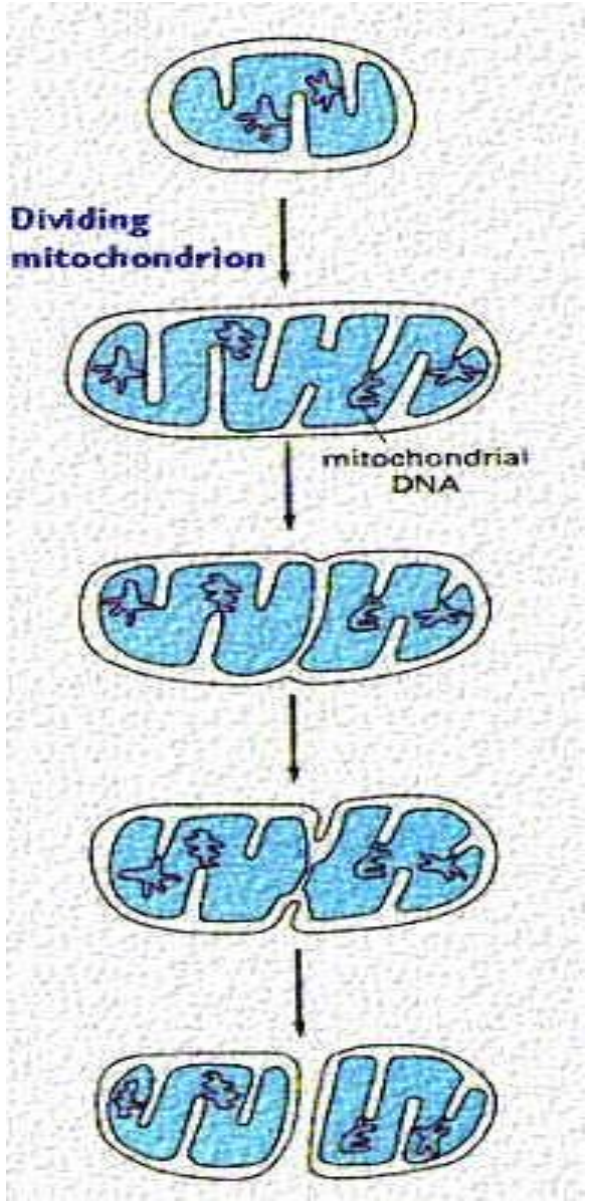
Dominance - in heterozygote alleles the trait that shows up in a new individual is dominant, while the other is recessive.

Mitochondria DNA

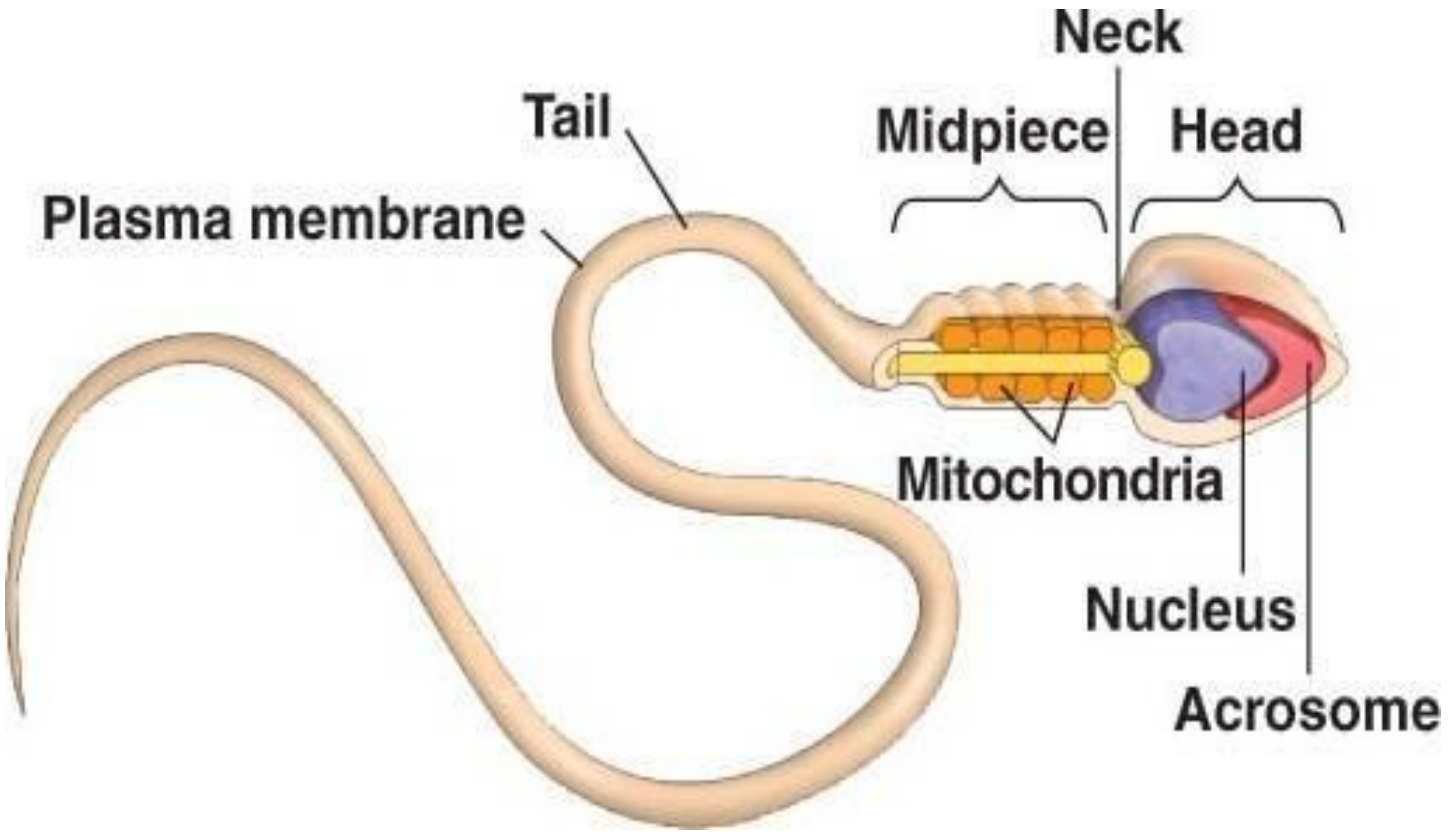
- Mitochondria DNA (mtDNA) was discovered in 1963*. They consist of circular chromosomes which collectively contain 37 genes, 22 of which encode for the production of the RNAs used in protein synthesis.
- mtDNA in humans is of maternal origin.
- Since mtDNA carries certain ethnic markers over many generations, it can be used to trace maternal linage back multiple generations.
- *Journal of Cell Biology, vol. 19, p593, 1963

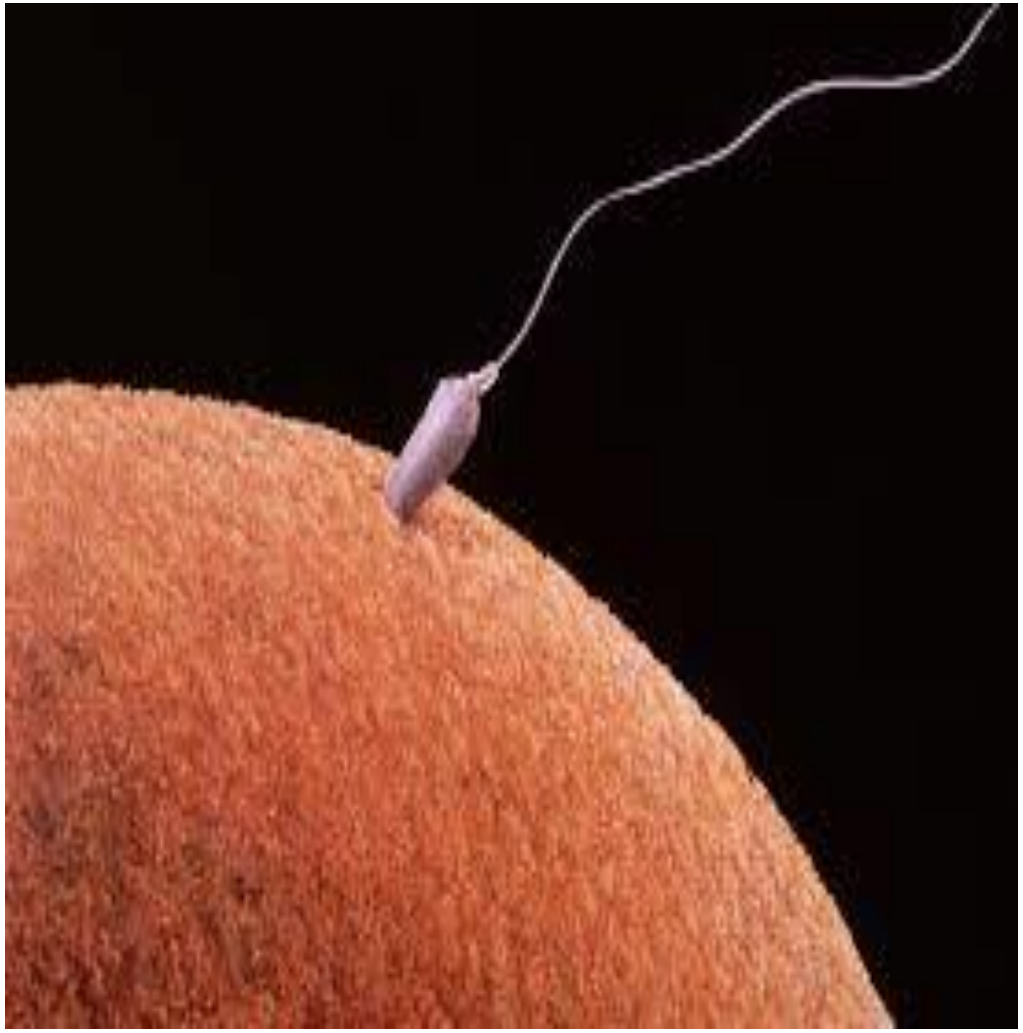



MATERNAL INHERITANCE OF MITOCHONDRIAL DNA MUTATIONS
mother with mild or no symptoms
small number of mother's mitochondria, selected randomly, goes into each early egg cell
contribution from mother
contribution from father
possible outcome
"Bottleneck Effect"
number of mitochondria increases
80% mutant + = child with severe disease?
50% mutant + = child with mild disease?
20% mutant + = child with no disease?
mother's cells may have 20% mutant mitochondria
cells that will become egg cells
mature egg cells
sperm cells (no mitochondria)

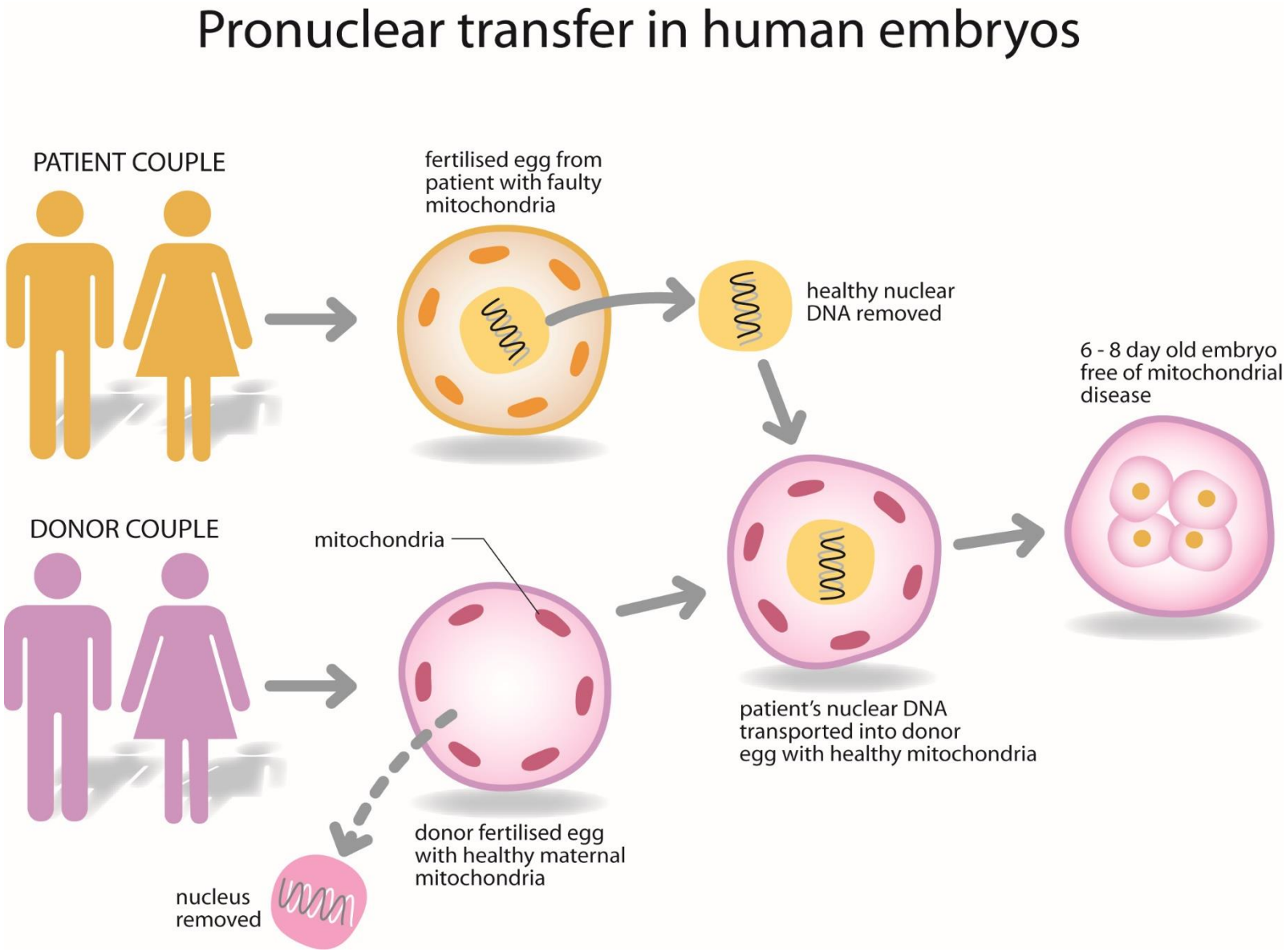

Dividing mitochondrion
mitochondrial DNA

Mitochondria in sperm provide energy for motion of the tail
Sperm tails get “lost” between ovum penetration and fertilization





An interesting sidebar



Function of Genes

Genes code for the synthesis of ***all*** proteins* within an organism

Overall process termed *genetic expression*

DNA to RNA to protein

Average time for completion: 2 min.

* DNA/genetic damage (e.g. with age) alters protein functions

Milestones of Genetic History (subjective)

1865 - Mendel published his genetic experiments.

1903 – chromosomes discovered.

1910 – Thomas Hunt Morgan (nephew of John Hunt Morgan) discovered that genes reside on chromosomes.

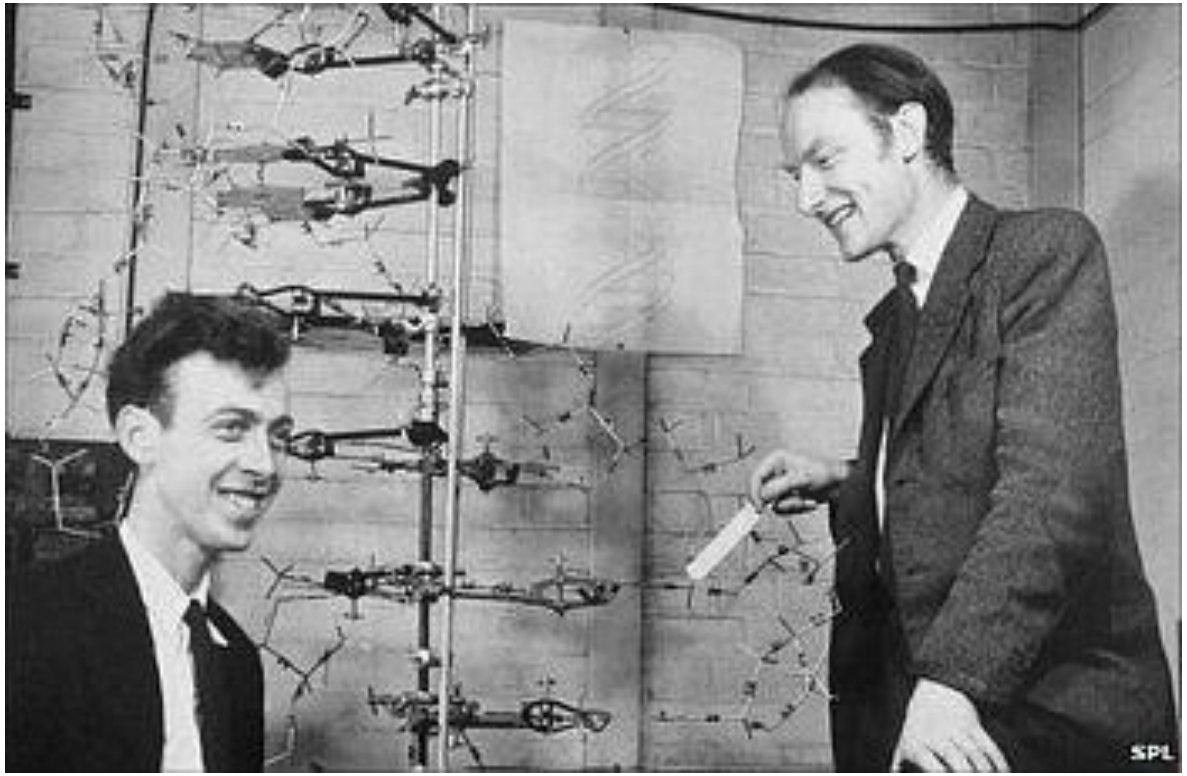
1953 – James Watson and Francis Crick elucidated the double helical structure of DNA.

2003 – Completion of the Human Genome Project.

Thomas Hunt Morgan, 1866-1945

John Hunt Morgan, 1825-1864

James Watson & Francis Crick
Cambridge, circa 1953



Watson and Crick, circa 2000

Human Genome Project

Genome: The complete set of genes of a biological organism

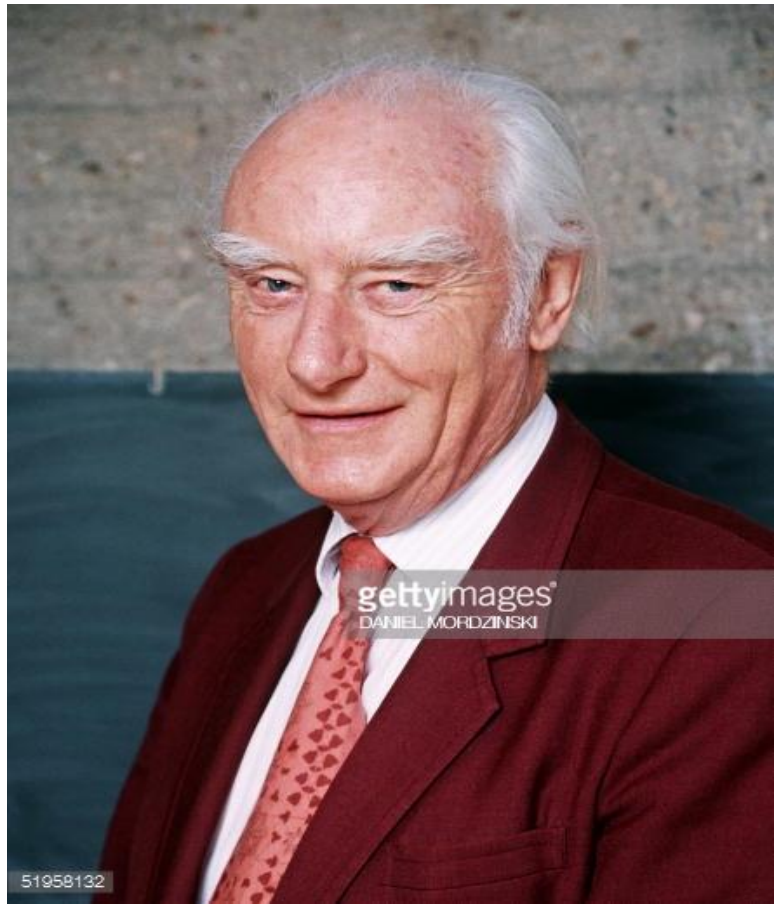
Initiated by the United States, the Human Genome Project is the largest and most comprehensive international biological project ever undertaken.

Objectives: 1) determine the sequence of the estimated three billion nucleotide base pairs that make up human DNA
2) to identify and map all of the genes of the human genome

Key dates: 1984 project proposed
1990 project initiated
2000 rough draft of completed project
2003 final draft of completed project

Directors of Human Genome Project, 1990 (start) to 2003 (completion)

James Watson, 1990-1992



Francis Collins 1992-2003

Human Genome Project: Continued

Funding sources: NIH, Dept of Energy, grants from other participating countries including: United Kingdom, Japan, France, Germany, Spain and China

Total cost: about three billion US dollars

Presidents involved: Ronald Reagan, George H. Bush, Bill Clinton, George W. Bush

Tony Blair and Bill Clinton: Joint announcement of rough draft of the completed genome project, 2000

Human Genome Project: Major results

Successful determination of the sequence of nucleotide bases in human DNA.

Identification of the set of genes within the human genome - 22,300 total.

Less than the 100,000 genes projected to be found on the basis of the fact that genes code for the manufacture of proteins and there are about 100,000 proteins in the human body.

Therefore, a third major result was the discovery that a given gene codes for more than one protein.

Human Genome Project: Applications and Benefits:

Genotyping of viruses to design effective treatment

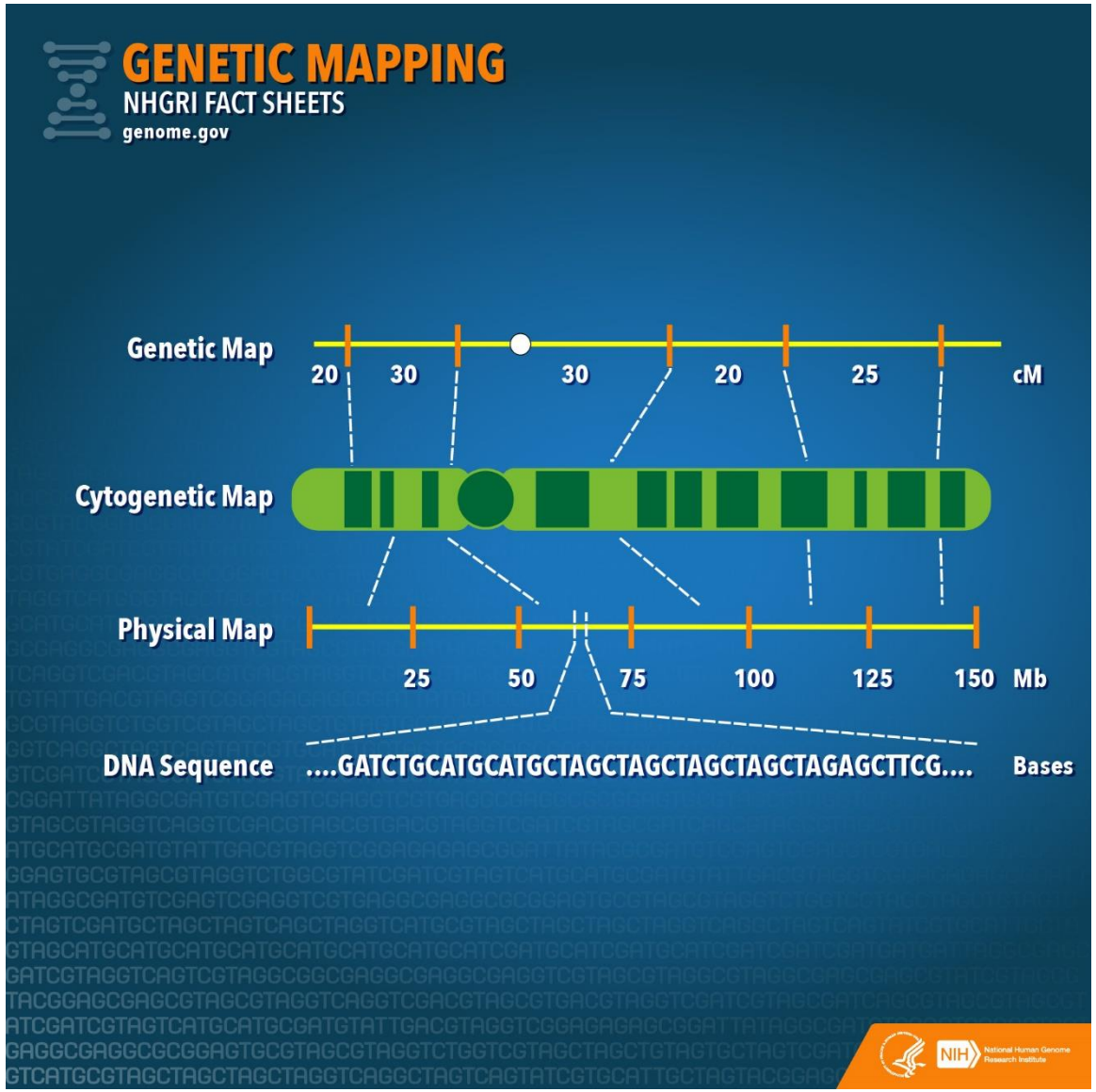
Identification of mutations linked to cancer

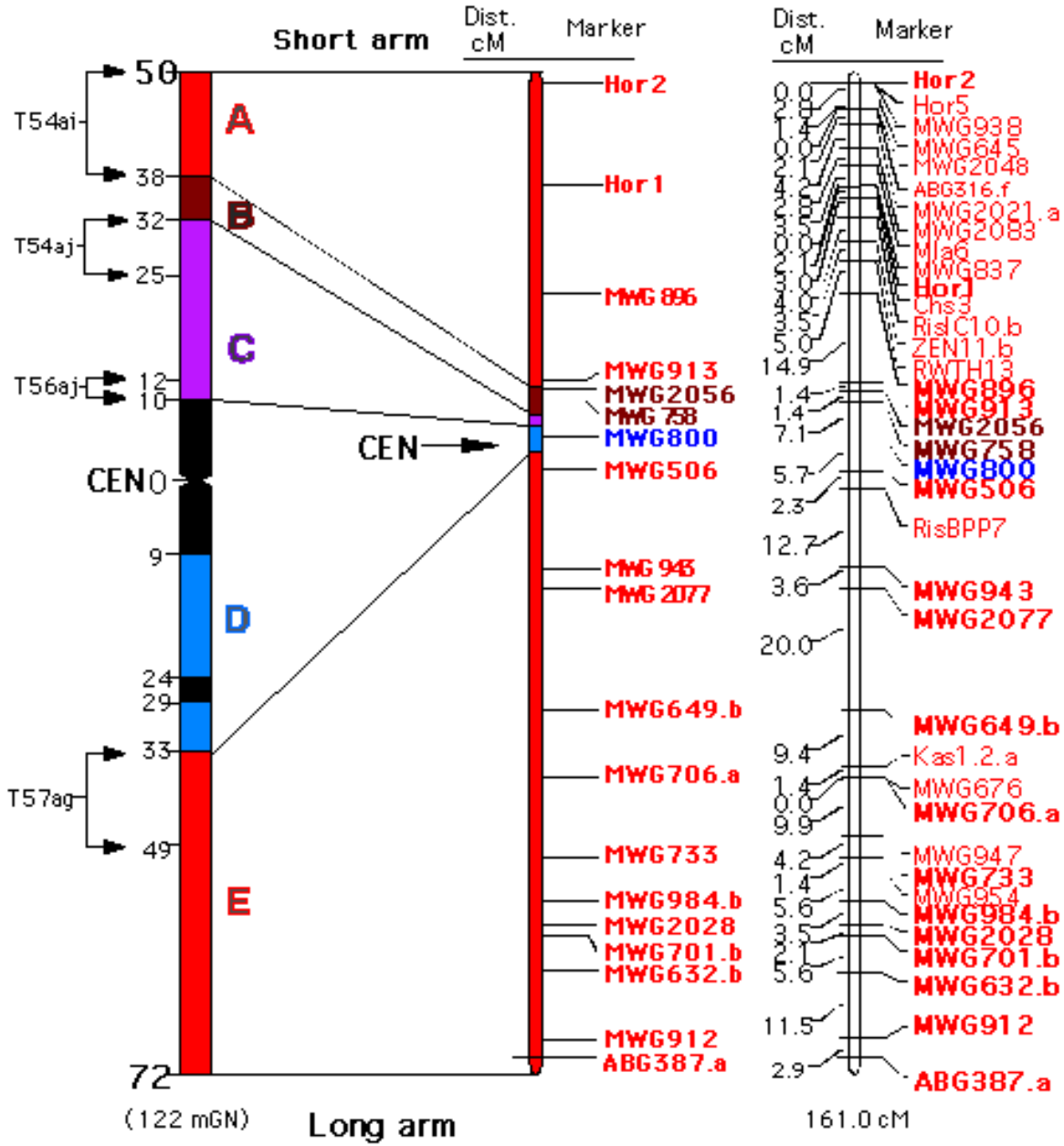
Genetic targeting of cancer cells

Design of designer genes to produce designer drugs

Advancement in forensic science

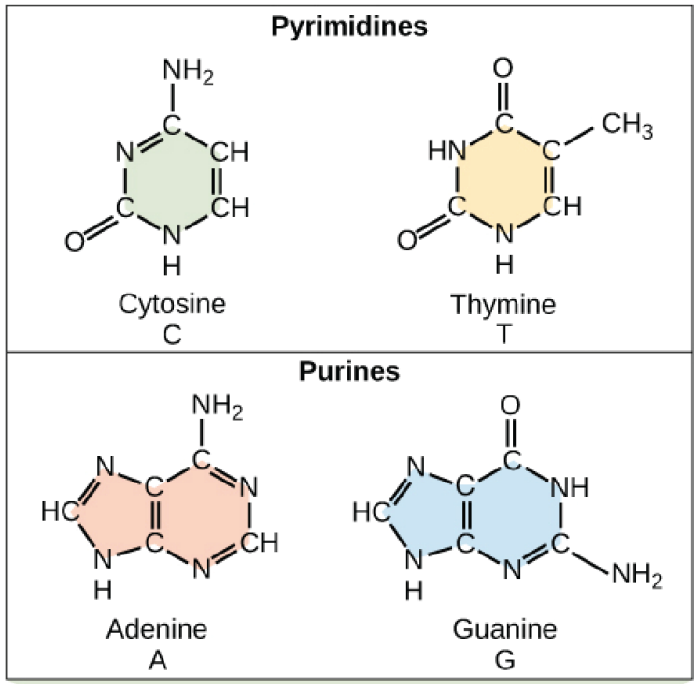
Assist in elucidating DNA modification and damage mechanisms of aging

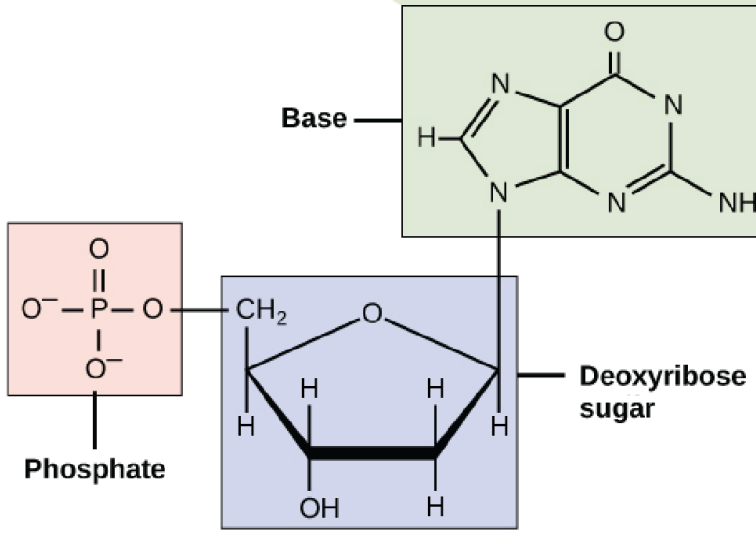

GENETIC MAPPING
NHGRI FACT SHEETS
genome.gov
Genetic Map
20
30
30
20
25
cM
Cytogenetic Map
Physical Map
25
50
75
100
125
150
Mb
DNA Sequence
....GATCTGCATGCATGCTAGCTAGCTAGCTAGCTAGAGCTTCG....
Bases
NIH
National Human Genome Research Institute

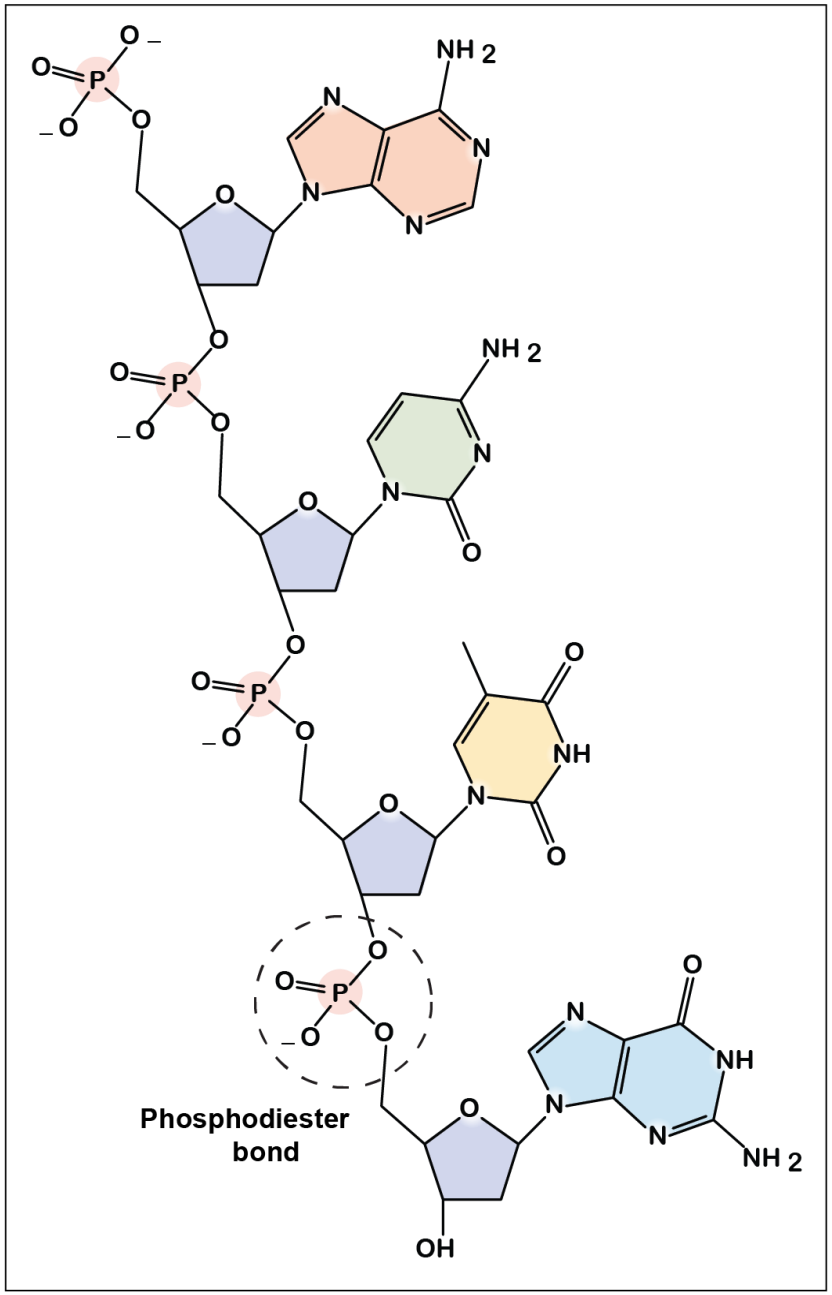

Short arm
Dist. cM
Marker
50
T54ai
38
32
T54aj
25
T56aj
12
10
CEN
0
9
24
29
33
T57ag
49
72
(122 mGN)
A
B
C
D
E
Hor2
Hor1
MWG896
MWG913
MWG2056
MWG758
MWG800
MWG506
MWG945
MWG2077
MWG649.b
MWG706.a
MWG733
MWG984.b
MWG2028
MWG701.b
MWG632.b
MWG912
ABG387.a
Long arm
Dist. cM
Marker
Hor2
Hor5
MWG938
MWG645
MWG2048
ABG316.f
MWG2021.a
MWG2083
Mla6
MWG837
Hor1
Chs3
RisIC10.b
ZEN11.b
RWTH13
MWG896
MWG913
MWG2056
MWG758
MWG800
MWG506
RisBPP7
MWG943
MWG2077
MWG649.b
Kas1.2.a
MWG676
MWG706.a
MWG947
MWG733
MWG954
MWG984.b
MWG2028
MWG701.b
MWG632.b
MWG912
ABG387.a
161.0 cM

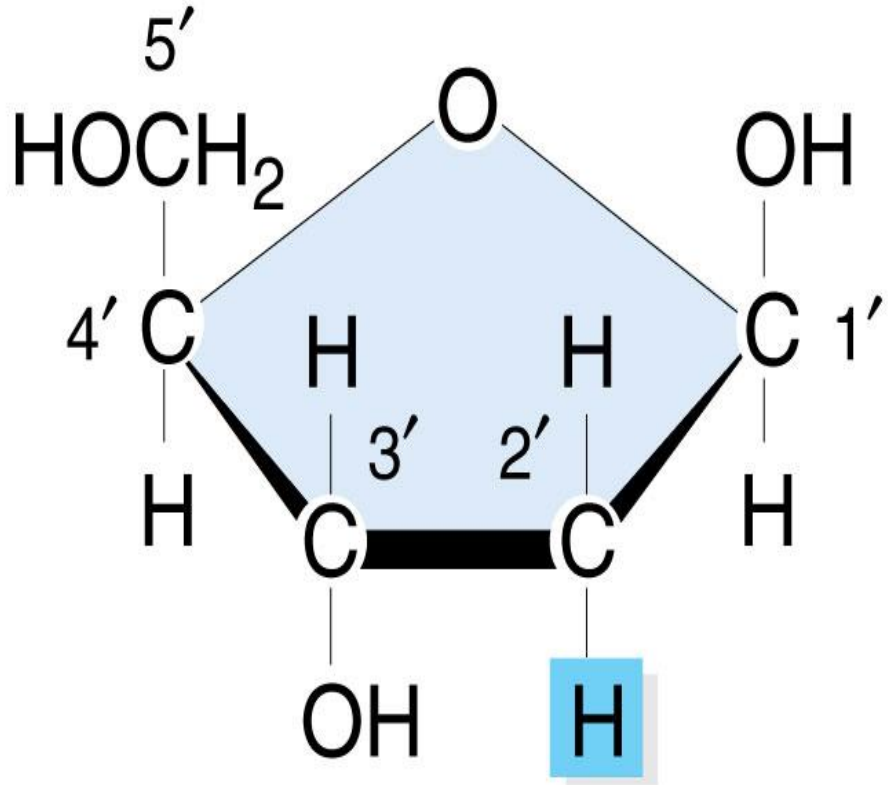
Nucleotides – the framework of DNA

Nucleotide bases

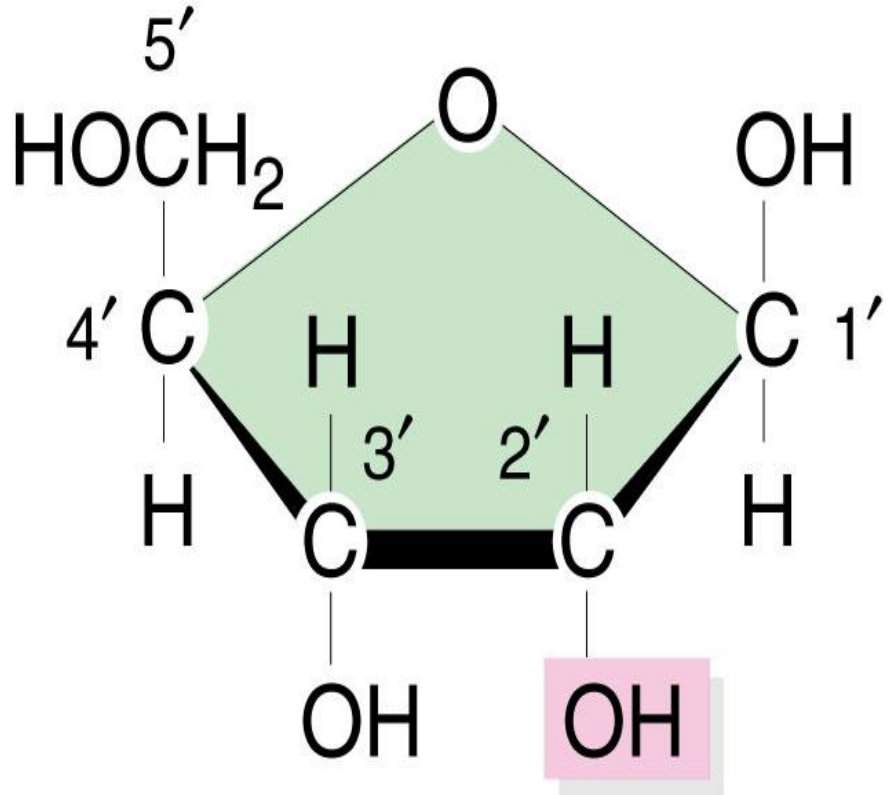




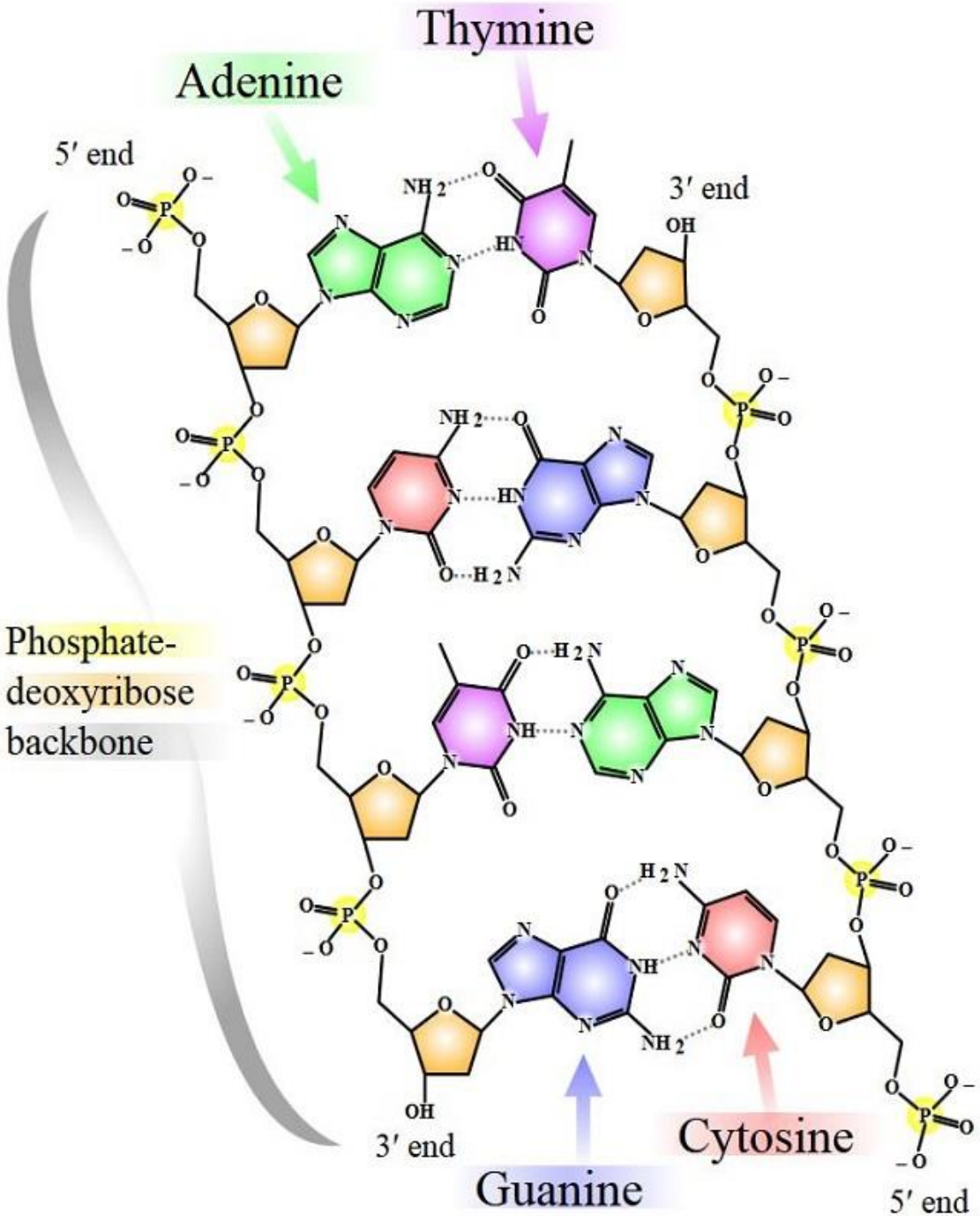


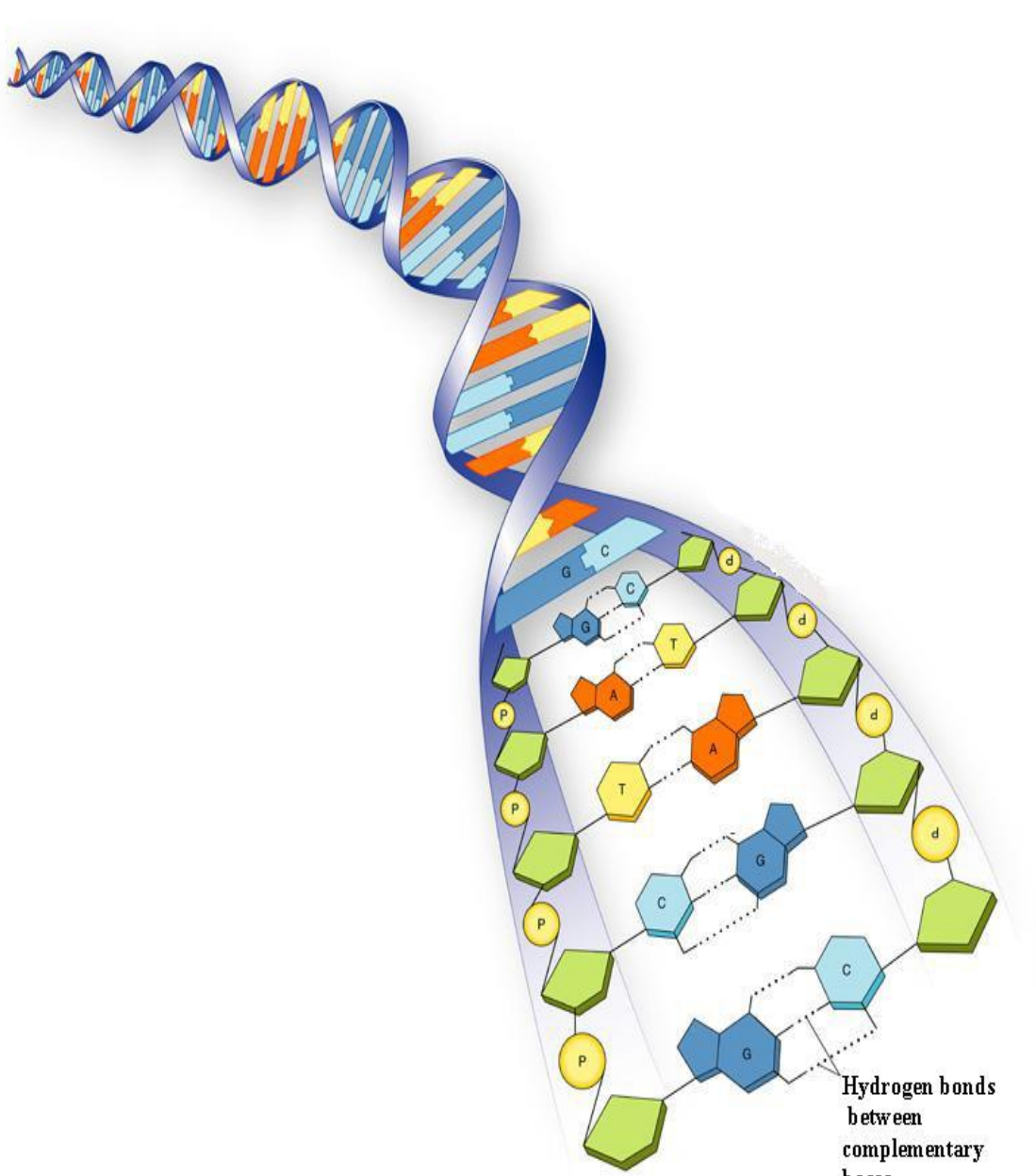


Deoxyribose

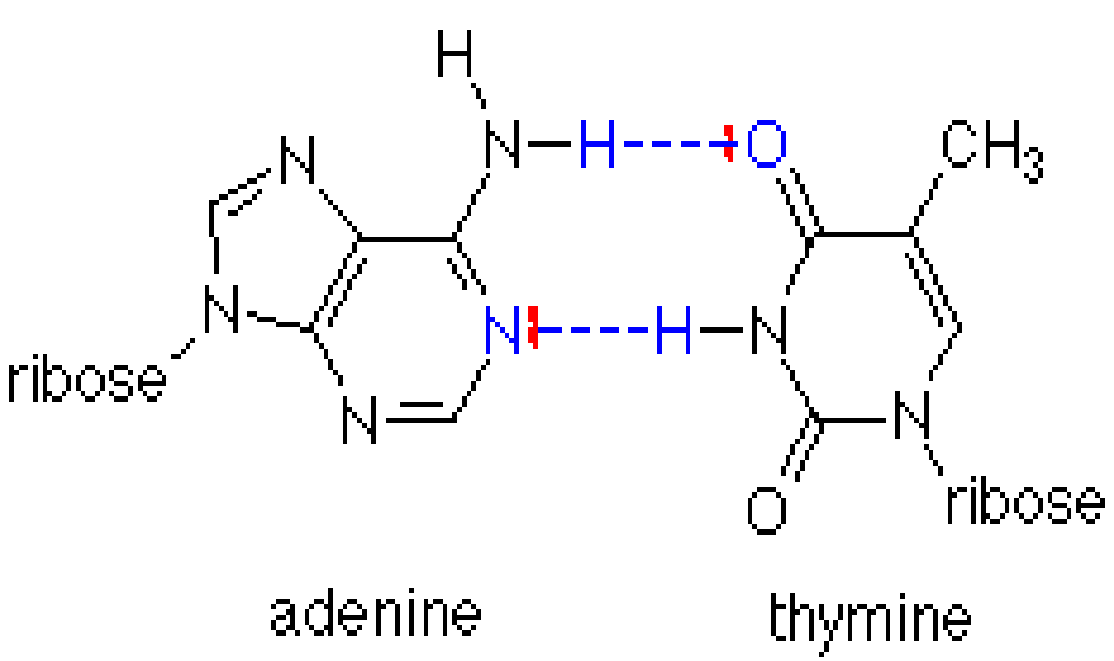


Ribose

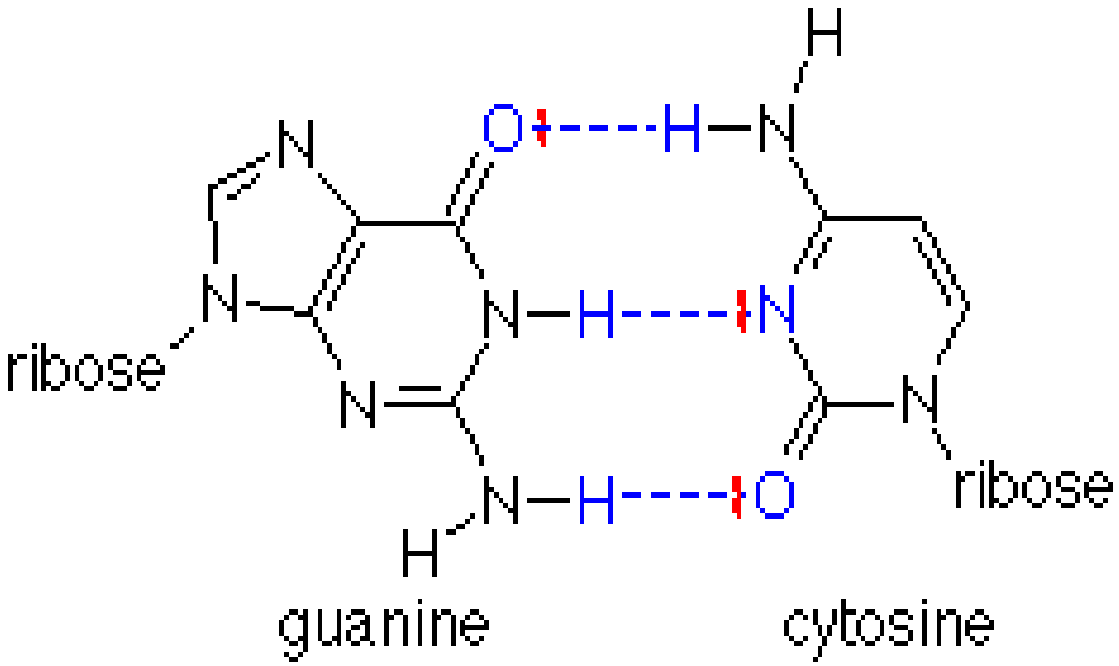




Original idea: Nucleotide bases held together by hydrogen bonding

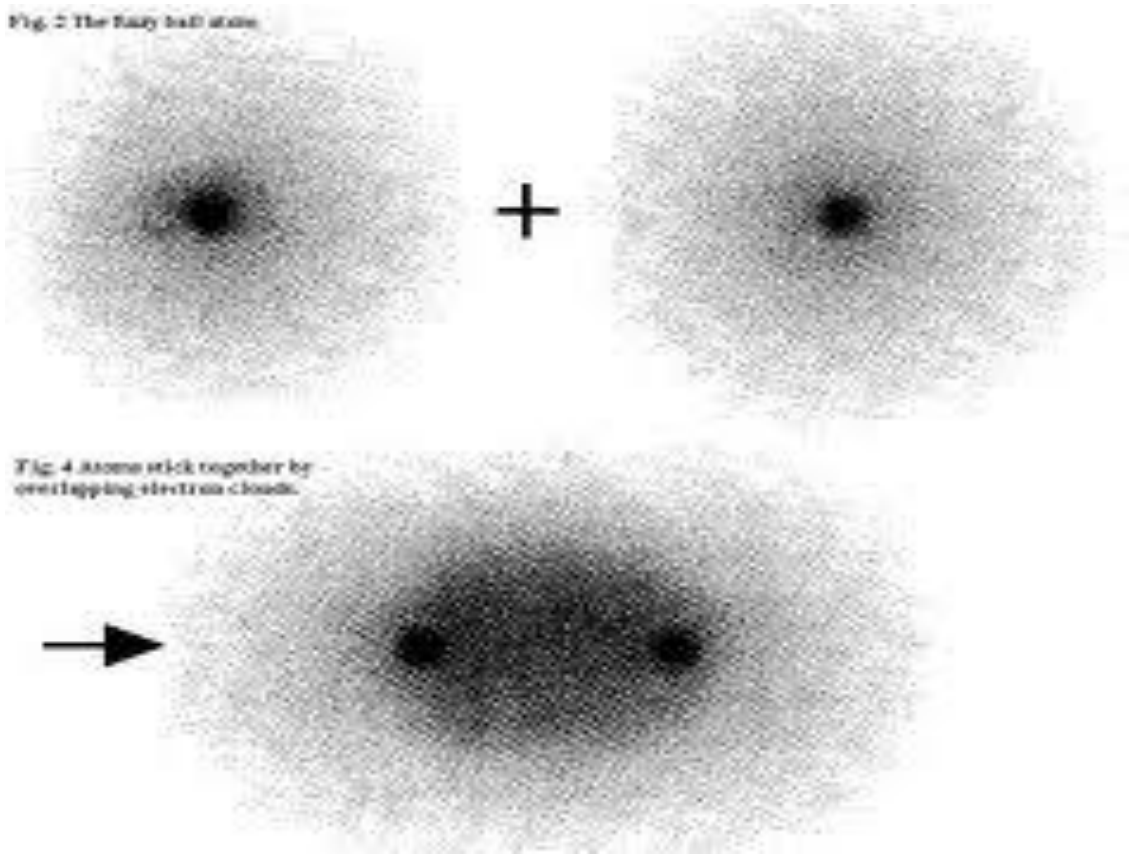


adenine thymine



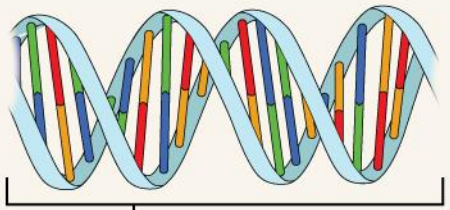
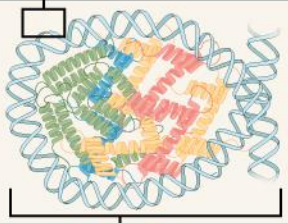
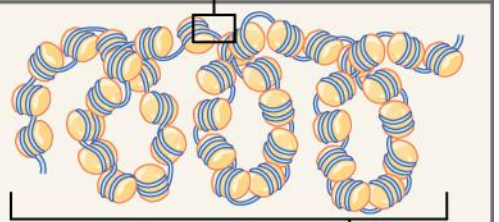
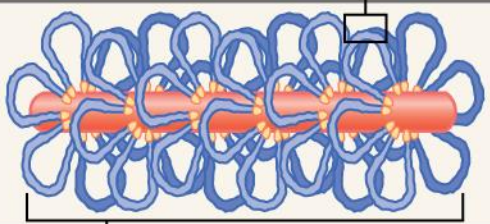
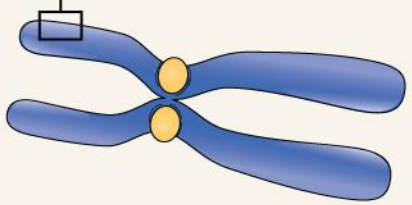
guanine cytosine

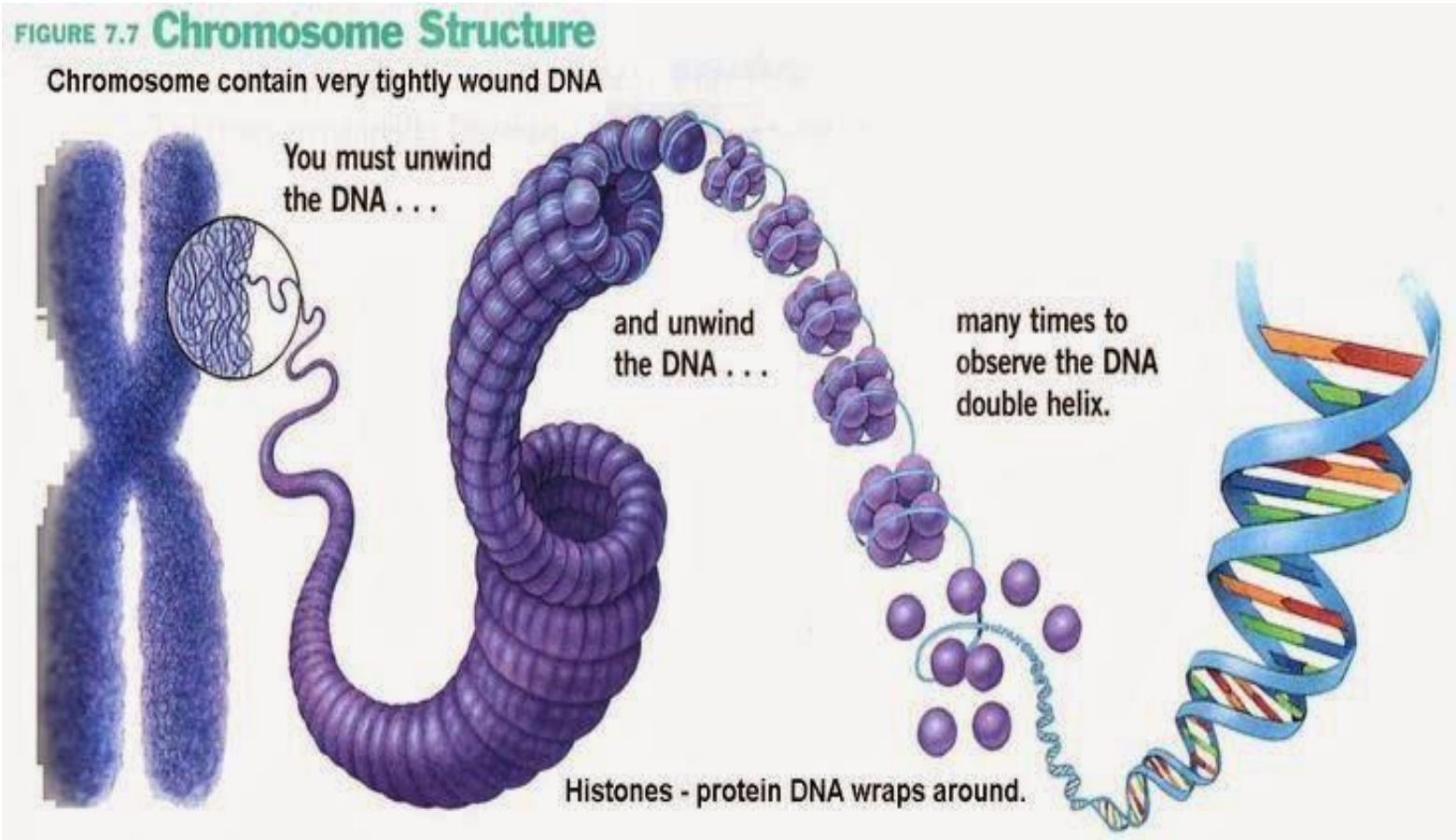
Recent idea: Entanglement of electron “fogs” from atoms on opposing bases



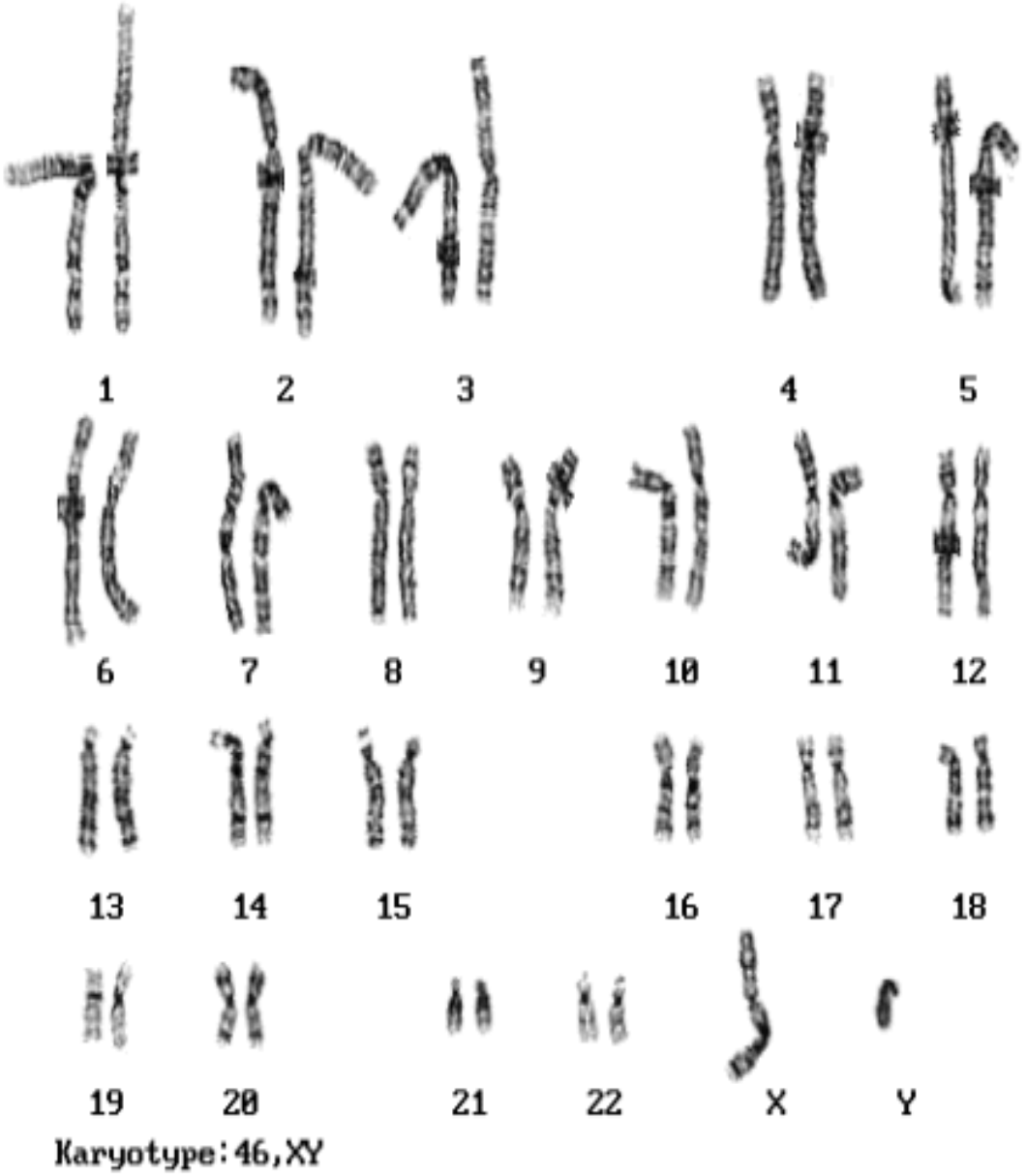
Nebula in center of the Milky Way resembling the structure of DNA

"*DNA may be created by a quantum template*" David Wilcock "The Source Field Investigations"

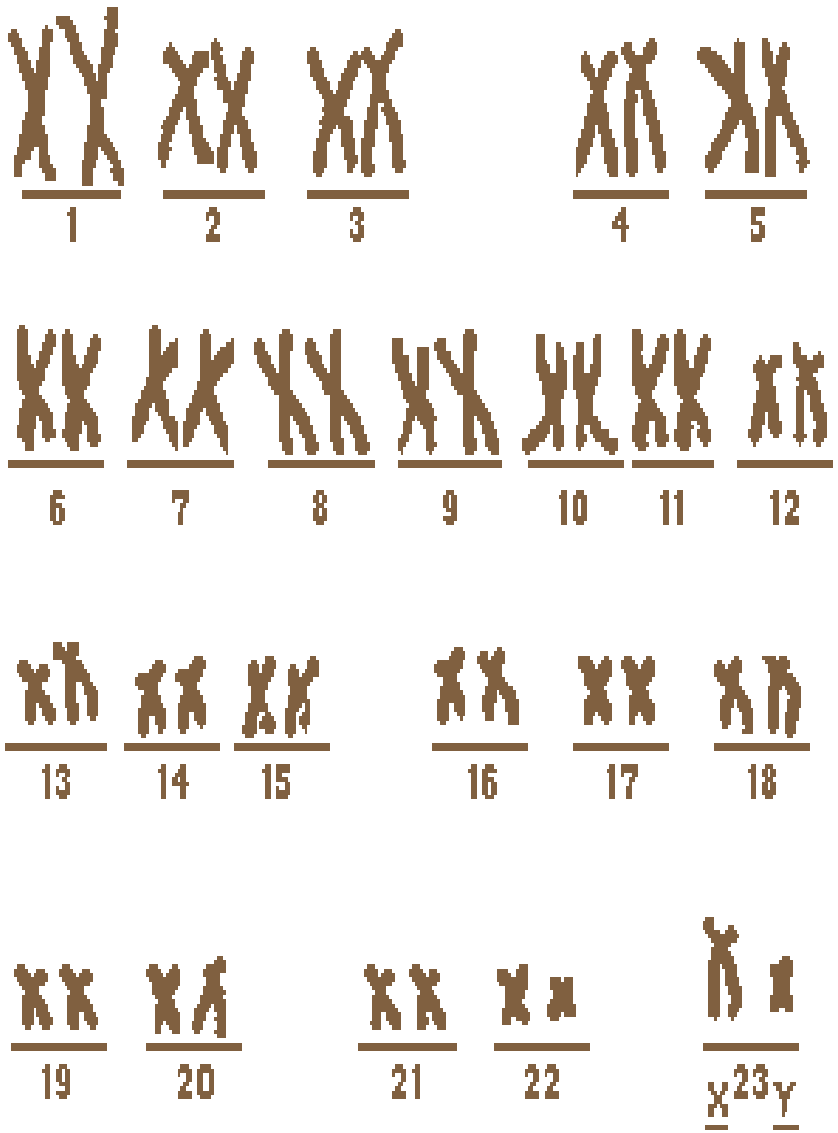
Organization of Eukaryotic Chromosomes	
DNA double helix	
DNA wrapped around histone	
Nucleosomes coiled into a chromatin fiber	
Further condensation of chromatin	
Duplicated chromosome	



human male chromosomes



chromosomes duplicated



Telomeres (telos = end; meros = part):

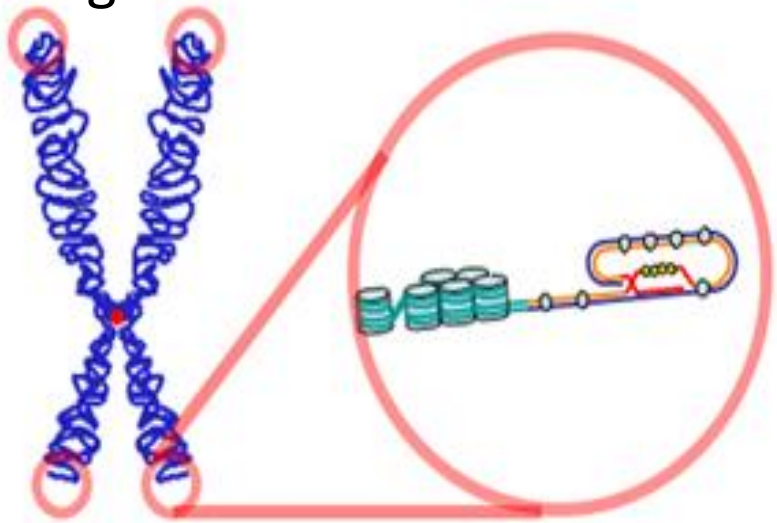
Repeating sequences of the base combination TTAGGG placed at the ends of a chromosome.

The role of telomeres is to keep the chromosomes from bonding to each other.

There are about 2,500 repeats of a telomere sequences at birth.

Every time a cell duplicates one or more sequences split off.

By old age the average duplicating cell is down to about a 900 sequences.



Lenard Hayflick, American anatomist discovered that dividing cells, such as skin and GI, divide on average 52 times (range 40-60) before division ceases (Stanford Univ. circa 1961).

Later shown to be due to Telomeres reaching a minimal number of replications.

Barbara McClintock, American botanist hypothesized end elements on chromosomes that prevented them from “sticking” together (1933)

1983 Nobel Prize for her work on genetic control elements

Elizabeth Blackburn discovered the structure of telomeres (Yale Univ. circa 1976)

Elizabeth Blackburn, Carol Greider and Jack Szostak; Nobel Prize in Physiology and Medicine for elucidating the mechanism of telomere protection of chromosomes (2009).

Epigenetics

Epi – high- or above- genetics

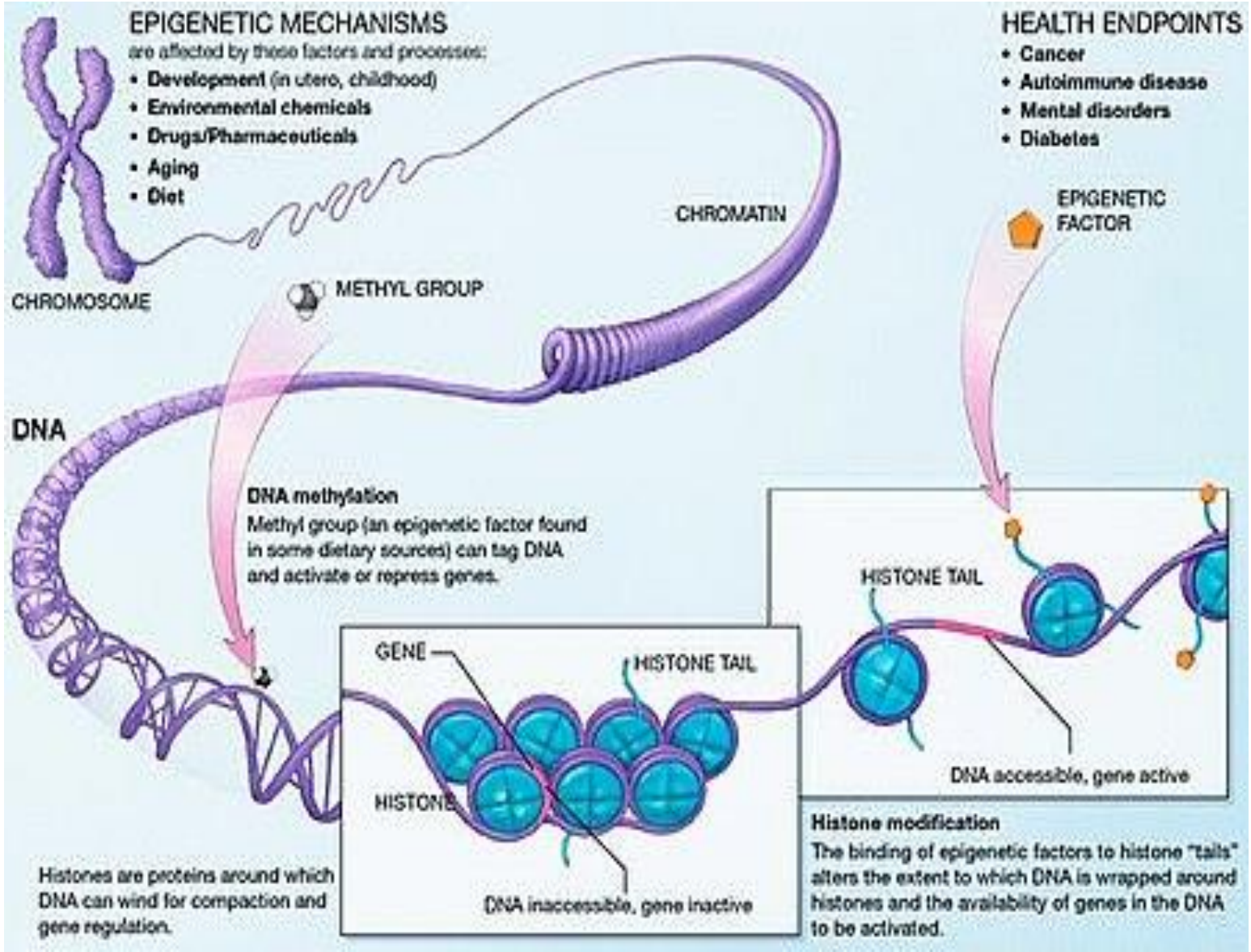
Epigenetics : transmittance of information through gene expression levels rather than changes in gene sequence

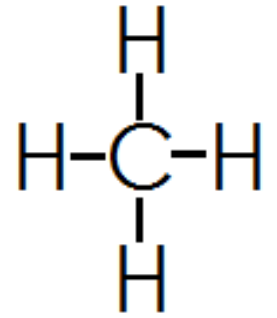
DNA methylation & histone modifications (methylation, acetylation, phosphorylation)

Epimutations faster than mutations

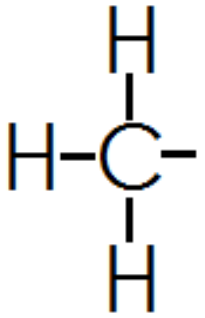
External environmental factors can alter epigenetic gene regulation.

Epigenetics: Study of the structure and function of surface molecules on DNA
Alterations in gene functions that do not involve DNA sequences





methane



methyl group

Conrad Waddington, British biologist coined the term epigenetics in 1942 (before structure of DNA was known) to refer to how genes might interact with the environment.

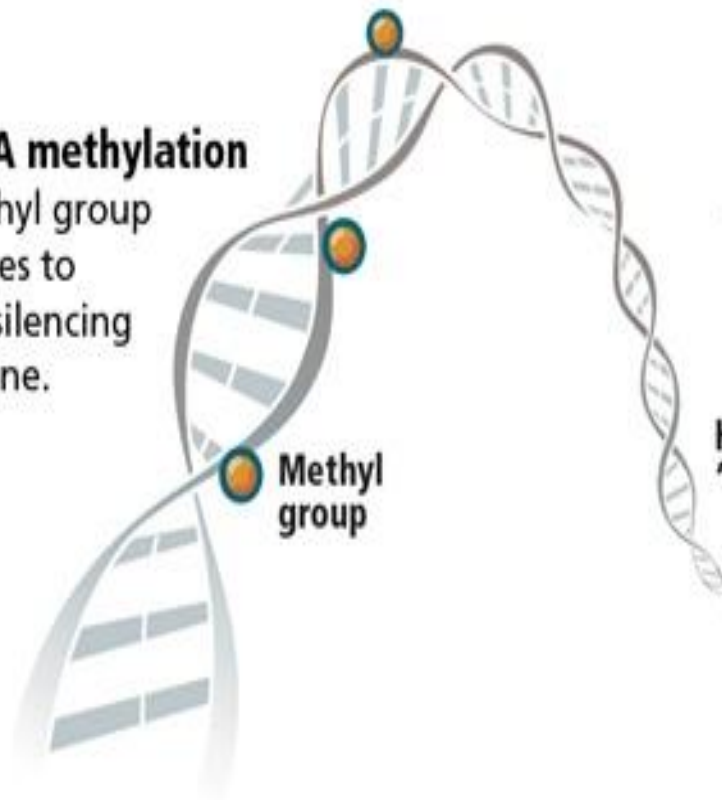
We now know that the environment does affect genes through the actions of epigenetic molecules.

Flipping the Switch

The addition of certain chemical markers can turn a gene on or off via one of two main epigenetic processes.

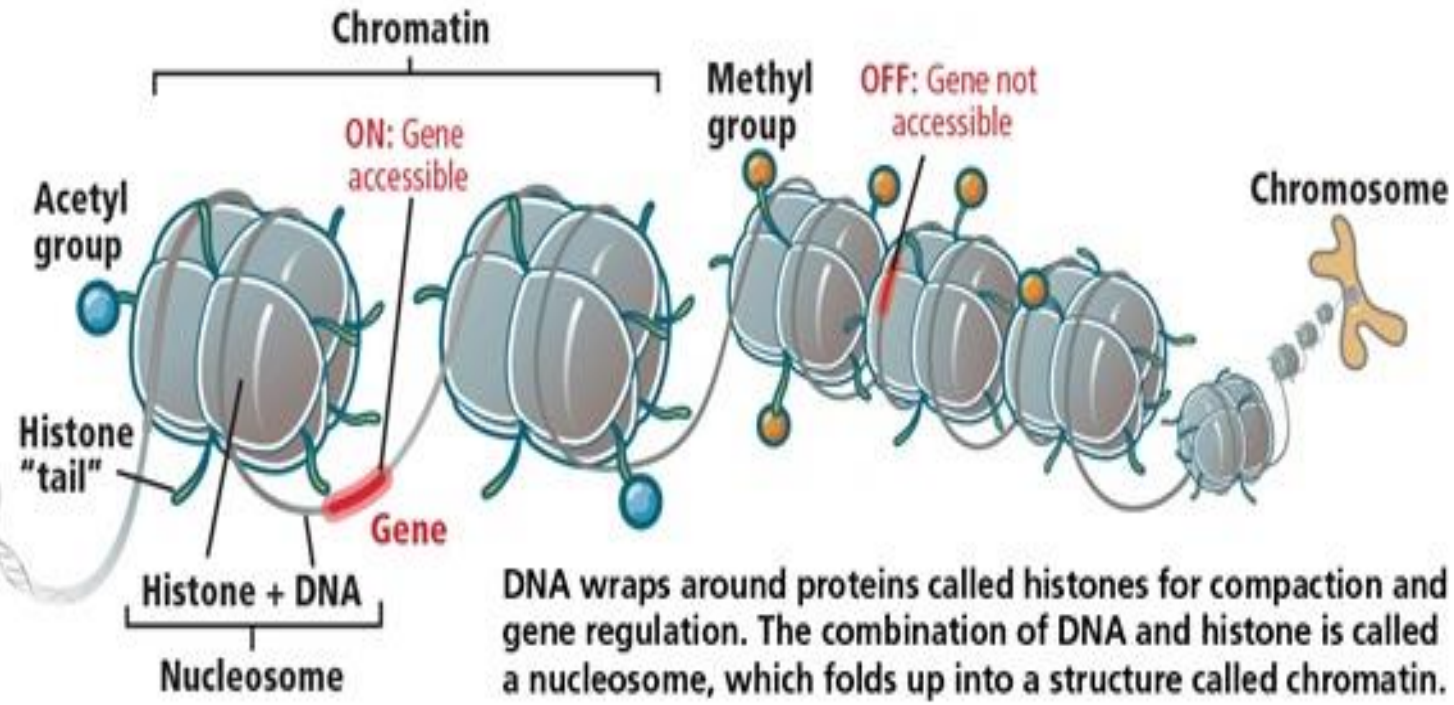
1. DNA methylation

A methyl group attaches to DNA, silencing the gene.



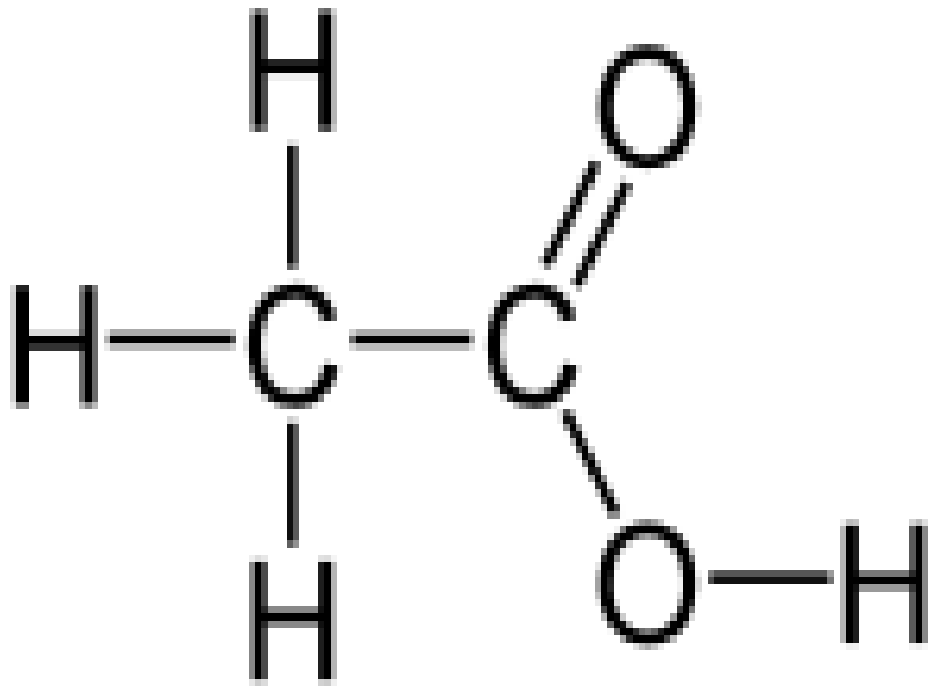
2. Histone modification

Epigenetic markers attach to the histone tail. An acetyl group causes the chromatin to unfurl, exposing the gene for transcription. Methyl groups have the opposite effect, causing the chromatin to pack tightly together, rendering the gene inaccessible.



DNA wraps around proteins called histones for compaction and gene regulation. The combination of DNA and histone is called a nucleosome, which folds up into a structure called chromatin.

Acetyl groups are compounds bonded to acetic acid



Sources of epigenetic molecule placement

Inheritance
Embryonic development
Environment and behaviors throughout life
- Dietary
- Physical activity
- Exposure to outdoor environment
  - Nature of outdoor environment
- Changes in environmental/behavioral factors elicit changes in epigenetic molecules

Diet

Psychological state

Diurnal/Seasonal correlations

Seasonal affective disorder

Social Interactions

EPIGENETIC MODULATION

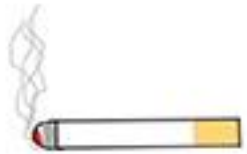
GENETIC

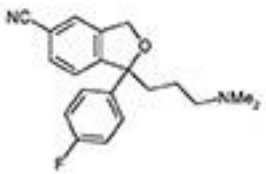
MODULATION

Disease exposure

Alternative medicine

Toxic Chemicals





Therapeutic Drugs

Drugs of Abuse

Microbiome

Exercise

Financial Status

Twins at 97

NASA confirms: Scott (left) and Mark Kelly still identical twins!
Only a 7% difference in the way certain genes are expressed.

Some, but not all, functions of epigenetic molecules

Cell differentiation:

Stem cell to muscle, nerve, liver, etc etc

Receptors of signals that initiate genetic expression

Can “select” conditions of genetic expression

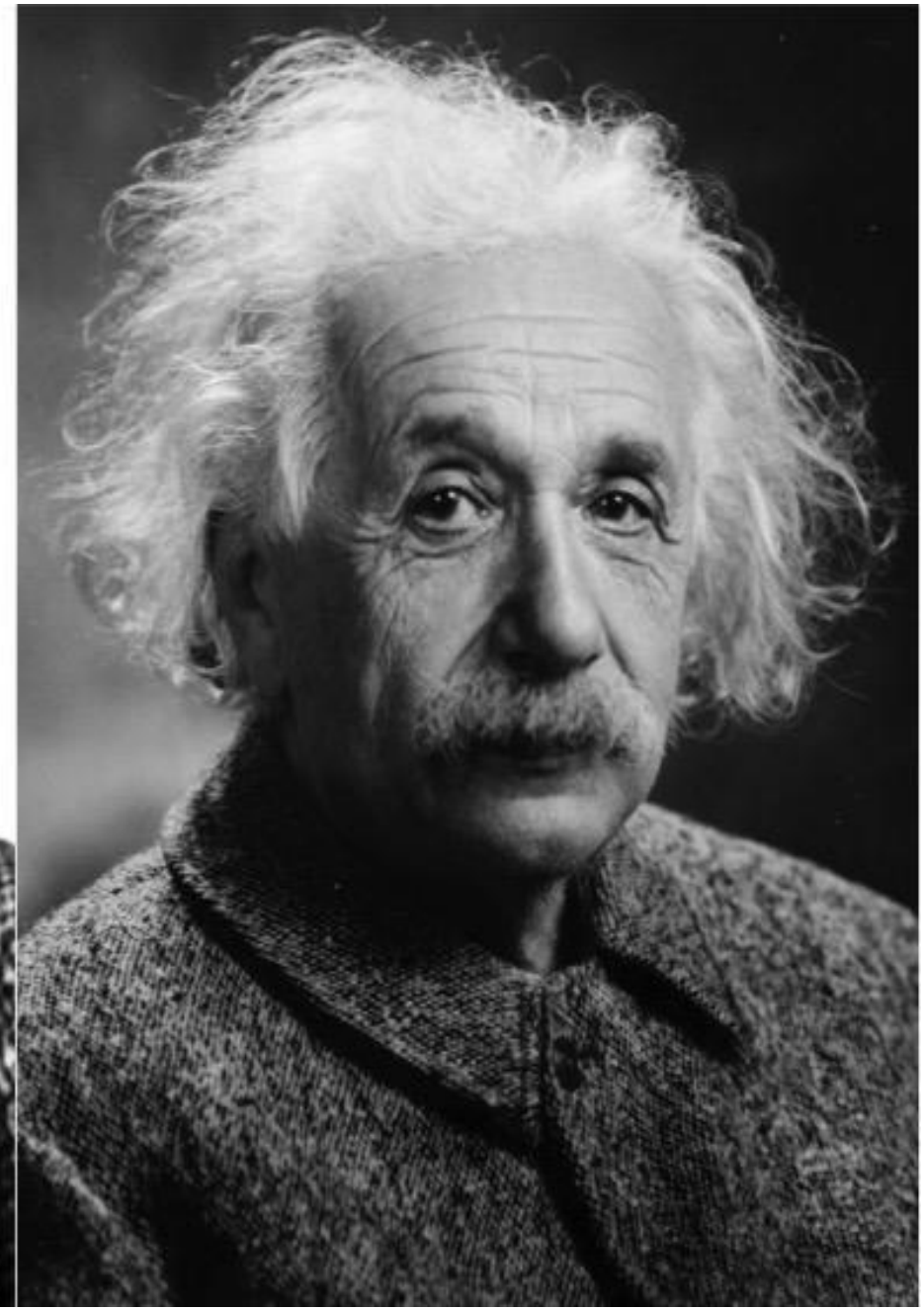
*Determination of phenotype:

The physical properties of an organism that are determined by interaction of their genotype with the environment.

*Contribute to repair of damaged DNA

But, epigenetic molecules can also be damaged along with DNA

*Determinants of aging



Biophotons as a component of DNA

Biophotons – photons emitted and absorbed by biological cells.

Absorption in humans occurs by:

- Consumption of plant food where:
  - Photons are byproducts of photosynthesis
- Exposure of eyes and skin to the sun.

Photons - energy carrying components of the electromagnetic spectrum

A blue photon

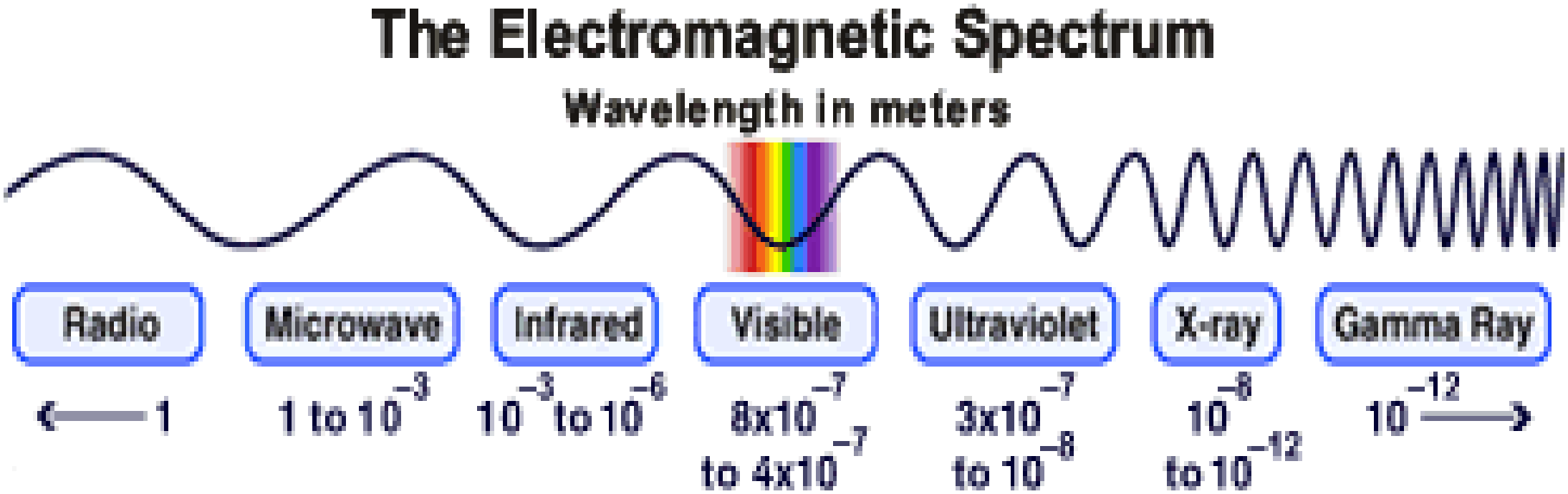
A red photon

$$E = h/\lambda$$

E = energy of a photon

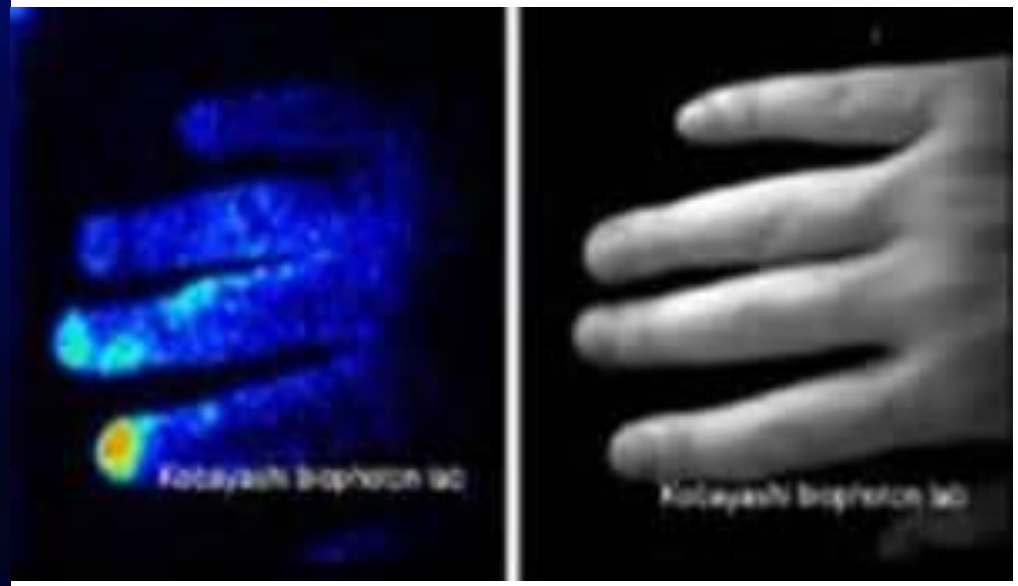
h = Planck's constant

λ = wave length of a photon



Fritz-Albert Popp (circa 1974)
Discovered single biophoton emissions from plants and humans

Photomultiplier (detects single photons) and recorded images of biophotons.



Biophotons have a wave length similar in size to a DNA helix

Enables them to be “stored” within DNA, and

Released as DNA unwinds during genetic expression

Biophotons are then thought to orchestrate genetic expression

Other roles of biophotons

Individual cells perform about 1,000 tasks per second
most, if not all, involving chemical reactions.

To fast to be totally due to chemical diffusion

By a process known as wave coherence, biophotons transmit information:

- Within cells
- Between cells
- Between different components of an organism
- Between organisms (e.g., individual people)
  - Thought to be mechanism of extrasensory perception

Emission of biophotons from neurons in the brain and their interaction with energy waves in the environment may be the mechanism of psychic phenomena and societal communication.

“Their (the pack) strength was not derived of muscularity or grace. Rather, it flowed from a single-minded intelligence. The individual animals converged into a lethal unit, cohering in the collective strength of the pack.”

Michael Punke, “The Revenant”

Chromosomes in brief

Chromosomes consist of a core of DNA surrounded by epigenetic molecules with the center of the DNA core containing a concentration of biophotons.

Each chromosome consists of hundreds to a thousand genes.

Each gene codes for the synthesis of *several* proteins, a process termed genetic expression.

Epigenetic molecules and biophotons within DNA regulate genetic expression.

Next Section:

Genetic expression and the genetic code