

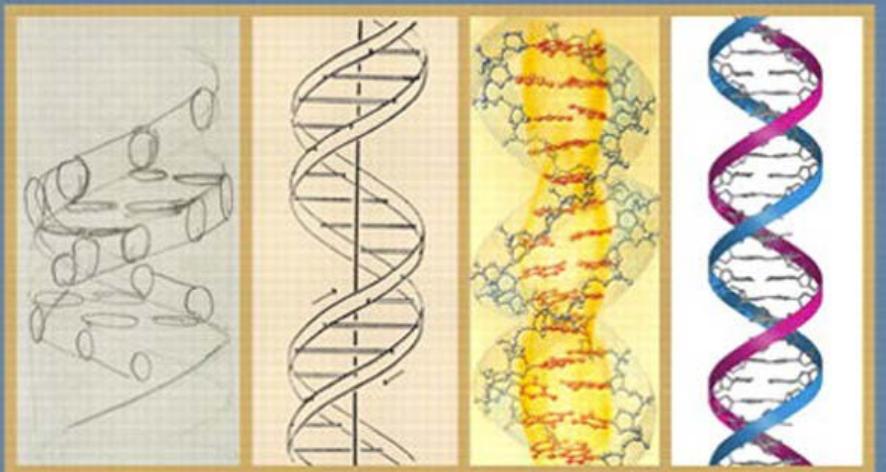
Molecular Biology of Gene Basics of Molecular Biology

Sulev Kuuse
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2022

LMR05.001 - 1

MOLECULAR BIOLOGY OF THE GENE

SEVENTH EDITION



WATSON • BAKER • BELL
GANN • LEVINE • LOSICK

To order the book:

http://www.estر.ee/record=b3351750*est

http://www.estر.ee/record=b3404652*est

To get the book from web:

<https://drive.google.com/file/d/1KV6aDhAhRfQT0JWpYtiFdN33DOULaVD/view?usp=sharing>

Watson, J.D., Baker, T.A., Bell, S.P., Gann, A., Levine, M., Losick, R.
Pearson Education & Cold Spring Harbor Laboratory Press, 2014

Lectures

Attendance in lectures is not obligatory but it is useful.

All slides are important to understand the contents of molecular biology. The best one for studying is the Book of Watson.

For better understanding of lecture material it is warmly recommended to read and check chapter(s) of next lecture over at home.

Lectures are interactive.

Tests

Four intermediate tests all account will sum up for final grade.

Final grade = Test1 + Test2 + Test3 + Test4

If each test for example is max 50 points,

Then You can collect max 200 points in total.

If one scores <100 points in tests, he or she has to take full written exam to pass the subject.

Exam

NB! Maximum grade based on test results will be A - it means You must collect at least 181 points.

If one for example has scored for example 161+ points (three-fourths, it means 80% or more of total maximum), he or she can come for an oral examination to upgrade B -> A.

In any case will B be not lowered.

SUM: If one scores <100 points (one-half) in tests, he or she has to take full written exam about our course of study to pass the subject.

22.03.2022	lecture	The Introduction, The Mendelian view of the world, Molecular biology off gene (chapters 1-2)
23.03.2022	lecture	The nucleic acids structure, The DNA topology (chapter 4)
25.03.2022.	lecture	The DNA stucture II, The DNA topology (chapter 4)
29.03.2022	lecture	The RNA Structure (chapter 5), The Protein structure (chapter 6)
30.03.2022	lecture	TheSstructure of Proteins (chapter 6) and Methods in Molecular Biology (ch 7)
01.04.2022	test I	



05.04.2022	lecture	Genome structure, Chromatin, histones and nucleosomes, Chromosome duplication and segregation (chapter 8)
06.04.2022	lecture	Histones and nucleosomes, Chromosome duplication and segregation (chapter 8)
08.04.2022	lecture	Replication (chapter 9)
12.04.2022	lecture	DNA damage and DNA repair (chapter 10)
13.04.2022	lecture	Homologous recombination (chapter 11)
15.04.2022	individual lesson	Good Friday
19.04.2022	test II	



- 20.04.2022 21 lecture Conservative site-specific recombination of DNA (chapter 12)
- 22.04.2022 lecture Transposition (chapter 12)
- 26.04.2022 lecture Transcription - initiation, elongation, termination (chapter 13)
- 27.04.2022 lecture Transcription in Eukaryotes (chapter 13)
- 29.04.2022 lecture RNA splicing (chapter 14)
- 03.05.2022 **test III**



04.05.2022	lecture	Translation I, mRNA, tRNA, starting capping, charging tRNA, aminoacylation (chapter 15)
06.05.2022	lecture	Translation II , Regulation of translation. Ribosome (chapter 15)
10.05.2022	lecture	Translation initiation, elongation and termination (chapter 15)
11.05.2022	lecture	Regulation of translation (chapter 15)
13.05.2022	lecture	Transcription regulation, RNAi, Gene 'Silencing', Regulatory RNAs (ch 18, 19, 20)
17.05.2022	test IV	
18.05.2022	e-learning	
20.05.2022	e-learning	
24.05.2022	full written exam or oral talking for upgrading test results from B to A	

Introduction & History

The Mendelian View of the World

How Nucleic Acids Convey
Genetic Information?

(Watson et al., 2014, chapters 1-2)

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Sulev Kuuse

Inst Mol Cell Biol



Gregor Johann Mendel (Czech: Řehoř Jan Mendel; 20 July 1822 – 6 January 1884)
He was the scientist in Moravia and Augustinian friar and since 1867 as the Abbot of the Monastery in Brno

Most known for his work on breeding experiments between strains of pea plants, *Pisum sativum* (1856 – 1863)

1865 presented a paper entitled “Experiments in Plant Hybridization”

In 1900, 16 years after Mendel’s death **Hugo de Vries, Karl Correns, and Erich von Tschermak-Seysenegg** and **William Jasper Spillman, William Bateson** working independently on different systems confirmed the significance of Mendel’s forgotten work.

Young Mendel was beekeeper or he worked with apiculture – the maintenance of bee colonies.

I Law - Mendels law of Dominance and uniformity (also called Menedels First Rule)

Peas differing in well-defined characteristics, like **seed shape** (round or wrinkled), **seed color** (yellow or green), **pod shape** (inflated or wrinkled), and **stem length** (long or short).

After ascertaining that each type of parental strain bred true—that is, produced progeny with particular qualities identical to those of the parents—Mendel performed a number of crosses between parents (P) differing in single characteristics (such as seed shape or seed color). All the progeny (F1 ¼ first filial generation) had the appearance of one parent only. For example, in a cross between peas having yellow seeds and peas having green seeds, all the progeny had yellow seeds. The trait that appears in the F1 progeny is called **dominant**, whereas the trait that does not appear in F1 is called **recessive**.

Hereditary transmission through the sperm and egg became known by 1860, and in 1868 Ernst Haeckel, noting that sperm consists largely of nuclear material, postulated that the nucleus is responsible for heredity. Almost 20 years passed before the chromosomes were singled out as the active factors, because the details of mitosis, meiosis, and fertilization had to be worked out first.

Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.

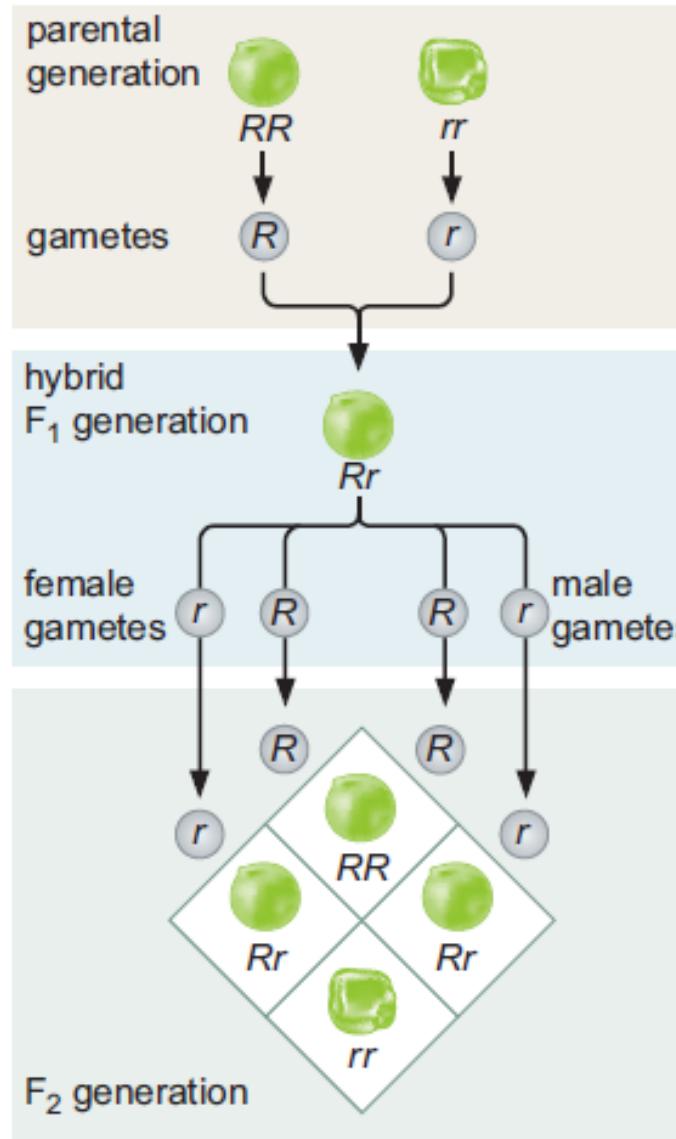
If two parents are mated with each other who differ in one genetic characteristic for which they are both homozygous (each pure-bred), all offspring in the first generation (F1) are equal to the examined characteristic in genotype and phenotype showing the dominant trait.

This uniformity rule or reciprocity rule applies to all individuals of the F1-generation.



II Law - Law of Segregation of Genes

The principle of independent segregation (also called Second Rule)



one gene = one trait

R – dominant; round seed
 r – recessive; wrinkled seed

FIGURE 1-1 How Mendel's first law (independent segregation) explains the 3:1 ratio of dominant to recessive phenotypes among the F_2 progeny. R represents the dominant gene and r the recessive gene. The round seed represents the dominant phenotype, the wrinkled seed the recessive phenotype.

F_2 progeny – the 3 : 1 ratio of dominant to recessive phenotypes and 1:2:1 ratio of genotype divergence

Law of Segregation of genes (the "Second Law")

The Law of Segregation states that **every individual organism contains two alleles for each trait**, and that **these alleles segregate (separate) during meiosis such that each gamete contains only one of the alleles**.

An offspring thus receives a pair of alleles for a trait by inheriting homologous chromosomes from the parent organisms: **one allele for each trait from each parent**.

Molecular proof of this principle was subsequently found through observation of meiosis by two scientists independently, the German botanist **Oscar Hertwig in 1876**, and the Belgian zoologist **Edouard Van Beneden in 1883**.

Paternal and maternal chromosomes get separated in meiosis and the alleles with the traits of a character are segregated into two different gametes.

Each parent contributes a single gamete, and thus a single, randomly successful allele copy to their offspring and fertilization.

No need to be recessive

Some alleles are neither Dominant nor Recessive

In the the crosses reported by Mendel, one member of each gene pair was clearly dominant to the other.

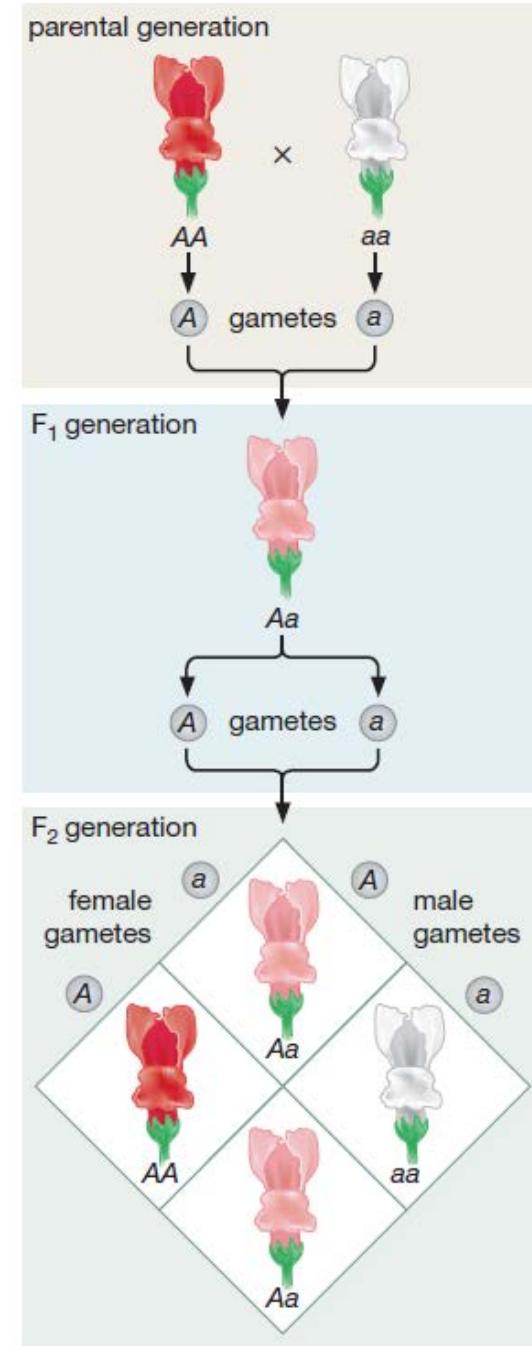
Thus, it is possible here to distinguish heterozygotes from homozygotes by their phenotype.

We also see that Mendel's laws do not depend on whether one allele of a gene pair is dominant over the other.

The ratio 1 : 2 : 1

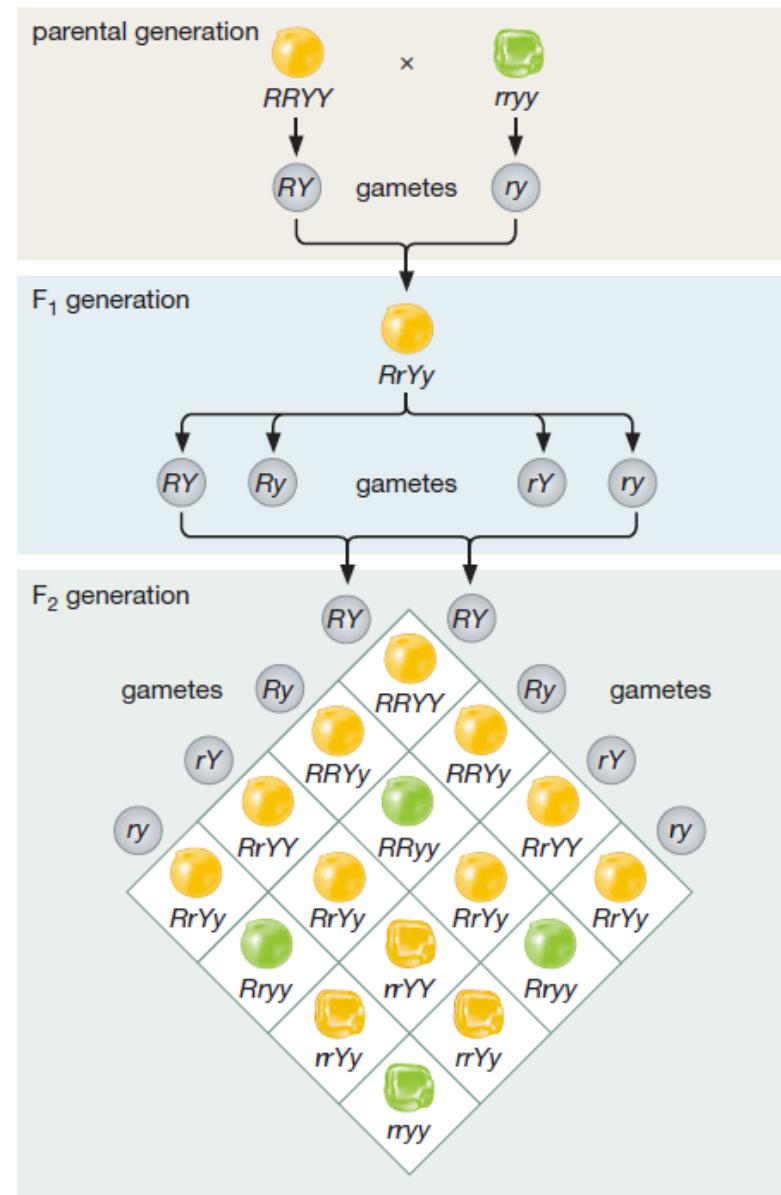
1 dominant-2 heterozygous-
1 recessive

FIGURE 1-2 The inheritance of flower color in the snapdragon. One parent is homozygous for red flowers (AA) and the other homozygous for white flowers (aa). No dominance is present, and the heterozygous F_1 flowers are pink. The 1:2:1 ratio of red, pink, and white flowers in the F_2 progeny is shown by appropriate coloring.





III Law - Law of Independent Assortment



G. Mendel postulated that the yellow- and green-seed genes are carried on a certain pair of chromosomes and the round- and wrinkled-seed genes are carried on a different pair.

This hypothesis immediately explains the experimentally observed 9:3:3:1 segregation ratio (9 different genotypes and 4 phenotypes).

The gene divergence by different two genes happens independently.

F₂ progeny:
R – round & yellow
r- wrinkled & green
+
Recombinants
wrinkled & yellow,
round & green

FIGURE 1-3 How Mendel's second law (independent assortment) operates. In this example, the inheritance of yellow (*Y*) and green (*y*) seed color is followed together with the inheritance of round (*R*) and wrinkled (*r*) seed shapes. The *R* and *Y* alleles are dominant over *r* and *y*. The genotypes of the various parents and progeny are indicated by letter combinations, and four different phenotypes are distinguished by appropriate shading.

Law of Independent Assortment (the "Third Law")

The Law of Independent Assortment states **that alleles for separate traits are passed independently of one another from parents to offspring**. That is, the **biological selection of an allele for one trait has nothing to do with the selection of an allele for any other trait**. Mendel found support for this law in his **dihybrid cross experiments** (Fig. 1-1). In his monohybrid crosses, an idealized 3:1 ratio between dominant and recessive phenotypes resulted. In dihybrid crosses, however, he found a **9:3:3:1 ratios** (Fig. 1-3). This shows that **each of the two alleles is inherited independently from the other, with a 3:1 phenotypic ratio for each**.

Independent assortment **occurs in eukaryotic organisms during meiotic prophase I (human)**, and produces a gamete with a mixture of the organism's chromosomes. The physical basis of the independent assortment of chromosomes is the random orientation of each bivalent chromosome along the metaphase plate with respect to the other bivalent chromosomes. **Along with crossing over, independent assortment increases genetic diversity** by producing novel genetic combinations.



Chromosomal theory of heredity

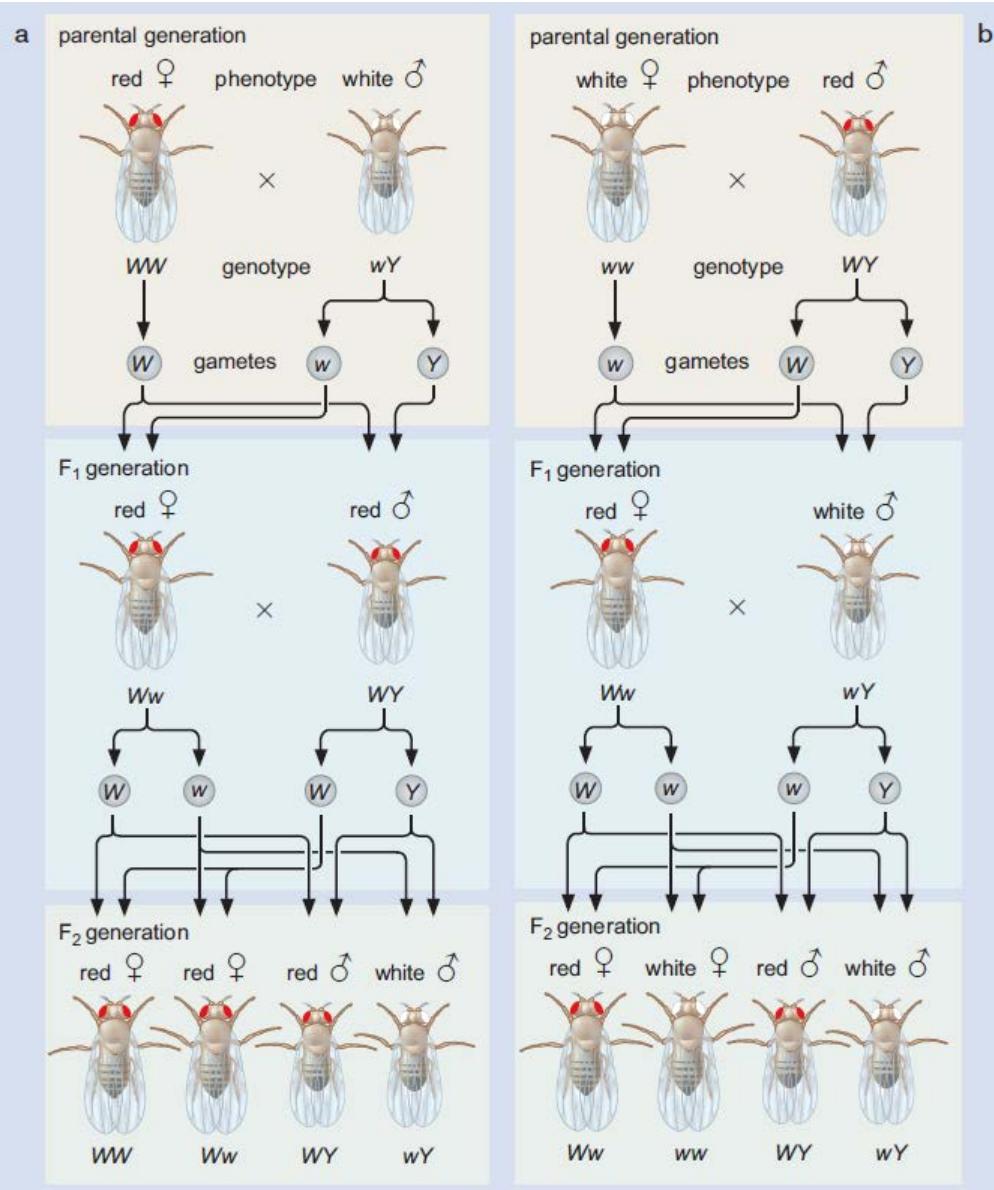
- 1903 **Walter S. Sutton** “The Chromosomes in Heredity”
 - Diploid chromosome groups contain two morphologically similar sets
 - During meiosis, each gamete receives only one chromosome of each homologous pair
 - Genes are parts of chromosomes
 - R (round) and Y (yellow) are carried by different chromosomes

The term gene was introduced by Danish botanist, plant physiologist and geneticist **Wilhelm Johannsen** in 1909!!!

Gene in ancient Greek (genos) means offspring or procreation or birth or generation!!!

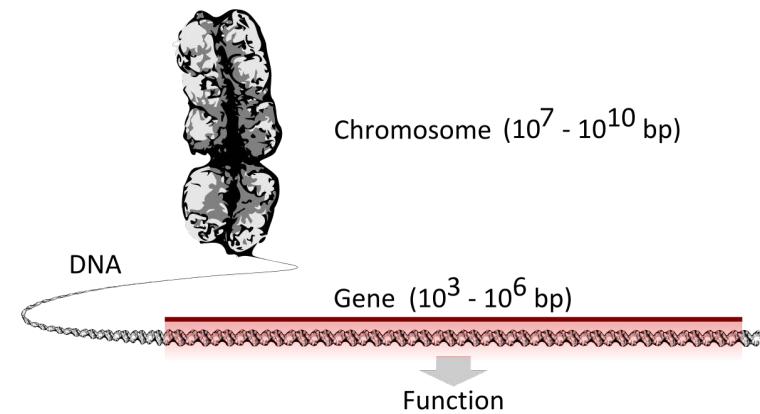
- Although **Sutton**'s paper did not prove the chromosomal theory of heredity, it was immensely important, for it brought together for the **first time** the independent disciplines of **genetics** (the study of breeding experiments) and **cytology** (the study of cell structure).
- A principal reason for the original failure to appreciate Mendel's discovery was the absence of firm facts about the behavior of chromosomes during meiosis and mitosis. This knowledge was available, however, when Mendel's laws were confirmed in 1900 and was seized upon in 1903 by American biologist Walter S. Sutton. In his classic paper "The Chromosomes in Heredity," **Sutton** emphasized the **importance of the fact that:**
 - **the diploid chromosome group consists of two morphologically similar sets, and**
 - **during meiosis, every gamete receives only one chromosome of each homologous pair.**

Genes are linked to Chromosomes



- Wild-type gene
- Mutant gene – the genes can change (mutate) to give rise to new genes

A gene is a region of DNA that encodes function. A chromosome consists of a long strand of DNA containing many genes. Each human chromosome can be up to 250 mega base pairs of DNA and it contains thousands of genes.



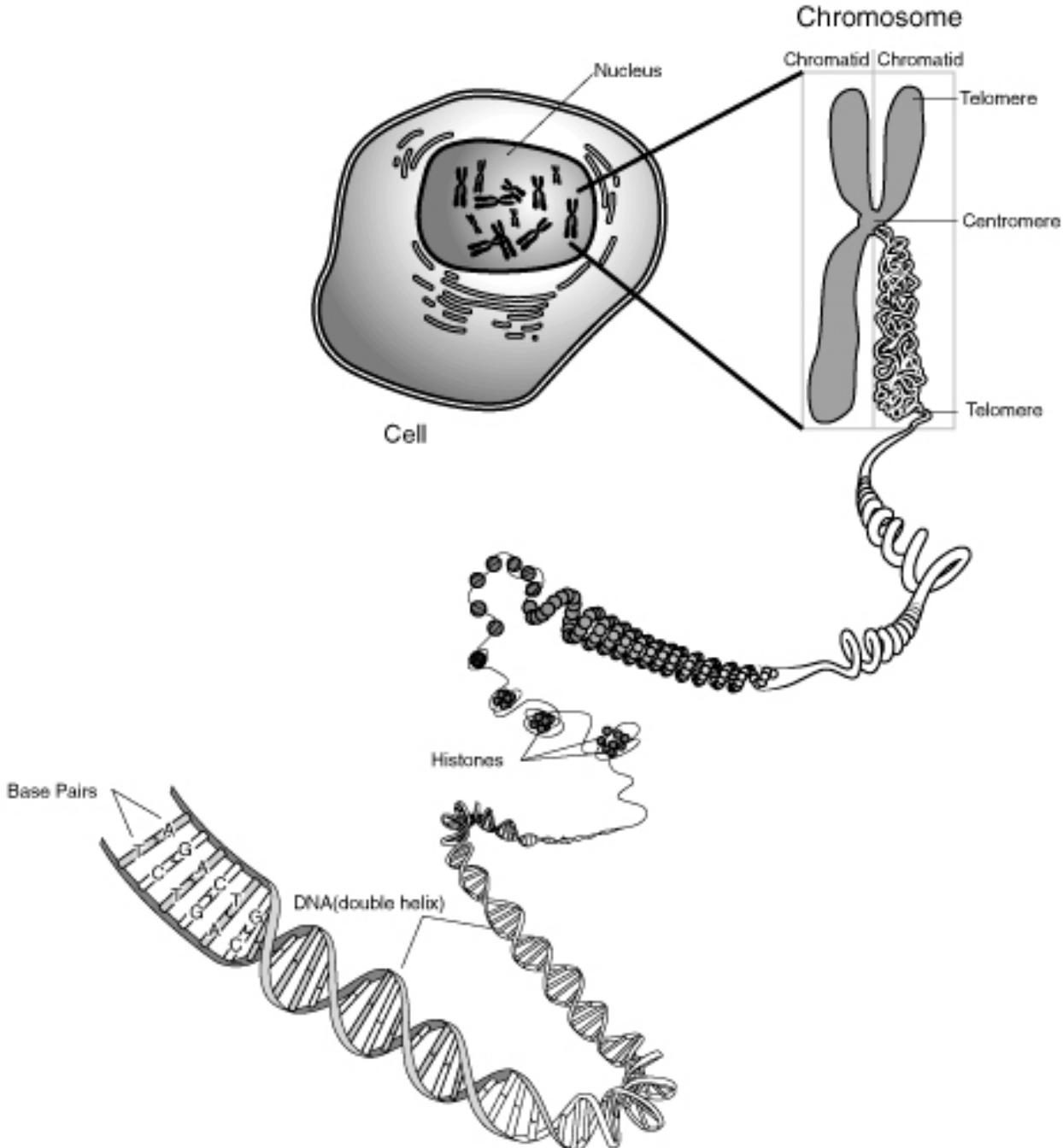
BOX 1-2 FIGURE 1 The inheritance of a sex-linked gene in *Drosophila*. Genes located on sex chromosomes can express themselves differently in male and female progeny, because if there is only one X chromosome present, recessive genes on this chromosome are always expressed. Here are two crosses, both involving a recessive gene (*w*, for white eye) located on the X chromosome. (a) The male parent is a white-eyed (*wY*) fly, and the female is homozygous for red eye (*WW*). (b) The male has red eyes (*WY*) and the female white eyes (*ww*). The letter *Y* stands here not for an allele, but for the Y chromosome, present in male *Drosophila* in place of a homologous X chromosome. There is no gene on the Y chromosome corresponding to the *w* or *W* gene on the X chromosome.

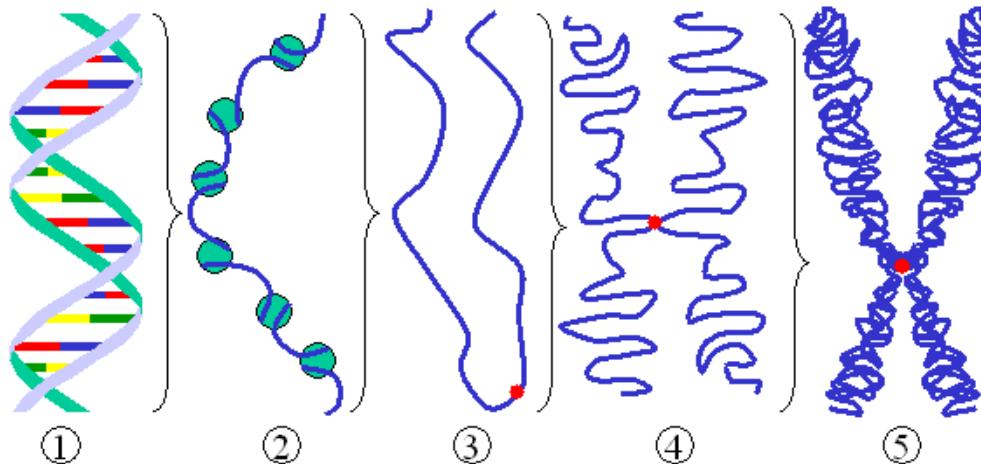
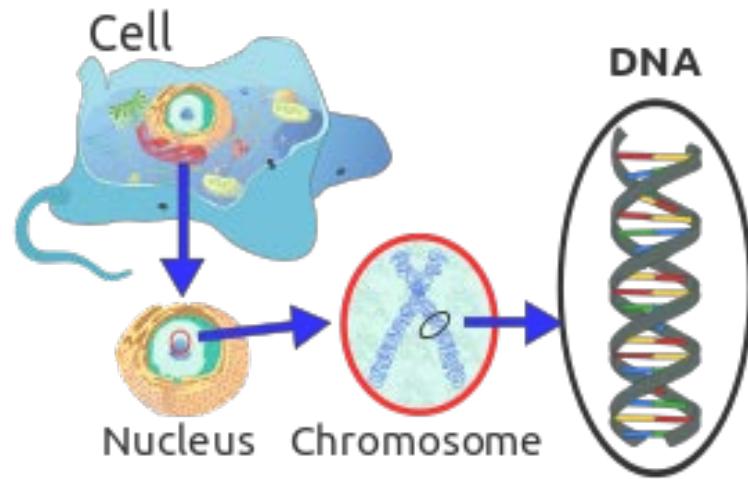
Reminder about chromosomes and mitosis and meiosis

Walter Sutton (his theory that the Mendelian laws of inheritance could be applied to chromosomes at the cellular level of living organisms) and

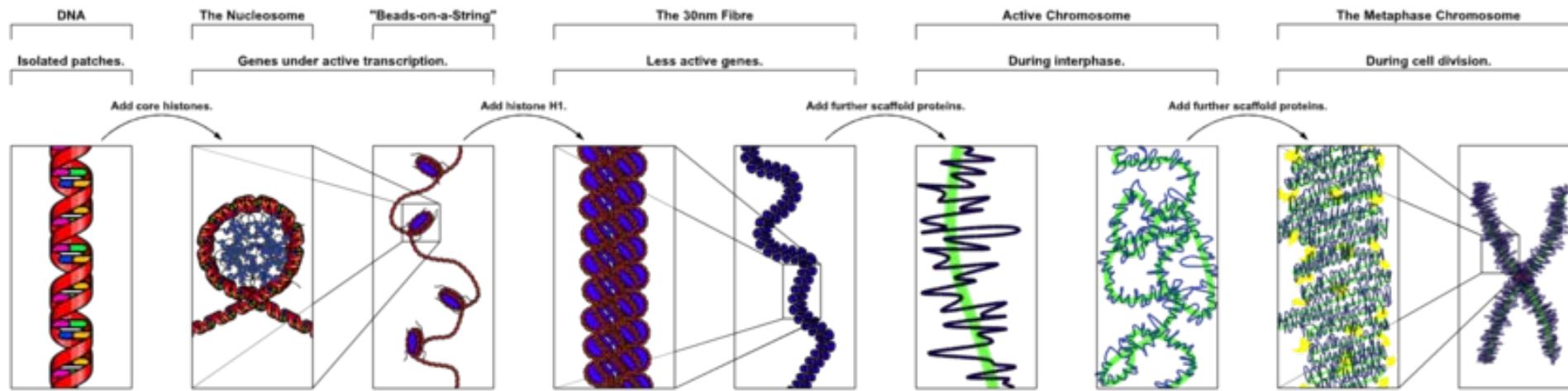
Theodor Boveri (the definitive demonstration that chromosomes are the vectors of heredity).

They independently developed **the chromosome theory of inheritance in 1902.**





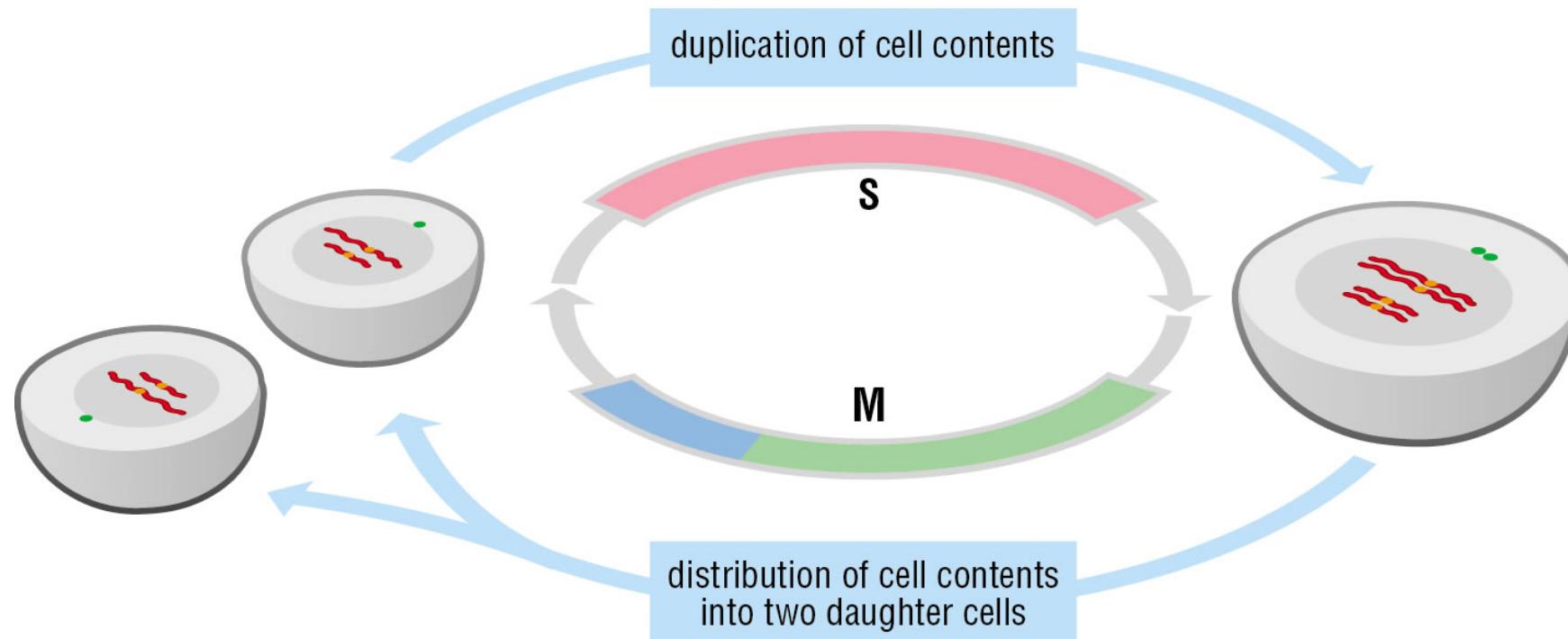
Different levels of DNA condensation in eukaryotes. (1) Single DNA strand. (2) Chromatin strand (DNA with histones). (3) Chromatin during interphase with centromere. (4) Two copies of condensed chromatin together during prophase. (5) Chromosome during metaphase.



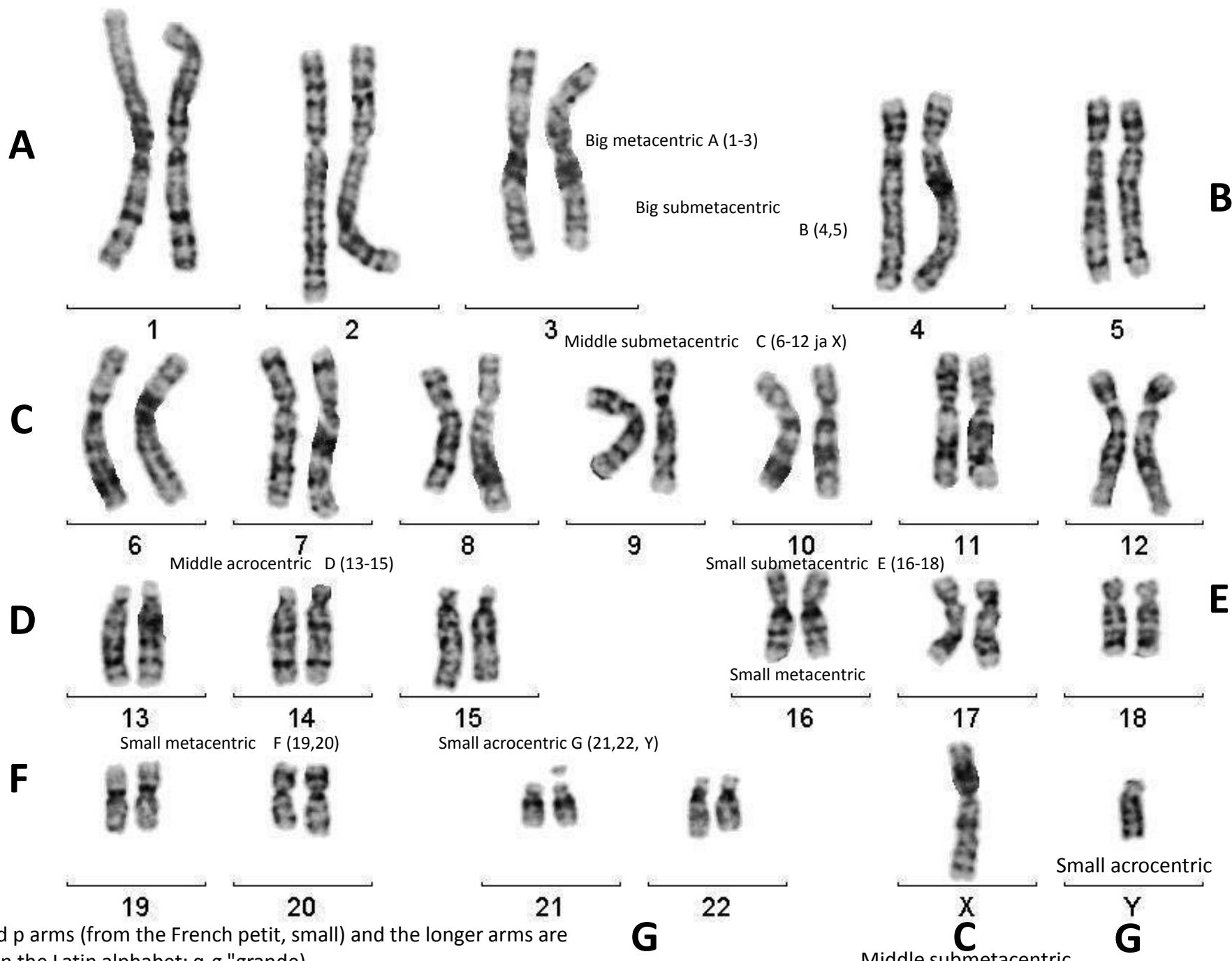
The major structures in DNA compaction: DNA, the nucleosome, the 10 nm "beads-on-a-string" fibre, the 30 nm fibre, active chromosomal structure during the interphase and the metaphase chromosome during the mitose or meiosis.

Mitosis

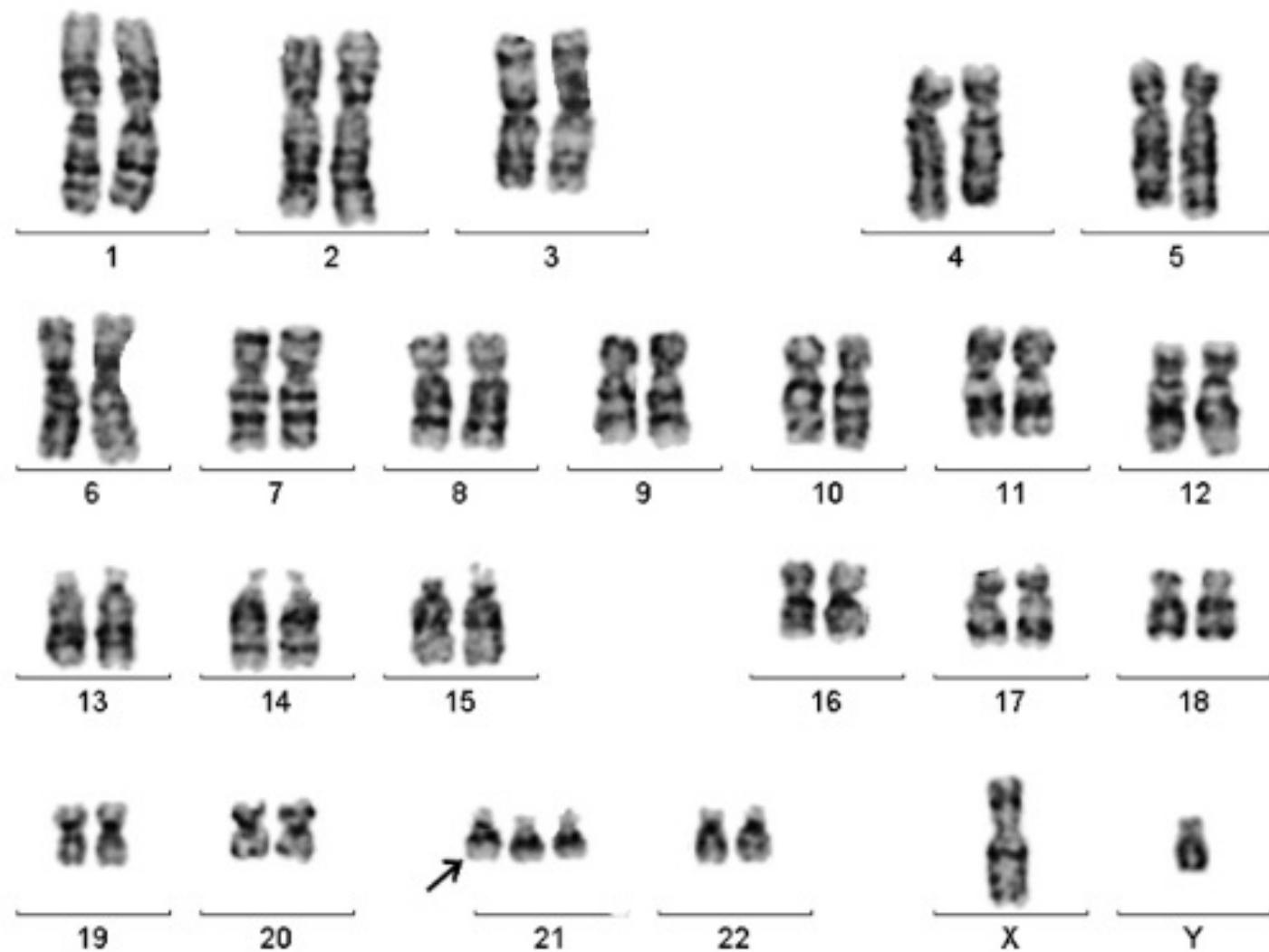
From **The Cell Cycle: Principles of Control** by David O Morgan



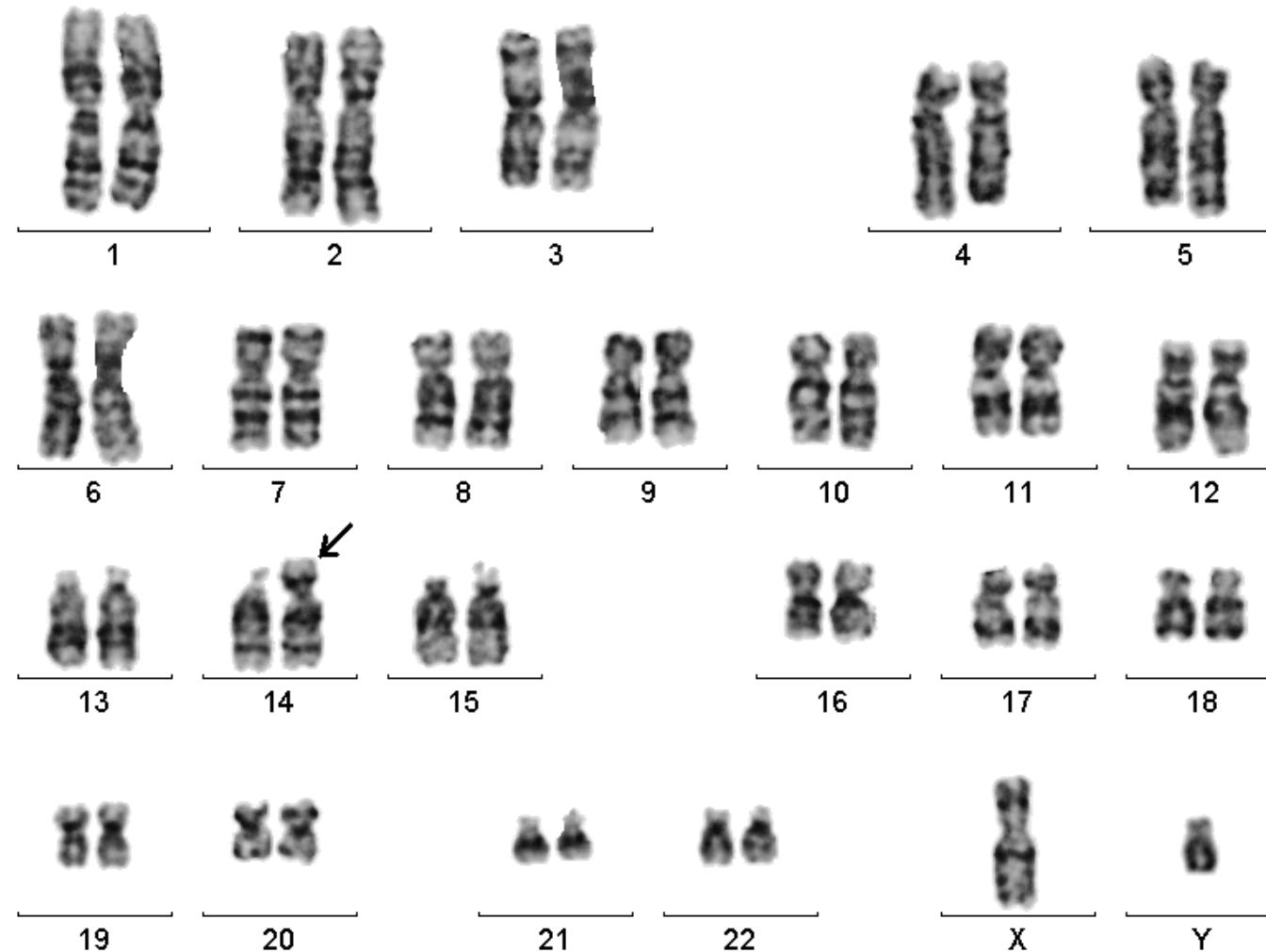
Human
Diploid Set of
Chromosomes

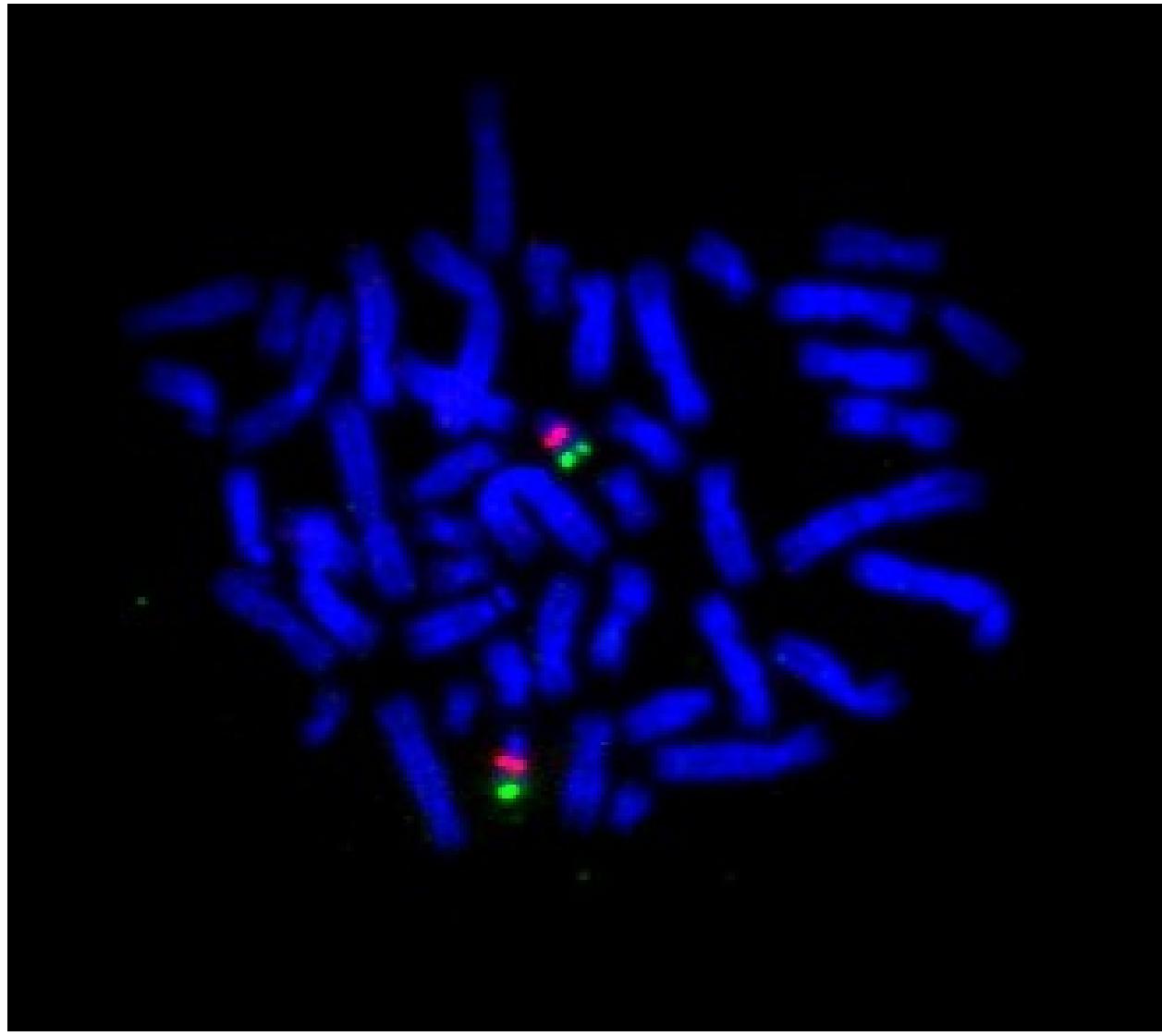


Down syndrome: 47,XY,+21

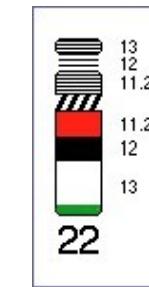


Down syndrome: 46,XY,t(14;21)(q10;q10),+21



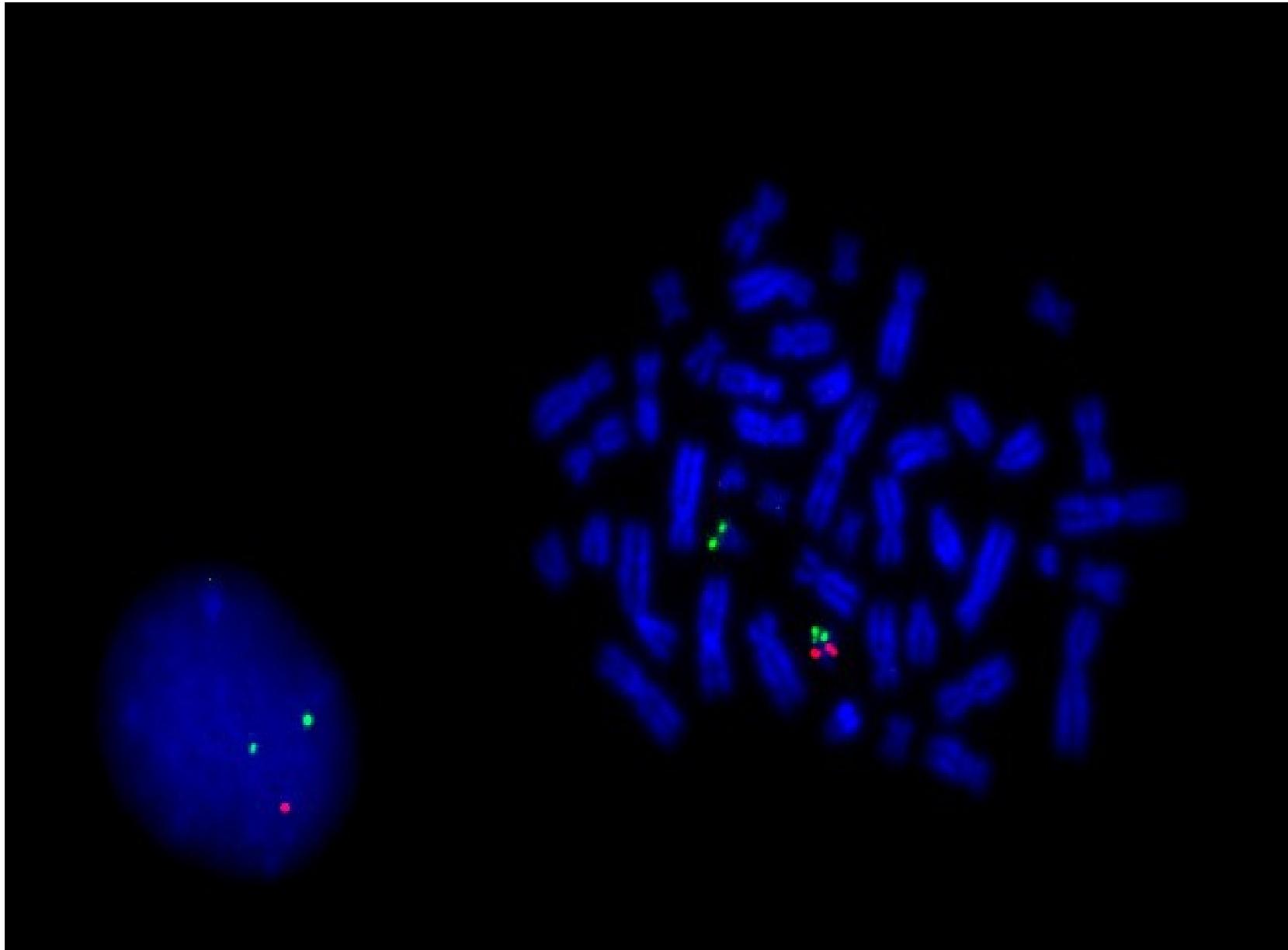


FISH-analysis (normal karyotype)

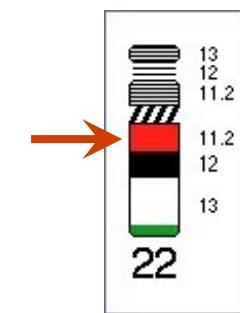




FISH-analysis: mickrodeletion 22q11.2 – DiGeorge syndrome



ish del(22)(q11.2q11.2)(TUPLE-1)



FISH-diagnostics

Specific probe TUPLE-1. It's shown the microdeletion on 22. chromosome regioon 11.2 (red fluorescence). In one chromosome it is clearly visible but it is absent on other.

Marker of chromosome 22 – green flourecence signal.

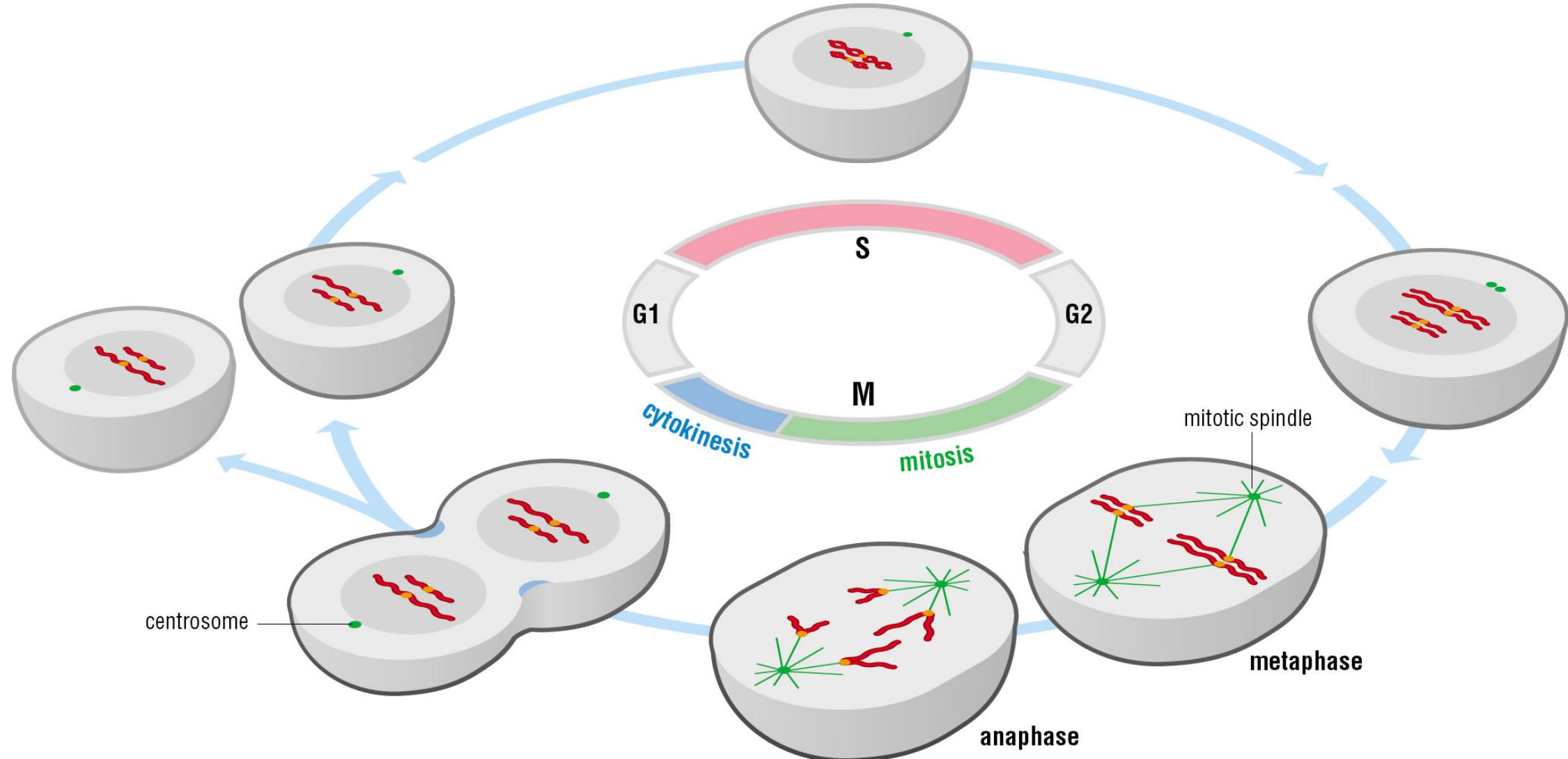
This microdeltion is known as DiGeorge syndrome.

We can use this method on the condensed mitotic metaphase chromosomes and on the cell nucleus of interphase.

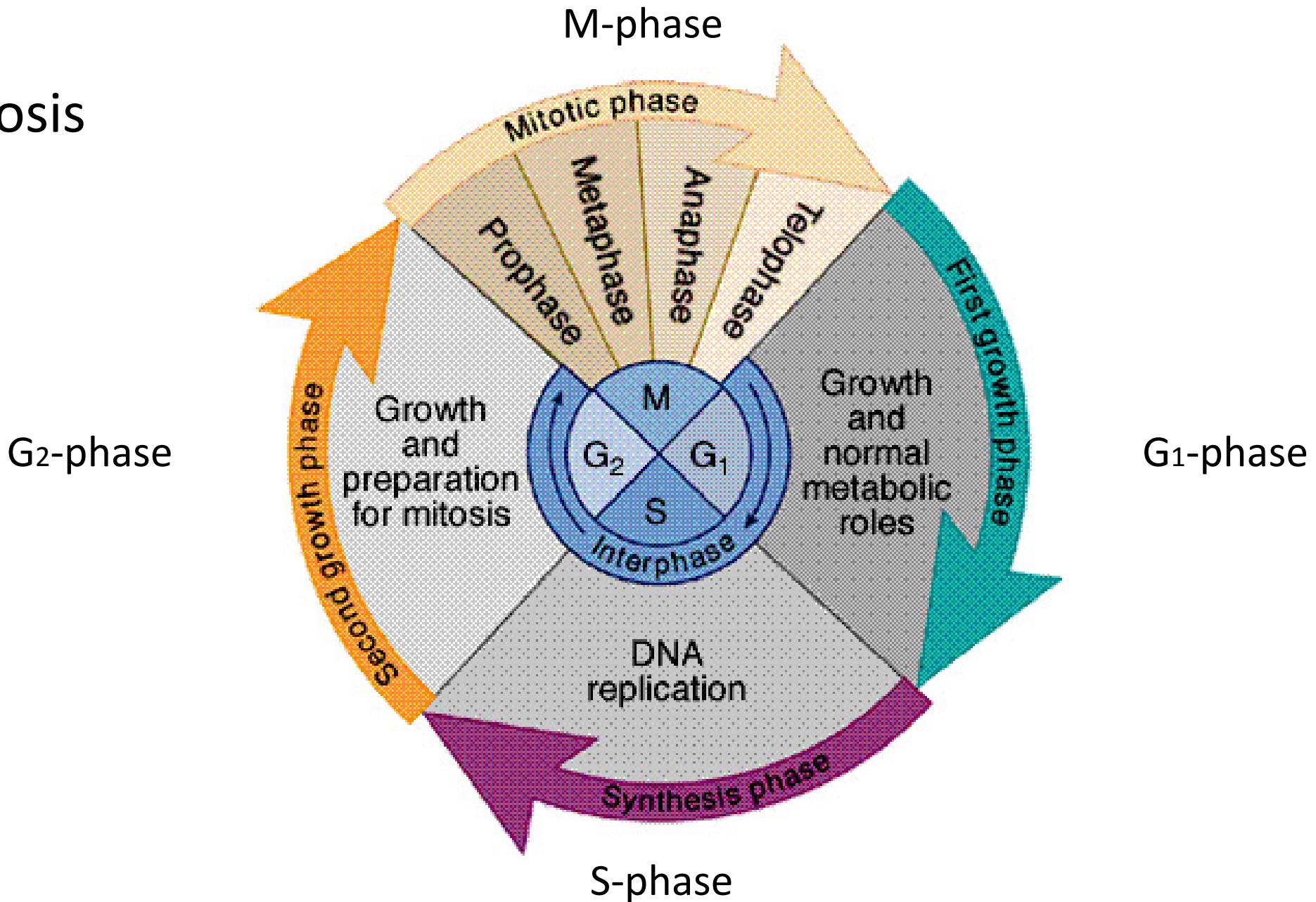
DiGeorge syndrome, more accurately known by a broader term — 22q11.2 deletion syndrome — is a disorder caused when a small part of chromosome 22 is missing. This deletion results in the poor development of several body systems.

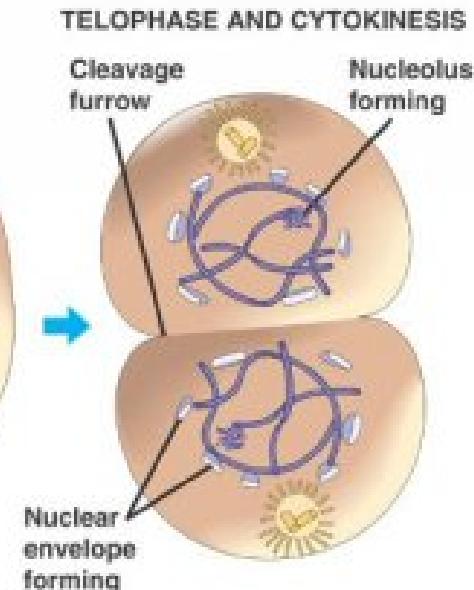
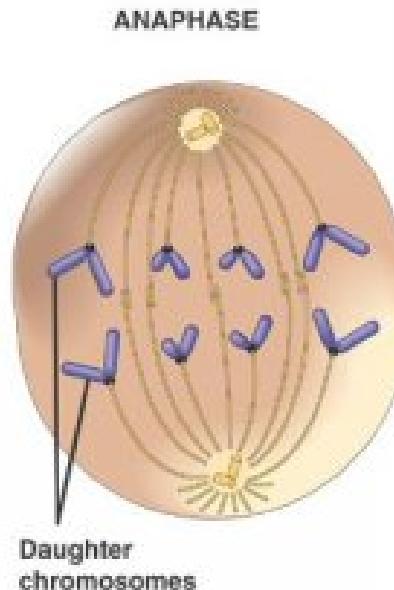
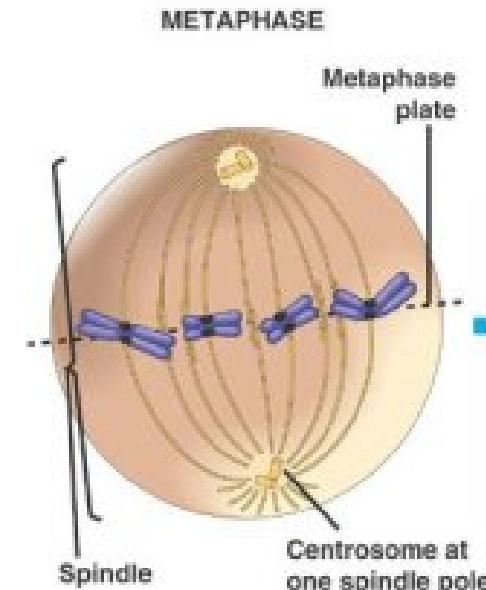
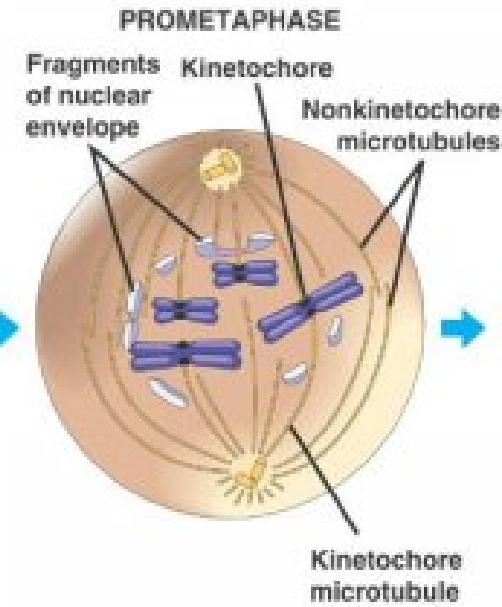
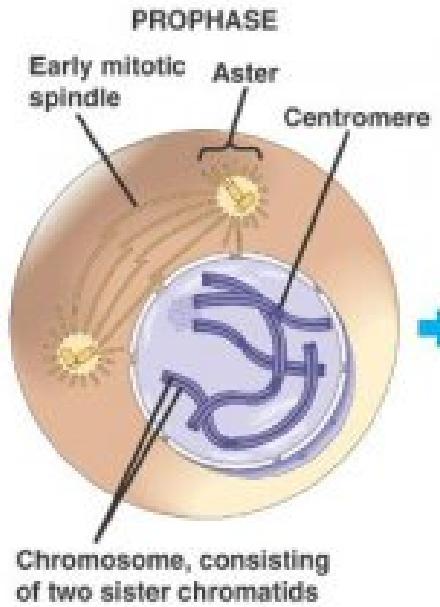
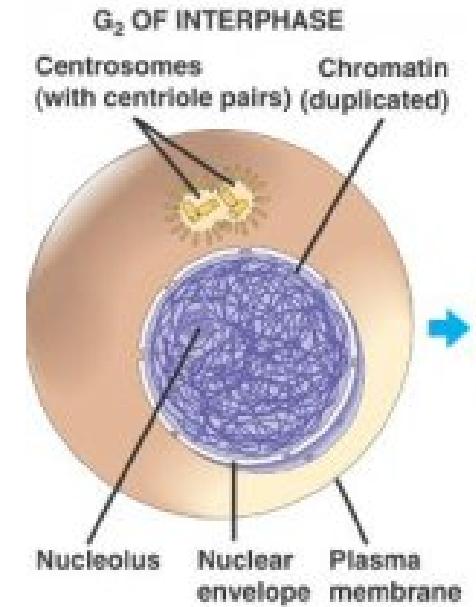
Medical problems commonly associated with 22q11.2 deletion syndrome include heart defects, poor immune system function, a cleft palate, complications related to low levels of calcium in the blood, and delayed development with behavioral and emotional problems.

From **The Cell Cycle: Principles of Control** by David O Morgan



Mitosis





The mitotic division of plant cells (basilar cells of root)

www.youtube.com/watch?v=m73i1Zk8EA0

The mitosis of cells of ovary cancer of Chinese Hamster (CHO) *in vitro* conditions

www.youtube.com/watch?v=NVfqzSKa_Bg&feature=related

<https://www.youtube.com/watch?v=ofjyw7ARP1c>

<https://www.youtube.com/watch?v=GhD-haQU4Og>

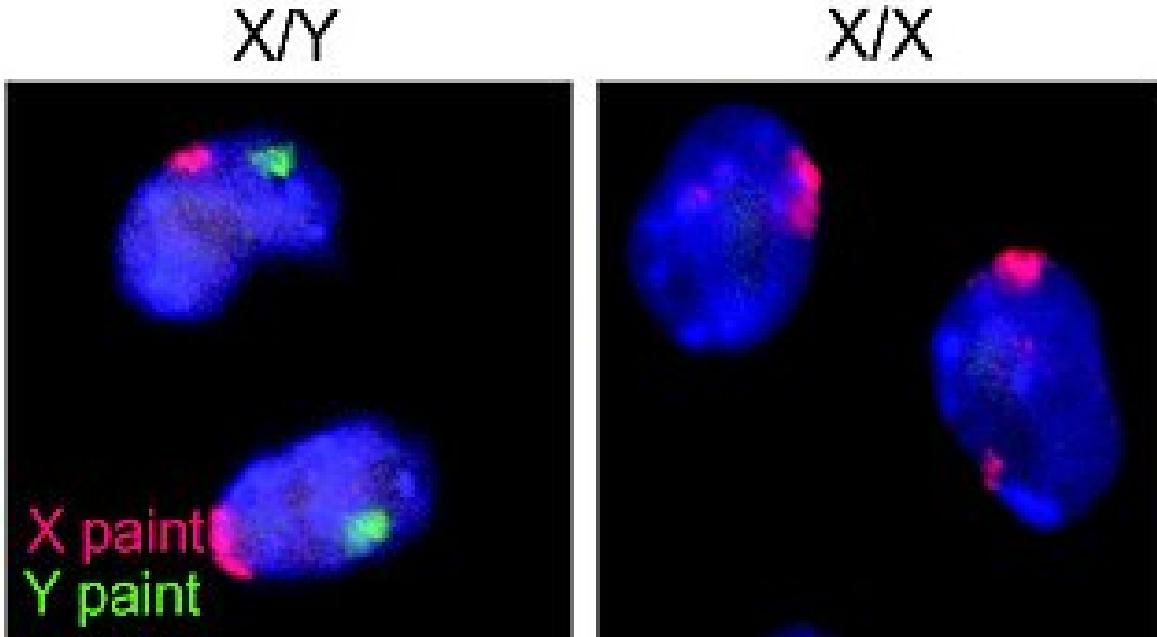
https://www.youtube.com/watch?v=L61Gp_d7evo

Meiosis

Meiosis (/mī'ōsɪs/ from Greek μείωσις, which means lessening) is a **special type of cell division that reduces the chromosome number by half**, creating **four haploid cells**, each genetically distinct from the parent cell that gave rise to them.

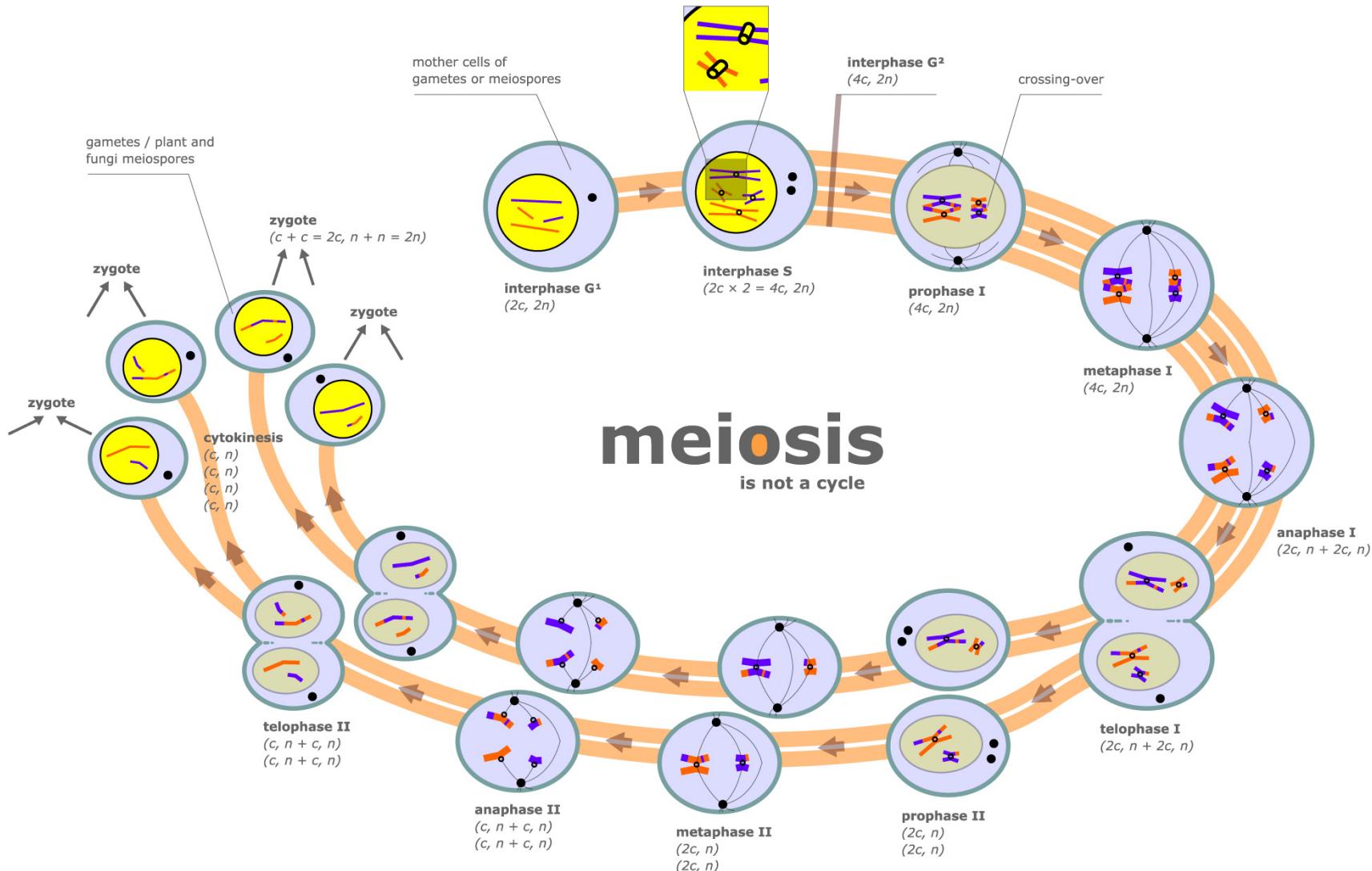
This process occurs in all sexually reproducing single-celled and multicellular eukaryotes, including animals, plants, and fungi. Errors in meiosis resulting in aneuploidy are the leading known cause of miscarriage and the most frequent genetic cause of developmental disabilities

Products of meiosis

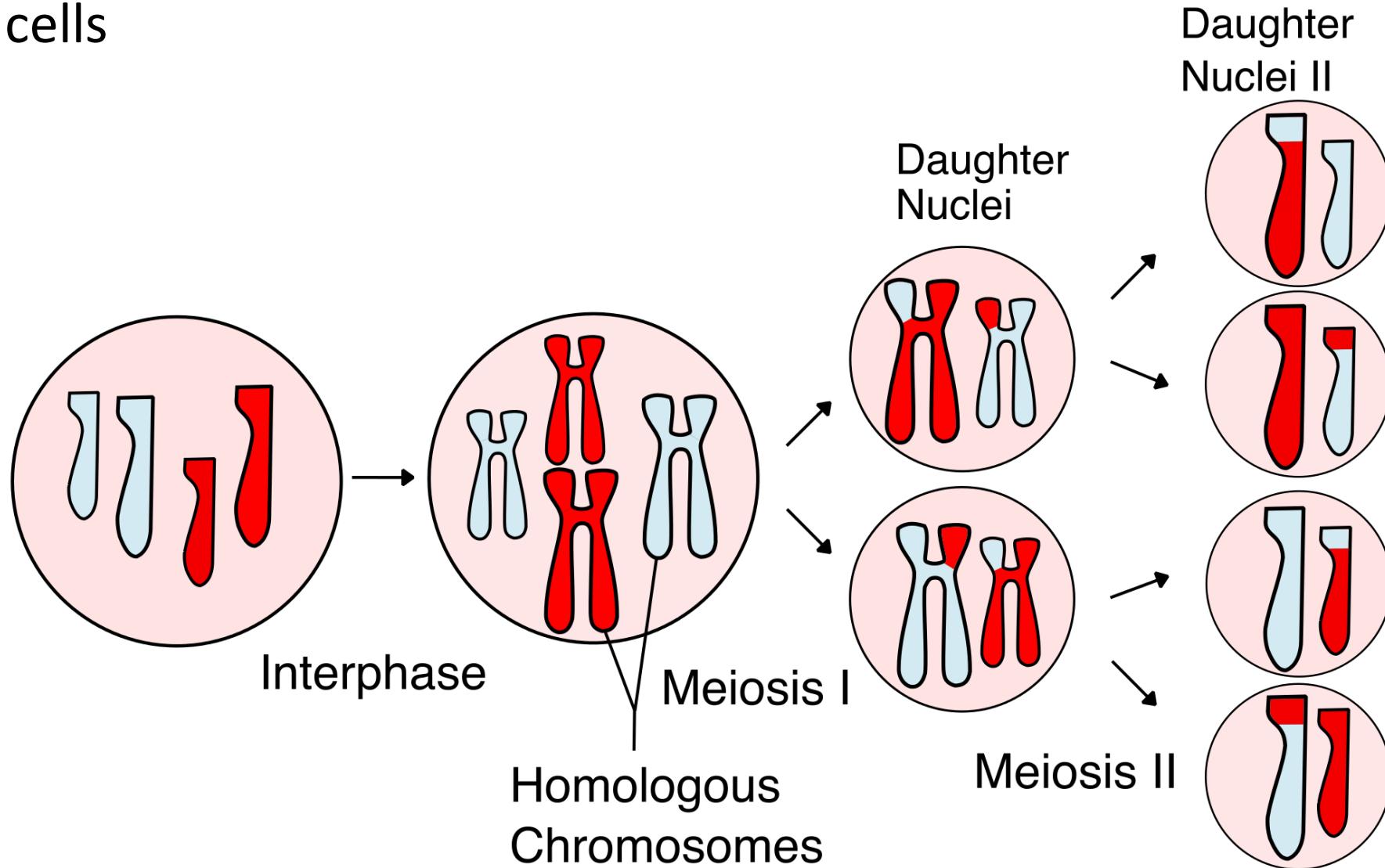


A **germ cell** is any biological cell that gives rise to the gametes of an organism that reproduces sexually. In many animals, the germ cells originate in the primitive streak and migrate via the gut of an embryo to the developing gonads. There, they undergo meiosis, followed by cellular differentiation into mature gametes, either eggs or sperm. Unlike animals, plants do not have germ cells designated in early development. Instead, germ cells can arise from somatic cells in the adult (such as the floral meristem of flowering plants).

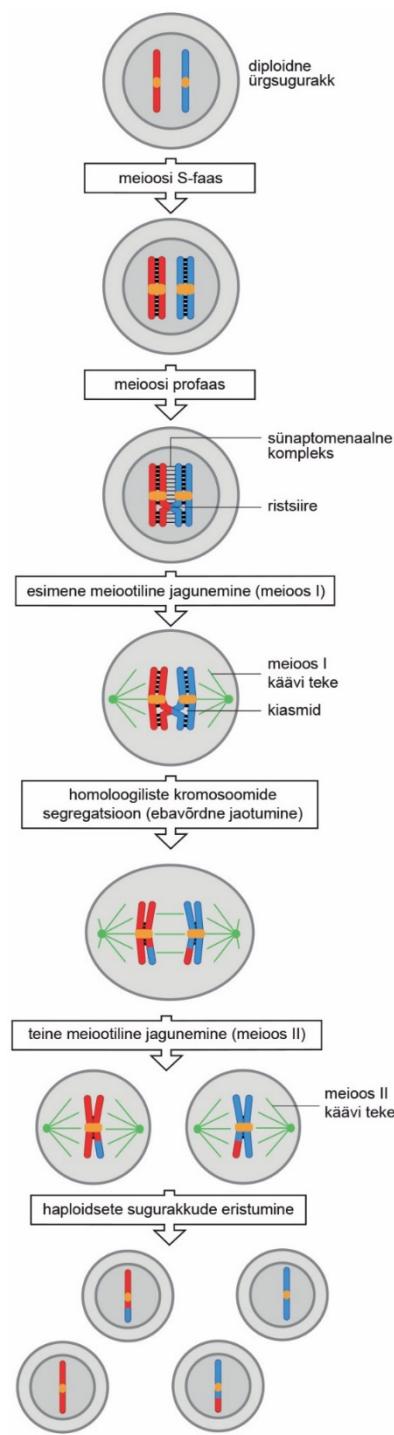
August Weismann (1834-1914) – the first describer of meiosis



The 1st and 2nd division - the meiotic cell cycle of germ cells



https://www.youtube.com/watch?v=n2cQP_260TM



Diploid gametogonium

The first division of meiosis; S-phase

Prophase

Synaptonemal complexes

Crossing over

Crossing over

The first meiotic division (I metaphase)

Spindle of I meiotic division

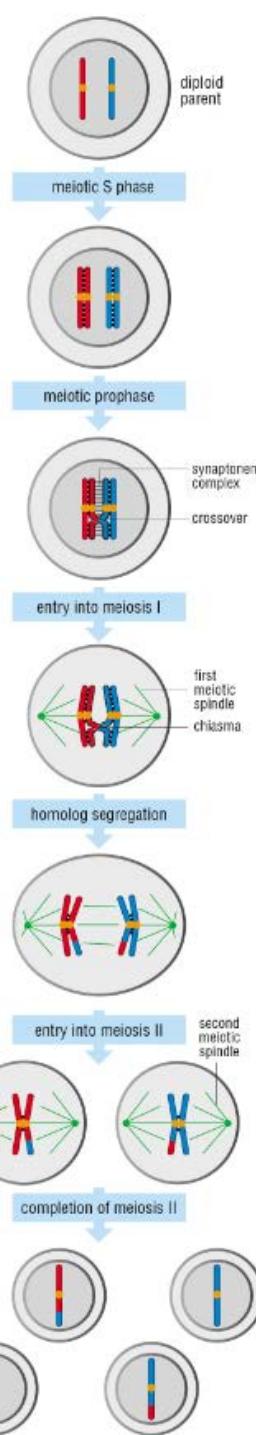
Chiasmata

Segregation of homologous chromosomes (nonequal division)

The second meiotic division (II metaphase)

The spindle of II meiotic division

Segregation of germ cells (equal division)



Crossing Over by Frans Alfons Janssens (1865-1924)

The variation in linkage suggests that there must be a mechanism for exchanging genes on homologous chromosomes.

It is ***crossing over ("chiasmatypie")*** at the stage of I prophase of meiosis

A subset of recombination events results in crossovers, which create physical links known as chiasmata (singular: chiasma, for the Greek letter Chi (X) between the homologous chromosomes

Chiasma is the point of contact, the physical link, between two (non-sister) chromatids belonging to homologous chromosomes

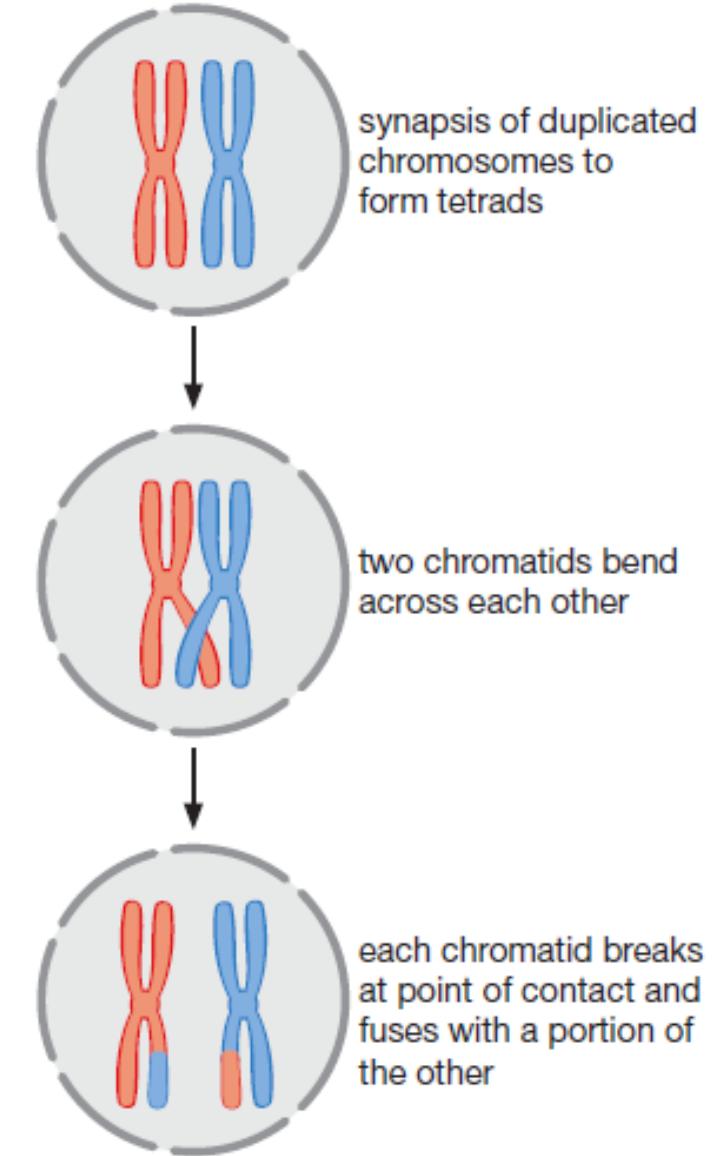


FIGURE 1-4 Janssens's hypothesis of crossing over.

Frans Alfons Janssens (1865 - 1924) was Catholic priest

He discoverer of **crossing-over of genes during meiosis**, which he called "**chiasmatypie**".

His work was continued by the Nobel Prize winner Thomas Hunt Morgan to develop the theory of genetic linkage.

<https://opened.cuny.edu/courseware/module/666/student/?task=3>

F.A. Jannsen postulated in 1909 that chromosomes physically interchange material during meiotic synapsis.

This knowledge was rediscovered in **1931** by **Barbara McClintock** and **Harriet B. Creighton** by working with *Zea mays*.

Jannsen's theory called as the **partial chiasmata type hypothesis** to.

Homologous chromosomes can exchange parts

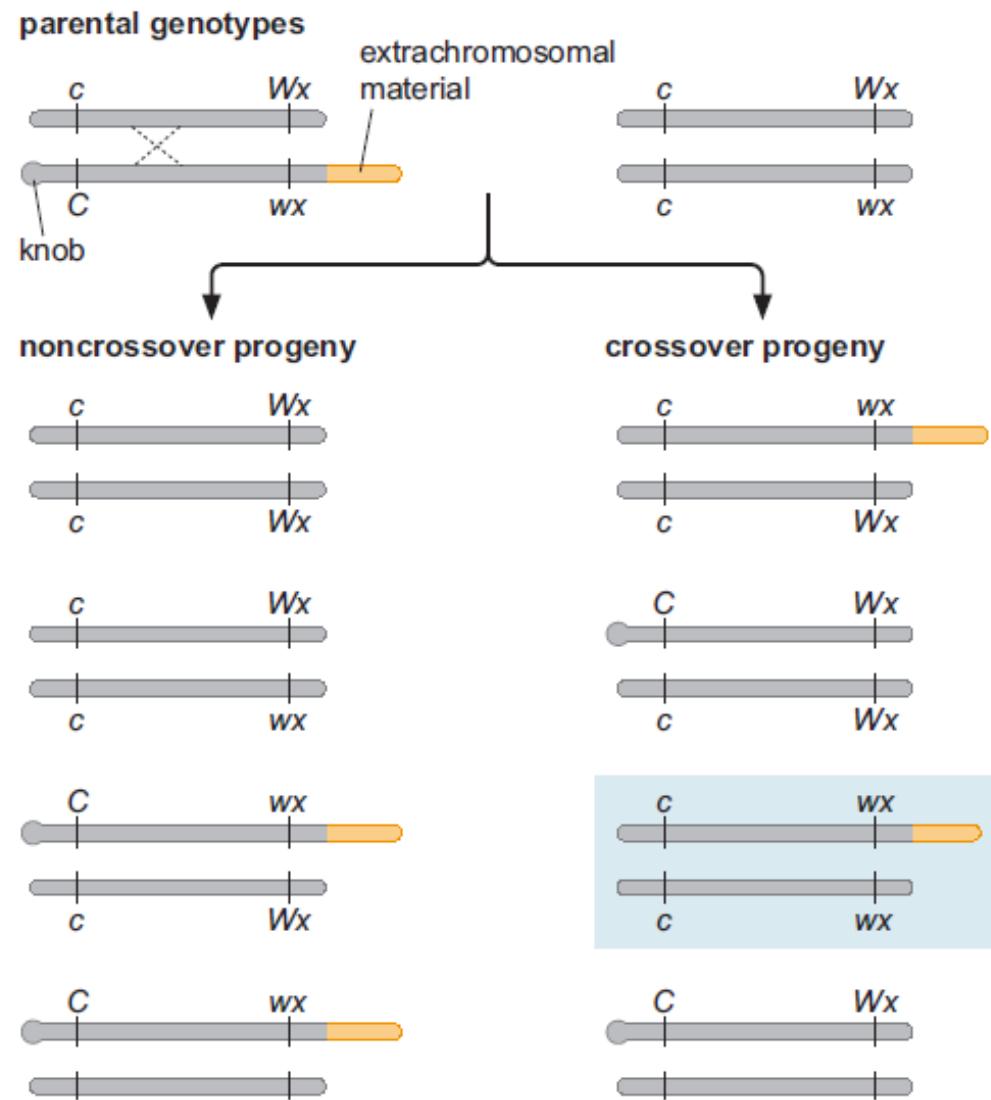
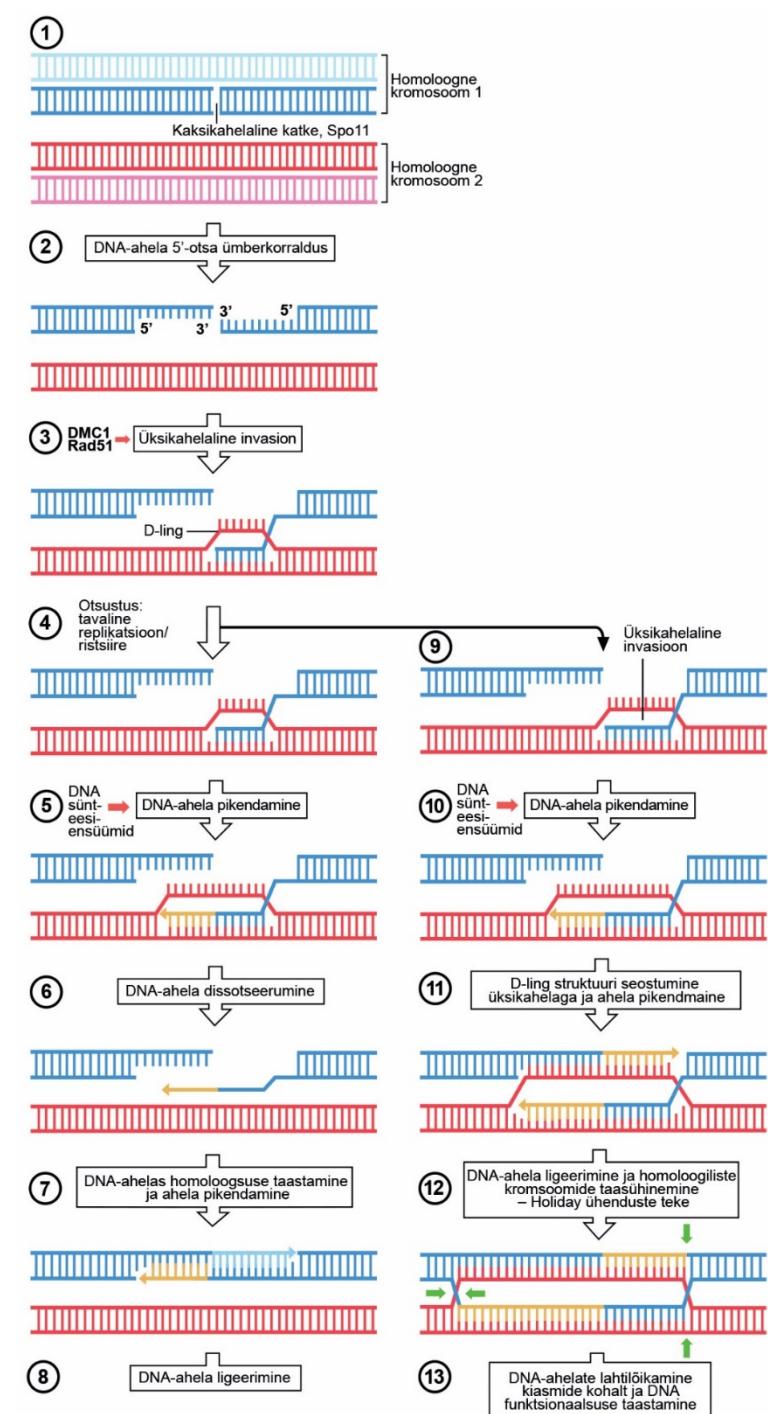
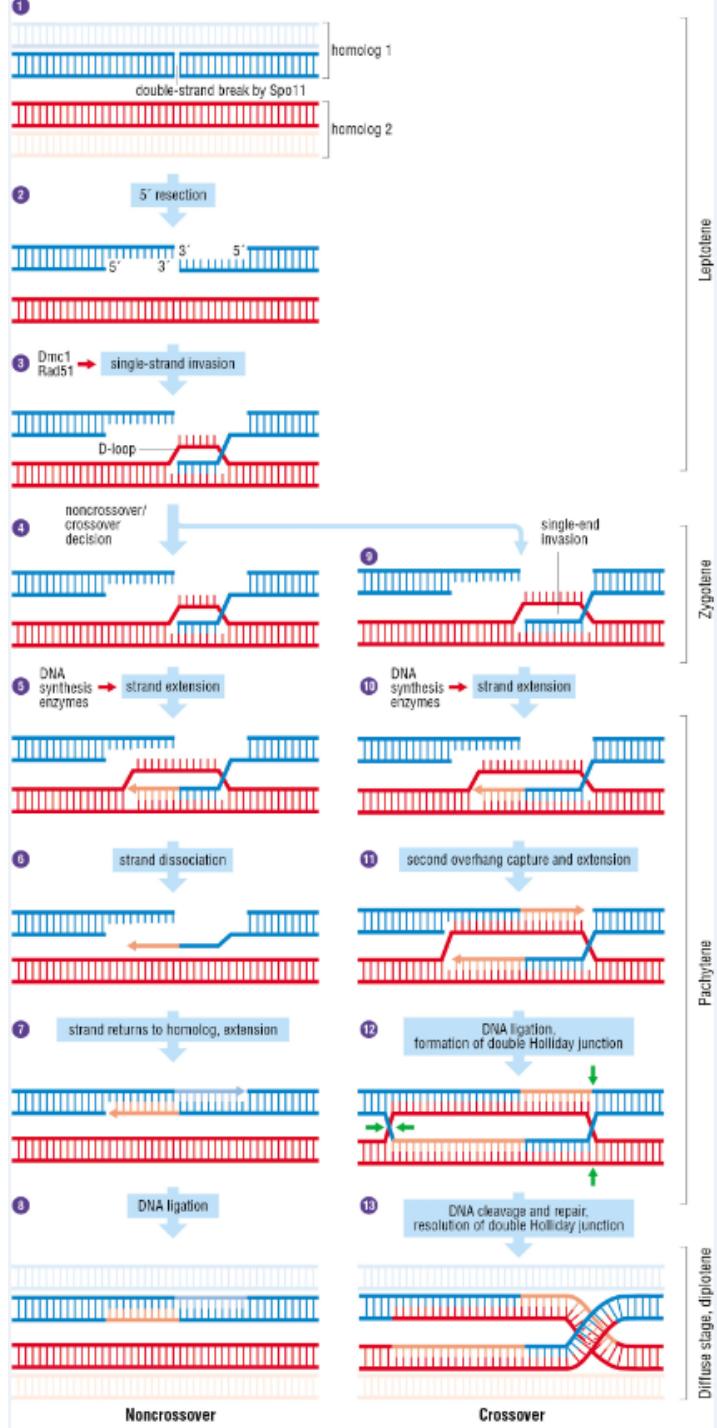


FIGURE 1-5 Demonstration of physical exchanges between homologous chromosomes. In most organisms, pairs of homologous chromosomes have identical shapes. Occasionally, however, the two members of a pair are not identical; one is marked by the presence of extrachromosomal material or compacted regions that reproducibly form knob-like structures. McClintock and Creighton found one such pair and used it to show that crossing over involves actual physical exchanges between the paired chromosomes. In the experiment shown here, the homozygous *c, wx* progeny had to arise by crossing over between the *C* and *wx* loci. When such *c, wx* offspring were cytologically examined, knobless *Wx* region had been physically replaced by a knobbed *wx* region. The colored box in the figure identifies the chromosomes of the homozygous *c, wx* offspring.

Homological recombination – the prophase of the first meiotic division.

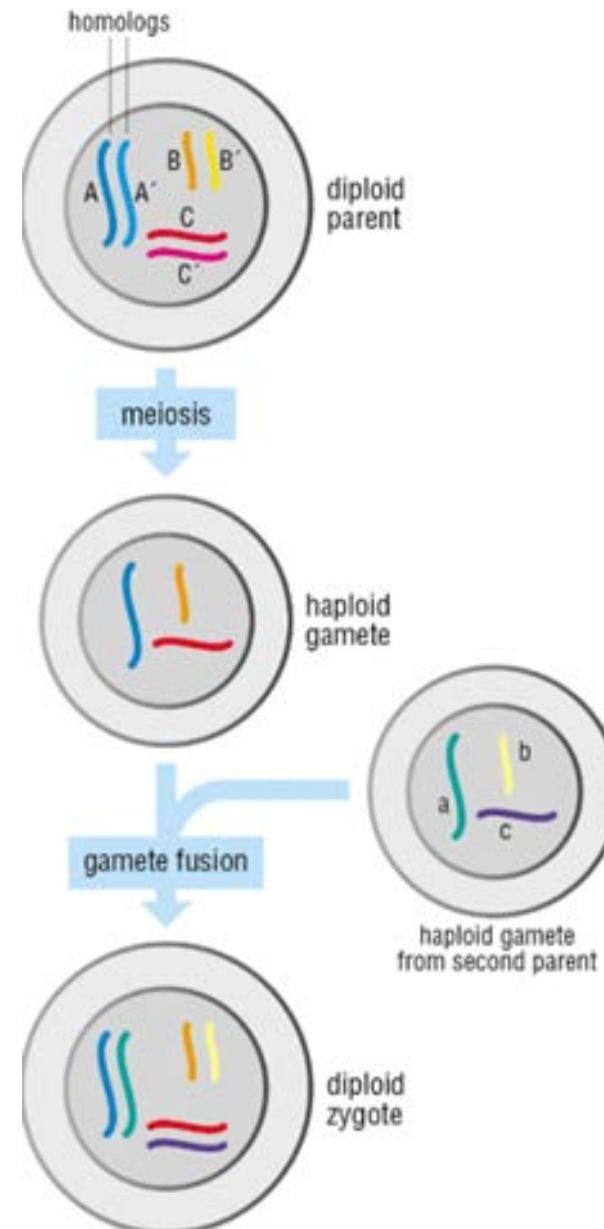
Linkage, however, is in effect never complete. The probability that two genes on the same chromosome will remain together during meiosis ranges from just less than 100% to nearly 50%. This variation in linkage suggests that there must be a mechanism for exchanging genes on homologous chromosomes. This mechanism is called **crossing over**. Its cytological basis was first described by Belgian cytologist F.A. Janssens.



Sexual multiplying cycle.

Diploid parent cell goes to dividing and after meiosis we have cell with haploid genome (germ cell) which contains only one homologous chromosome from the pair of two parental chromosomes.

After fertilization the haploid gametes shall join to the diploid zygote which contains in each chromosome one sister chromosome (homologous) from mother and another sister (homologous) chromosome from father.



Conclusions:

For example, diploid human cells contain totally 23 pairs of chromosomes including 1 pair of sex chromosomes (46 total), half of maternal origin and half of paternal origin.

Meiosis produces haploid gametes (ova and sperm) that contain one set of 23 chromosomes.

When two gametes (an egg and a sperm) fuse, the resulting zygote is once again diploid, with the mother and father each contributing 23 chromosomes.



Genes can be linked

Three genes (A , B and C) are located close together on the same chromosome

How are they organized? (use two-factor crosses)

AB and $ab \rightarrow AB, ab, Ab, aB$

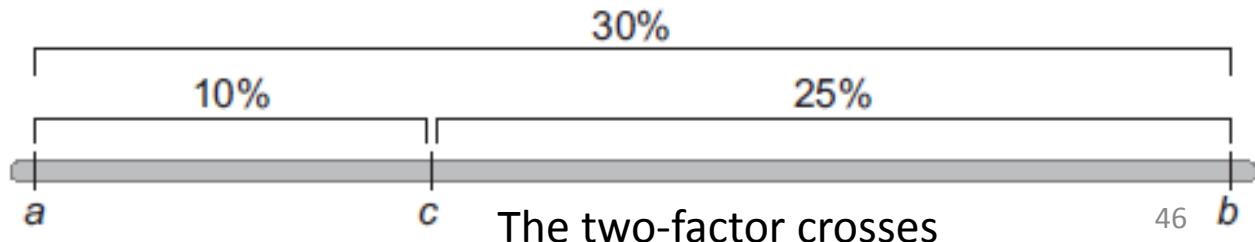
AC and $ac \rightarrow AC, ac, Ac, aC$

BC and $bc \rightarrow BC, bc, Bc, bC$

A cross between AB and ab yields four progeny types: the two parental genotypes (AB and ab) and two recombinant genotypes (Ab and aB). A cross between AC and ac similarly gives two parental combinations as well as the Ac and aC recombinants, whereas a cross between BC and bc produces the parental types and the recombinants Bc and bC . Each cross will produce a specific ratio of parental to recombinant progeny.

The first cross gives 30% recombinants, the second cross 10%, and the third cross 25%. This tells us that genes a and c are closer together than a and b or b and c and that the genetic distances between a and b and b and c are more similar. The gene arrangement that best fits these data is $a-c-b$

FIGURE 1-6 Assignment of the tentative order of three genes on the basis of three two-factor crosses.



Gene can be linked

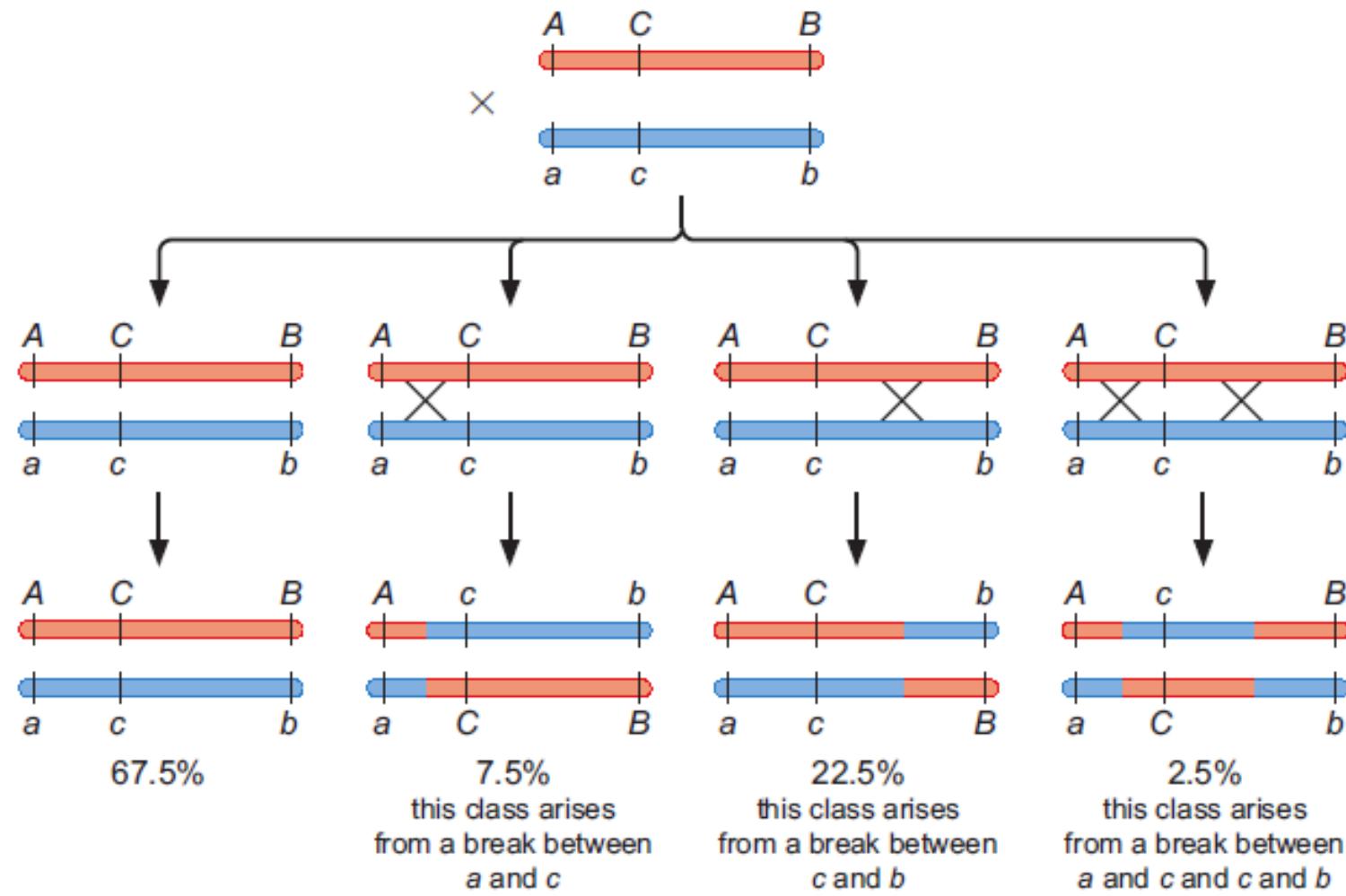


FIGURE 1-7 The use of three-factor crosses to assign gene order. The least frequent pair of reciprocal recombinants must arise from a double crossover. The percentages listed for the various classes are the theoretical values expected for an infinitely large sample. When finite numbers of progeny are recorded, the exact values will be subject to random statistical fluctuations.

The three-factor crosses

Gene Linkage -> Genetic Maps

Thomas Hunt Morgan – *Drosophila*
1915 – more than 85 mutant genes

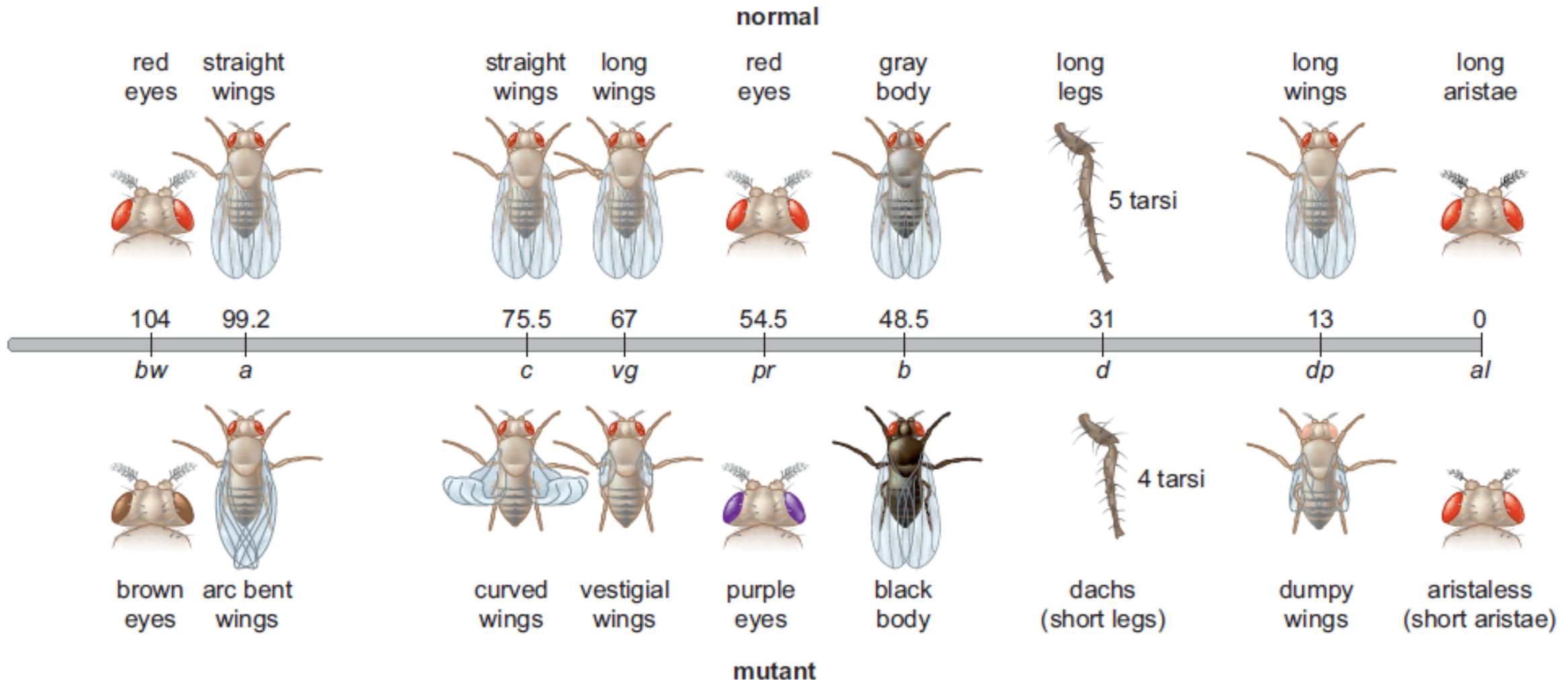


FIGURE 1-8 The genetic map of chromosome 2 of *Drosophila melanogaster*.

Using such reasoning, the Columbia University group headed by Morgan had by 1915 assigned locations to more than 85 mutant genes in *Drosophila* (Table 1-1), placing each of them at distinct spots on one of the four linkage groups, or chromosomes.

What means cM - centimorgan? It is map unit (m.u.) for measuring genetic linkage.

It is defined as the distance between chromosome positions (also termed loci or markers) for which the expected average number of intervening chromosomal crossovers in a single generation is 0.01. It is often used to infer distance along a chromosome. However, it is not a true physical distance. Note that non-syntenic genes (genes residing on different chromosomes) are inherently unlinked, and cM distances are not applicable to them.

Most importantly, all the genes on a given chromosome were located on a line. The gene arrangement was strictly linear and never branched. The genetic map of one of the chromosomes of *Drosophila* is shown in Figure 1-8.

Distances between genes on such a map are measured in map units, which are related to the frequency of recombination between the genes. Thus, if the frequency of recombination between two genes is found to be 5%, the genes are said to be separated by five map units. Because of the high probability of double crossovers between widely spaced genes, such assignments of map units can be considered accurate only if recombination between closely spaced genes is followed.

In 1915, Morgan, with his students Alfred H. Sturtevant, Hermann J. Muller, and Calvin B. Bridges, published their definitive book *The Mechanism of Mendelian Heredity*, which first announced the general validity of the chromosomal basis of heredity. We now rank this concept, along with the theories of evolution and the cell, as a major achievement in our quest to understand the nature of the living world.

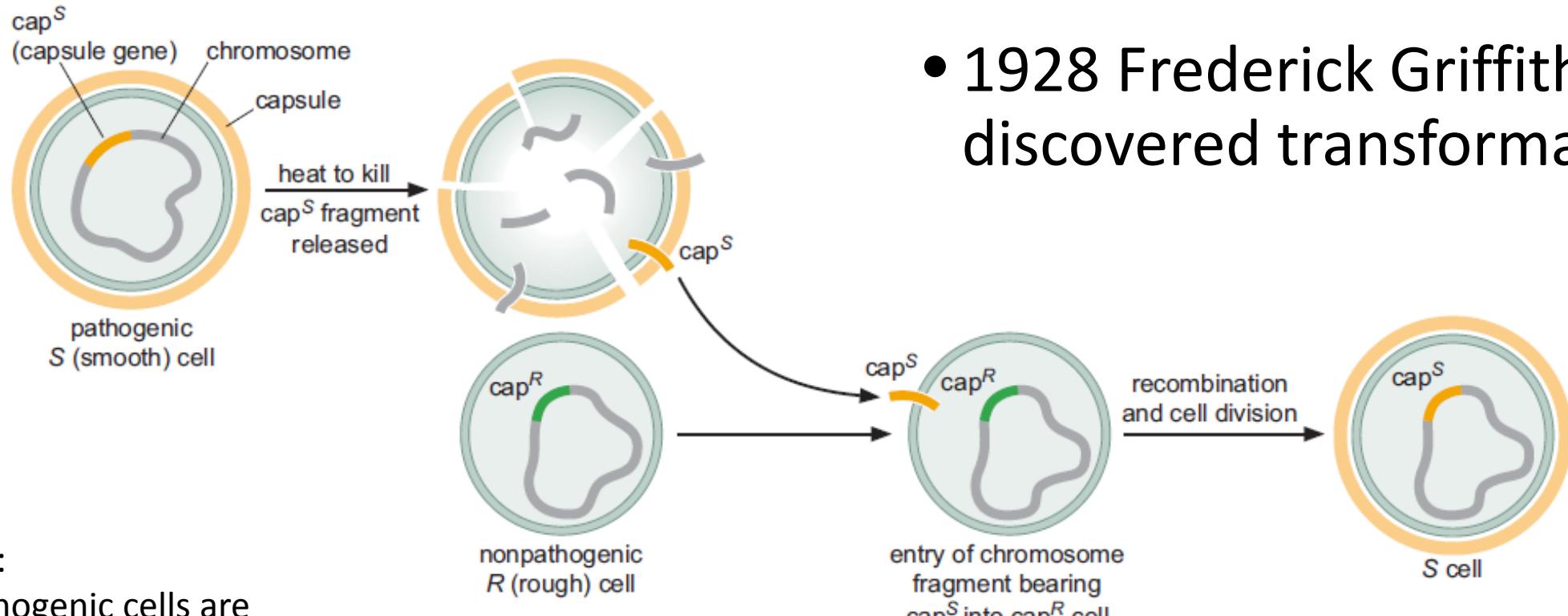
What are genes?

- Chromosomes contain proteins and nucleic acids
- Genes must be self-duplicating, how?
- 1927 Hermann Joseph Muller (Nobel prize 1946) „for the discovery that mutations can be induced by X-rays") and
- L.J. Stadler discovered independently that X-rays induce mutations
- 1909 Archibald E. Garrod's general hypothesis – gene-enzyme relationship
- 1930s work on pigments - **flower** pigments by John B.S. Haldane and Rose Scott-Moncrieff in England, **hair** pigment of the guinea pig by Sewall G. Wright in the United States, and pigments of **insect eyes** by A. Kuhn in Germany and by Boris Ephrussi and George W. Beadle

Nucleic acids Convey Genetic Information

- It was known by mid-1940s that chromosomes contained DNA – deoxyribonucleic acid
- All known enzymes were proteins
- The simplest hypothesis was that genetic information within genes determines the order of the 20 different amino acids within the polypeptide chains
- How?

Transformation of genetic characteristic makes non-virulent bacteria virulent



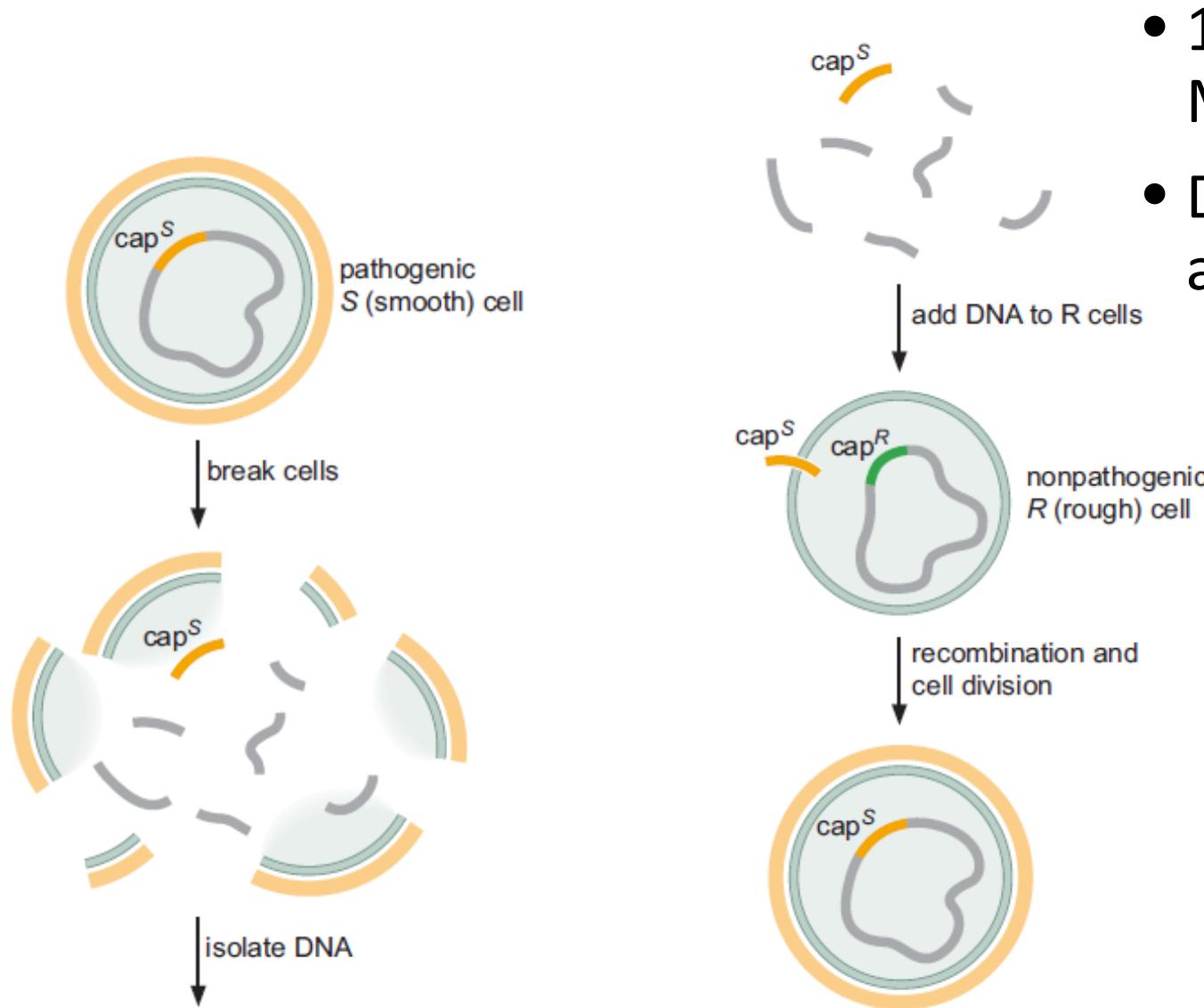
Summary:

when pathogenic cells are killed by heat, their genetic components remain undamaged

- 1928 Frederick Griffith discovered transformation

FIGURE 2-1 Transformation of a genetic characteristic of a bacterial cell (*Streptococcus pneumoniae*) by addition of heat-killed cells of a genetically different strain. Here we show an R cell receiving a chromosomal fragment containing the capsule gene from a heat-treated S cell. Since most R cells receive other chromosomal fragments, the efficiency of transformation for a given gene is usually less than 1%.

DNA is transforming agent



- 1944 Oswald T. Avery, Colin M. MacLeod and Maclyn McCarty
- DNase destroys transforming activity

FIGURE 2-2 Isolation of a chemically pure transforming agent. (Adapted, with permission, from Stahl F.W. 1964. *The mechanics of inheritance*, Fig. 2.3. © Pearson Education, Inc.)

It therefore came as a great surprise when in **1944**, after some 10 years of research, U.S. microbiologist Oswald T. Avery and his colleagues at the Rockefeller Institute in New York, Colin M. MacLeod and Maclyn McCarty, made the momentous announcement that the **active genetic principle was DNA** (Fig. 2-2).

Supporting their conclusion were key experiments showing that the transforming activity of their highly purified active fractions was destroyed by deoxyribonuclease, a recently purified enzyme that specifically degrades DNA molecules to their nucleotide building blocks but has no effect on the integrity of protein molecules or RNA. In contrast, the addition of either ribonuclease (which degrades RNA) or various proteolytic enzymes (which degrade proteins) had no influence on the transforming activity.

Most people still thought proteins are genes!

Viruses contain nucleic acids

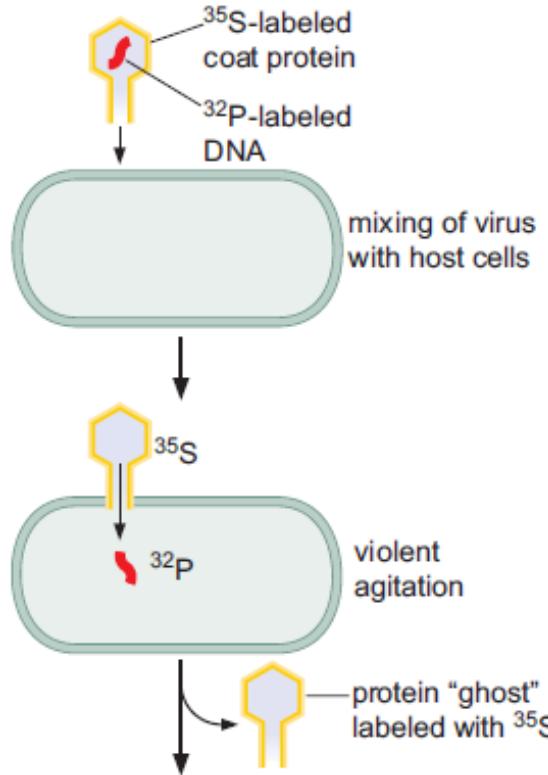
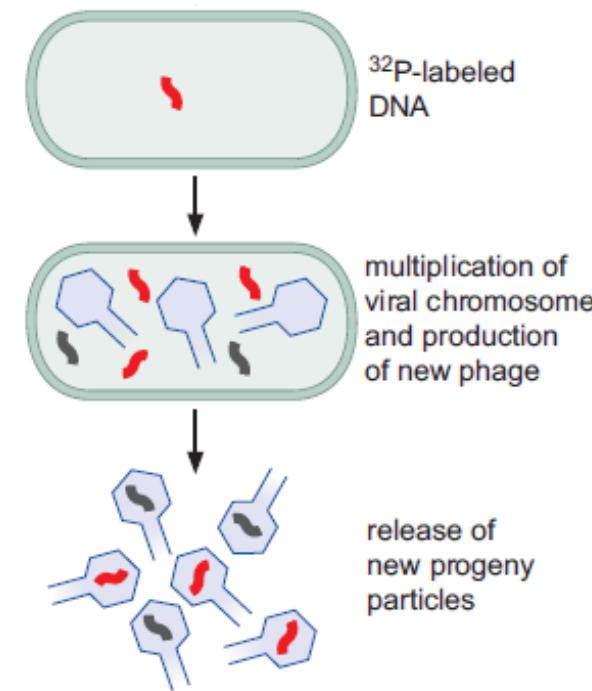


FIGURE 2-3 Demonstration that only the DNA component of the bacteriophage T2 carries the genetic information and that the protein coat serves only as a protective shell.

- 1952 Alfred D. Hershey and Martha Chase, CSHL
- Parental nucleic acid and none of the parental protein was detected in the progeny phage



DNA as a double helix

Photo 51

is the nickname given to an X-ray diffraction image of crystallized DNA taken by **Raymond Gosling** in May 1952, working as a PhD student under the supervision of **Rosalind Franklin**, at King's College London in Sir **John Randall's** group. It was critical evidence in identifying the structure of DNA.

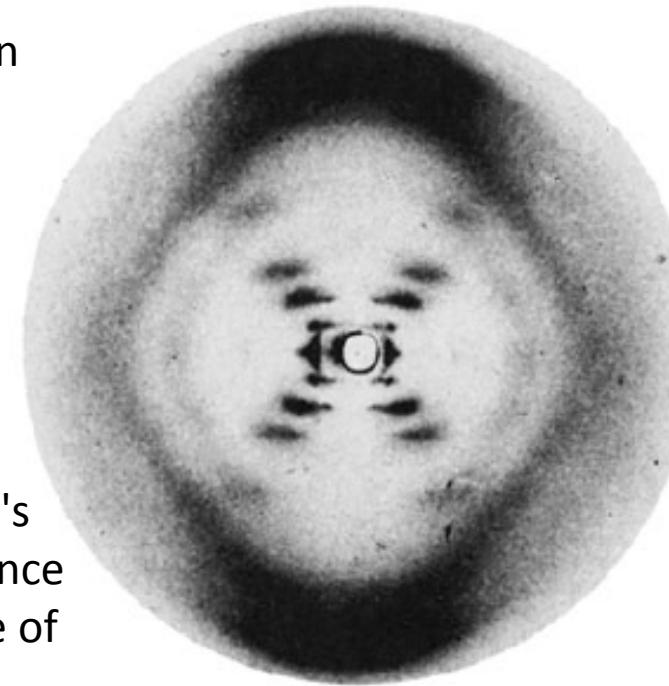


FIGURE 2-4 The key X-ray photograph involved in the elucidation of the DNA structure. This photograph, taken by Rosalind Franklin at King's College, London, in the winter of 1952–1953, confirmed the guess that DNA was helical. The helical form is indicated by the crossways pattern of X-ray reflections (photographically measured by darkening of the X-ray film) in the center of the photograph. The very heavy black regions at the top and bottom reveal that the 3.4-Å-thick purine and pyrimidine bases are regularly stacked next to each other, perpendicular to the helical axis. (Printed, with permission, from Franklin R.E. and Gosling R.G. 1953. *Nature* 171: 740–741. © Macmillan.)

- 1938 William Astbury took first diffraction pattern

William Thomas Astbury (also Bill Astbury; 1898 - 1961

was an English physicist and molecular biologist who made pioneering X-ray diffraction studies of biological molecules. His work on keratin provided the foundation for **Linus Pauling's** discovery of the alpha helix. He also studied the structure for DNA in 1937 and made the first step in the elucidation of its structure.

- 1950s **Maurice Wilkins** and **Rosalind Franklin** took high-quality diffraction photographs

These photographs suggested not only that the underlying DNA structure was helical but that it was composed of more than one polynucleotide chain—either two or three.

DNA structure

No. 4356 April 25, 1953

N A T U R E

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

GENETICAL IMPLICATIONS OF THE STRUCTURE OF DEOXYRIBONUCLEIC ACID

By J. D. WATSON and F. H. C. CRICK

Our model suggests possible explanations for a number of other phenomena. For example, spontaneous mutation may be due to a base occasionally occurring in one of its less likely tautomeric forms.

For the moment, the general scheme we have proposed for the reproduction of deoxyribonucleic acid must be regarded as speculative. Even if it is correct, it is clear from what we have said that much remains to be discovered before the picture of genetic duplication can be described in detail. What are the polynucleotide precursors? What makes the pair of chains unwind and separate? What is the precise role of the protein? Is the chromosome one long pair of deoxyribonucleic acid chains, or does it consist of patches of the acid joined together by protein?

Despite these uncertainties we feel that our proposed structure for deoxyribonucleic acid may help to solve one of the fundamental biological problems—the molecular basis of the template needed for genetic replication. The hypothesis we are suggesting is that the template is the pattern of bases formed by one chain of the deoxyribonucleic acid and that the gene contains a complementary pair of such templates.

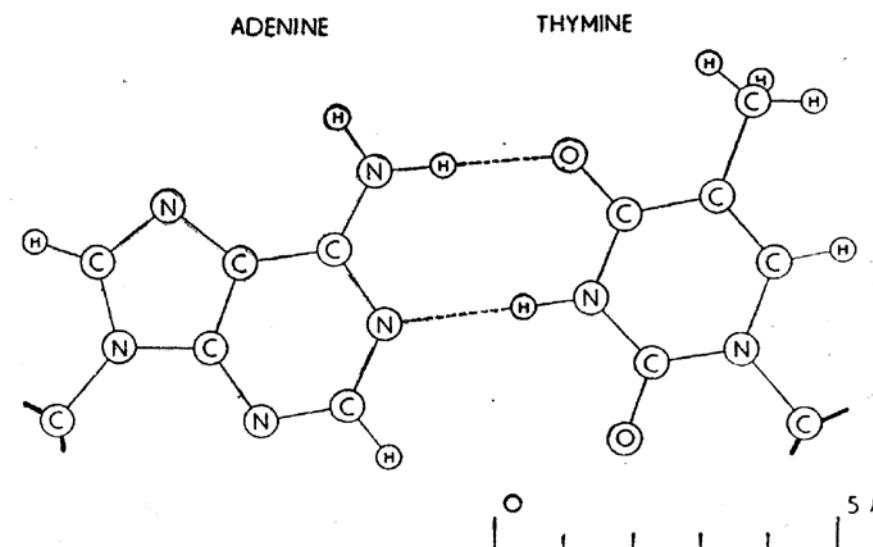


Fig. 4. Pairing of adenine and thymine. Hydrogen bonds are shown dotted. One carbon atom of each sugar is shown

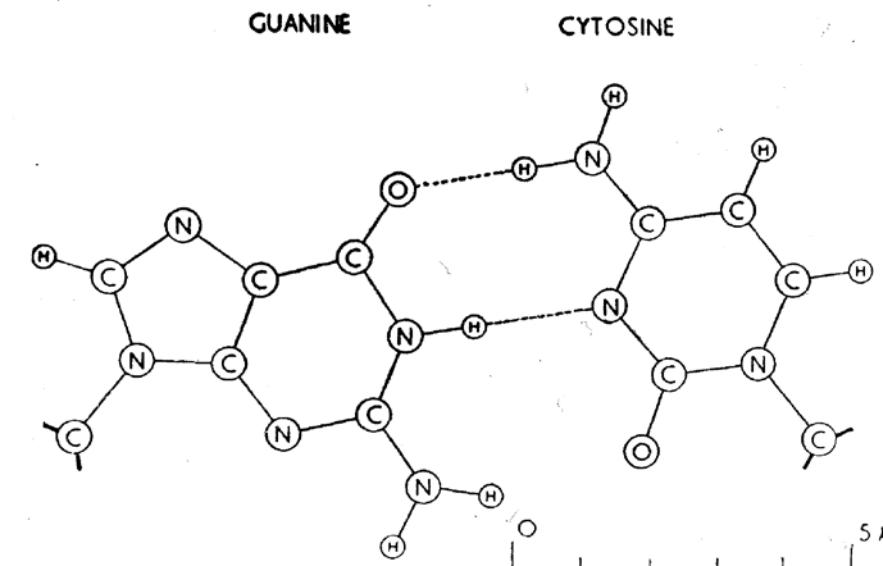
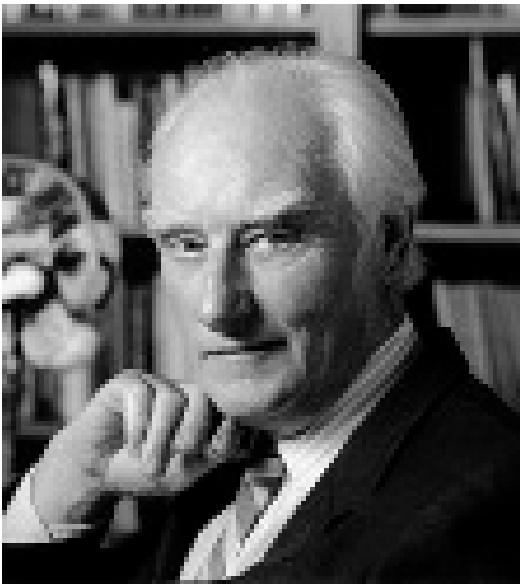


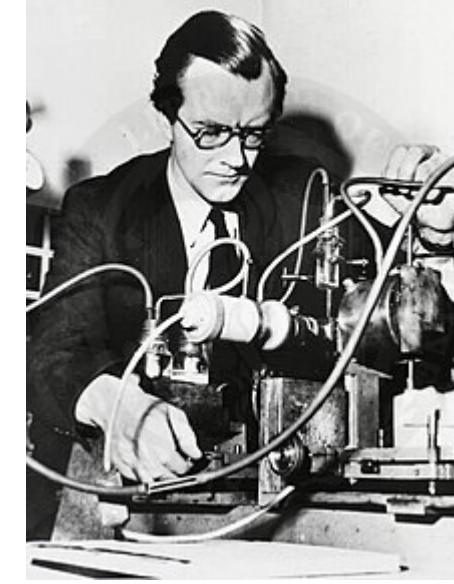
Fig. 5. Pairing of guanine and cytosine. Hydrogen bonds are shown dotted. One carbon atom of each sugar is shown



James Dewey Watson (born April 6, 1928) is an American [molecular biologist](#), [geneticist](#) and [zoologist](#). In 1953, he co-authored with [Francis Crick](#) the academic paper proposing the [double helix structure](#) of the [DNA molecule](#). Watson, Crick, and [Maurice Wilkins](#) were awarded the 1962 [Nobel Prize in Physiology or Medicine](#) "for their discoveries concerning the molecular structure of [nucleic acids](#) and its significance for information transfer in living material".



Francis Harry Compton Crick (8 June 1916 – 28 July 2004) was a British [molecular biologist](#), [biophysicist](#), and [neuroscientist](#). The results were based partly on fundamental studies done by [Rosalind Franklin](#), [Raymond Gosling](#) and M. Wilkins.



Maurice Hugh Frederick Wilkins (15 December 1916 – 5 October 2004) was a New Zealand-born [British physicist](#) and [molecular biologist](#), and [Nobel laureate](#) whose research contributed to the scientific understanding of [phosphorescence](#), [isotope separation](#), [optical microscopy](#) and [X-ray diffraction](#), and to the development of [radar](#). He is best known for his work at [King's College London](#) on the structure of [DNA](#).



R. G. Gosling was the co-author with R. Franklin of one of the three DNA double helix papers published in Nature in April 1953.

Raymond George Gosling (15 July 1926 – 18 May 2015) was a British scientist. While a PhD student at King's College, London he worked under the supervision of Rosalind Franklin. Their crystallographic experiments, together with those of Maurice Wilkins of the same laboratory, produced data that **helped** James Watson and Francis Crick to infer the structure of DNA.

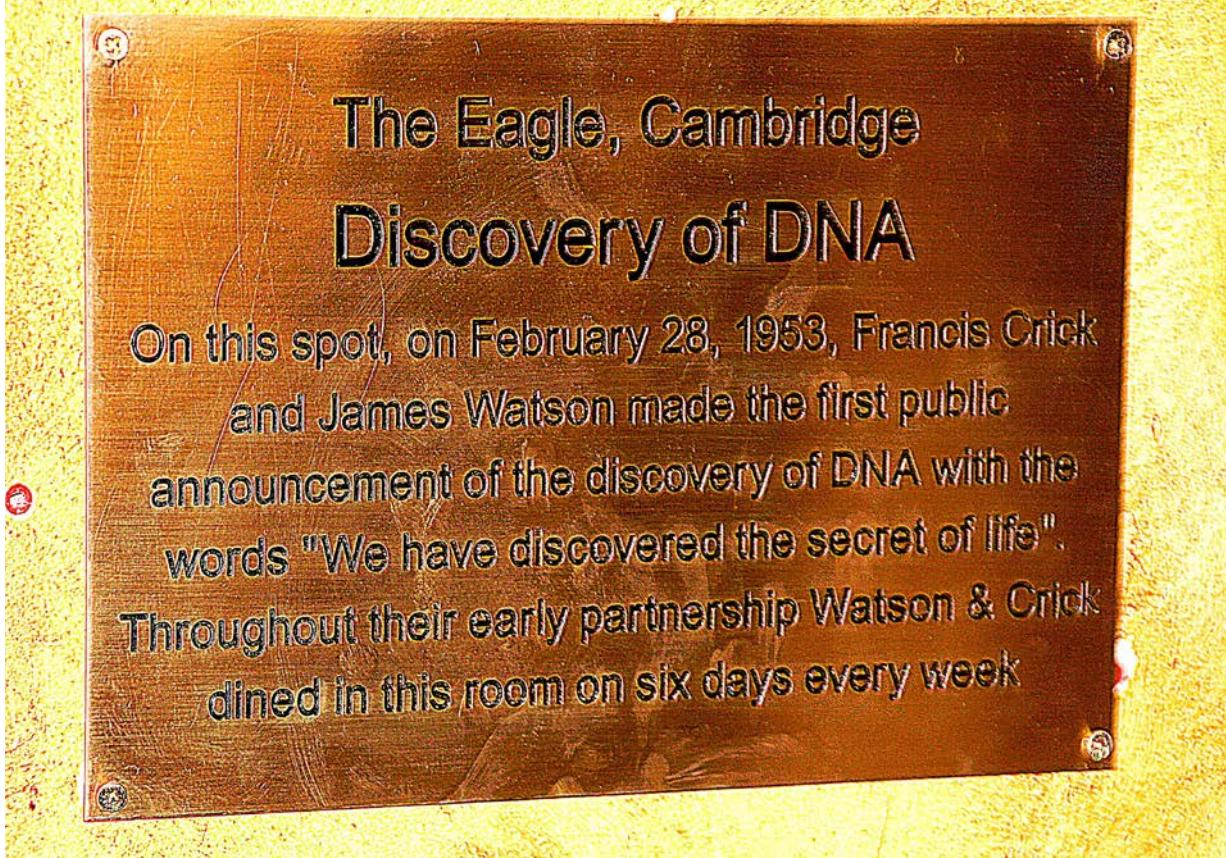


Rosalind Elsie Franklin (25 July 1920 – 16 April 1958) was an English [chemist](#) and [X-ray crystallographer](#) who made contributions to the understanding of the molecular structures of [DNA](#) (deoxyribonucleic acid), [RNA](#) (ribonucleic acid), [viruses](#), [coal](#), and [graphite](#).^[2] Although her works on coal and viruses were appreciated in her lifetime, her contributions to the discovery of the structure of DNA were largely recognised posthumously.

R. Franklin is best known for her work on the X-ray diffraction images of DNA, particularly Photo 51, while at King's College London, which led to the discovery of the DNA double helix for which James Watson, Francis Crick and Maurice Wilkins shared the Nobel Prize in Physiology or Medicine in 1962. Watson suggested that Franklin would have ideally been awarded a Nobel Prize in Chemistry, along with Wilkins, but, although there was not yet a rule against posthumous awards, the Nobel Committee generally does not make posthumous nominations.

Double helix:

William Astbury
Oswald Avery
Florence Bell
Lawrence Bragg
Francis Crick
Erwin Chargaff
Michael Creeth
Jerry Donohue
Rosalind Franklin
Raymond Gosling
Frederick Griffith
John Masson Gulland
Denis Jordan
Phoebus Levene
Friedrich Miescher
Fred Neufeld
Sir John Randall
Alex Stokes
James Watson
Maurice Wilkins
Herbert Wilson
Photo 51



When The University Cavendish Laboratory was at Cambridge old site, the „Eagle“ pub was a popular lunch destination for staff working there. Thus, it became the place where [Francis Crick](#) interrupted patrons' lunchtime on 28 February 1953 to announce that he and [James Watson](#) had "discovered the secret of life" after they had come up with their proposal for the structure of [DNA](#).

Also in 1953 Watson and Crick worked over lunch in the Eagle to draw up a list of the 20 canonical [amino acids](#). This has been a very influential rubric for molecular biology, and was a key development in understanding the protein-coding nature of DNA.



There are blue plaque next to the entrance of „Eagle“, and two plaques in the middle room by the table where Crick and Watson lunched regularly. Today the pub serves a special ale to commemorate the discovery, dubbed "Eagle's DNA".

Originally opened in 1667 as the "Eagle and Child", **The Eagle** is one of the larger pubs in Cambridge, England, on the north side of Benet' Street in the centre of the city.

<https://www.greeneking-pubs.co.uk/pubs/cambridgeshire/eagle/>

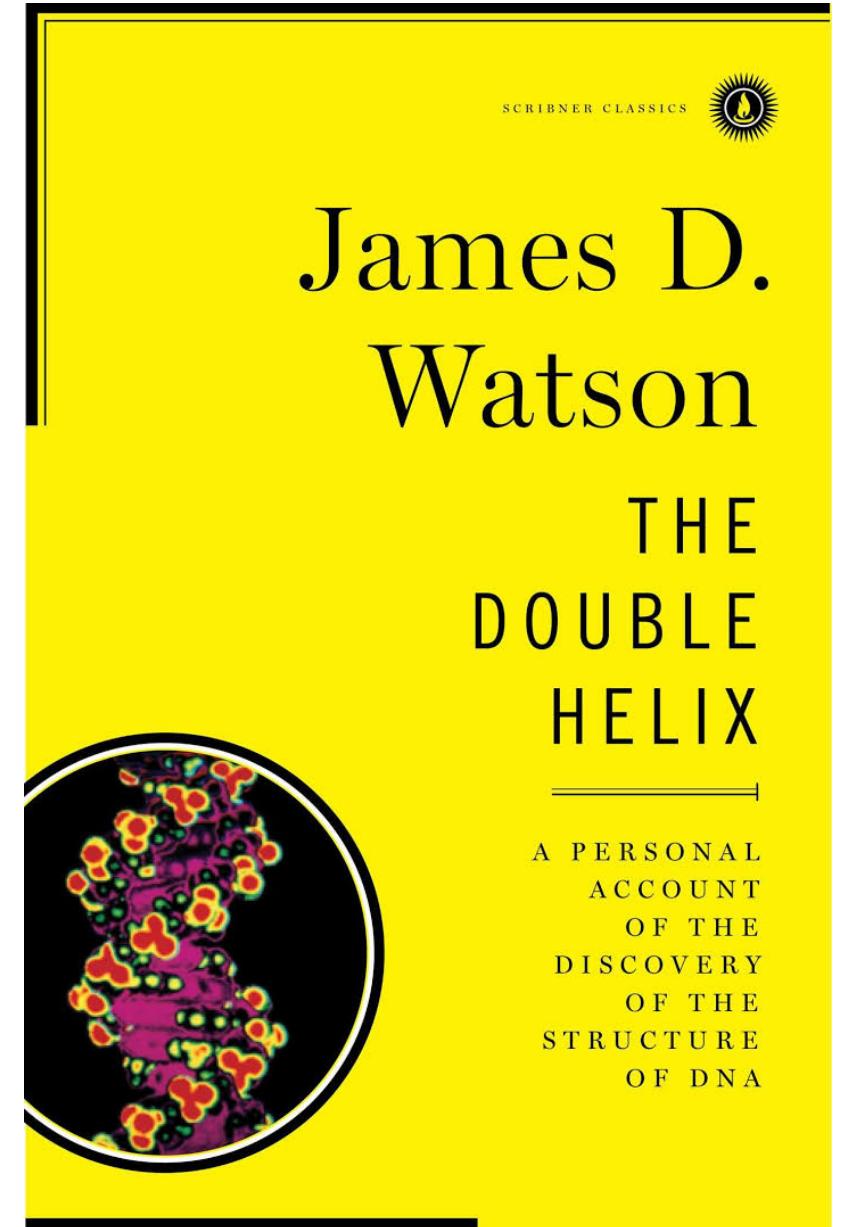
SCRIBNER CLASSICS



Discovery of DNA Structure and Function: Watson and Crick

By: Leslie A. Pray, Ph.D. © 2008 Nature Education

<https://www.nature.com/scitable/topicpage/discovery-of-dna-structure-and-function-watson-397>



James D.
Watson

THE
DOUBLE
HELIX

A PERSONAL
ACCOUNT
OF THE
DISCOVERY
OF THE
STRUCTURE
OF DNA

DNA chemical Structure (the link between the nucleotides of DNA)

- 1952 Alexander Todd *et al*
showed that 3'-5' phosphodiester
bonds regularly link together the
nucleotides of DNA

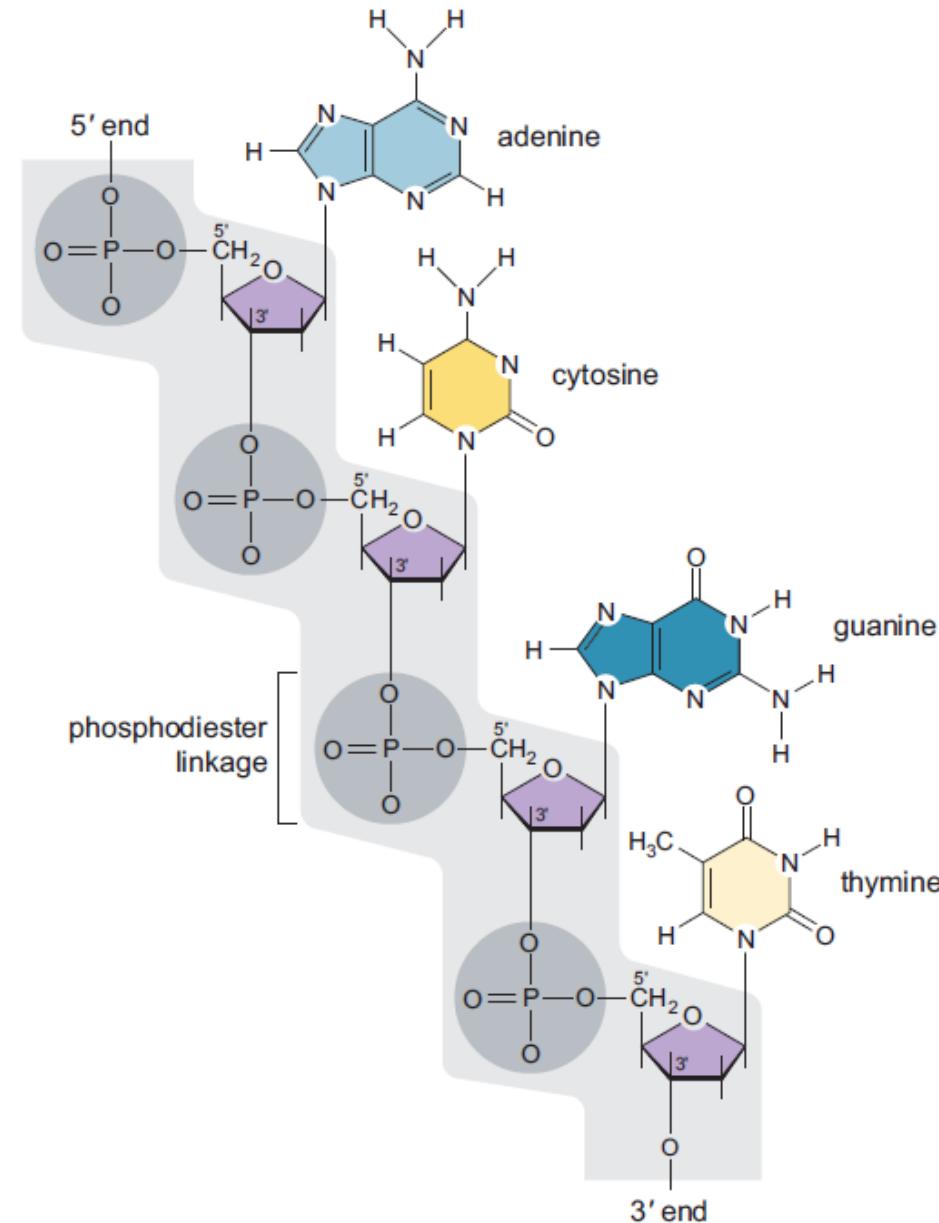


FIGURE 2-5 A portion of a DNA polynucleotide chain, showing the $3' \rightarrow 5'$ phosphodiester linkages that connect the nucleotides. Phosphate groups connect the 3' carbon of one nucleotide with the 5' carbon of the next.

Nucleotides, building blocks of DNA

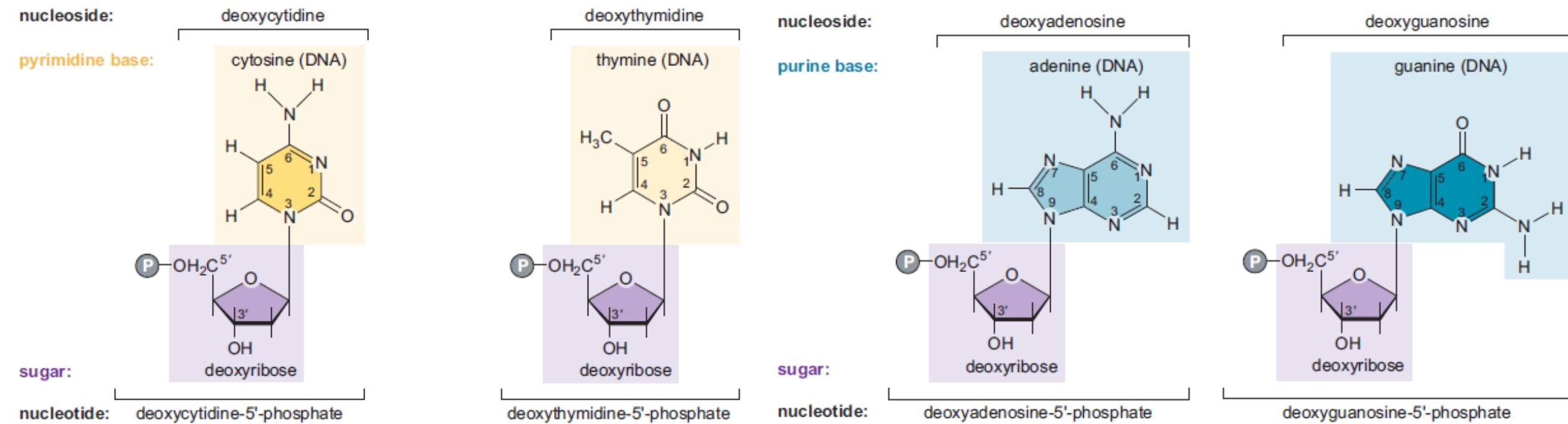


FIGURE 2-7 The nucleotides of DNA. The structures of the different components of each of the four nucleotides are shown.

Nucleic acids are the biopolymers, or small biomolecules, essential to all known forms of life. The term *nucleic acid* is the overall name for DNA and RNA. They are composed of nucleotides, which are the monomers made of three components:

- 5-carbon sugar,
- phosphate group
- nitrogenous base
- If the sugar is a compound ribose, the polymer is RNA (ribonucleic acid); if the sugar is derived from ribose as deoxyribose, the polymer is DNA (deoxyribonucleic acid).

- Nuclein were discovered by Friedrich Miescher in **1869**.
- In the early 1880s Albrecht Kossel further purifies the substance and discovers its highly acidic properties. He later also identifies the nucleobases.
- In **1889** Richard Altman creates the term nucleic acid
- In **1938** Astbury and Bell published the first X-ray diffraction pattern of DNA.
- In **1953** Watson and Crick determined the structure of DNA.



The Swiss scientist Friedrich Miescher discovered nucleic acids (DNA) in 1869. Later, he raised the idea that they could be involved in heredity.

He called the material 'nuclein' since it was found in the nucleus.

How these components makes DNA?

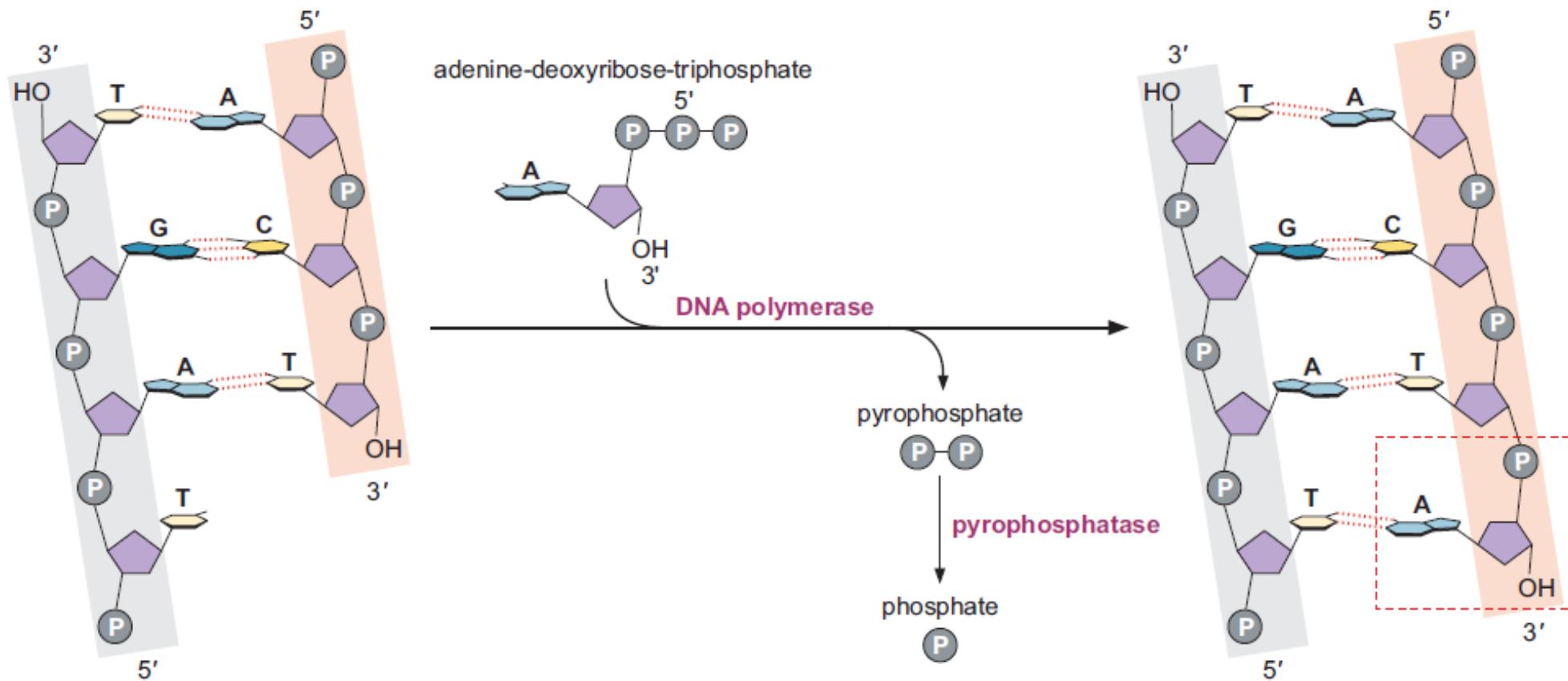


FIGURE 2-8 Enzymatic synthesis of a DNA chain catalyzed by DNA polymerase I. This image shows the addition of a nucleotide to a growing DNA strand as catalyzed by DNA polymerase. Although the DNA polymerase can catalyze DNA synthesis by itself, in the cell the released pyrophosphate molecule is rapidly converted to two phosphates by an enzyme called pyrophosphatase, making the forward reaction of nucleotide addition even more favorable.

Chargaff's rules of Base pairing

- 1949 Erwin Chargaff - 1905 - 2002 (an austrian chemist) showed that four different nucleotides are not present in equal amounts and the exact ratios of the four nucleotides vary

BOX 2-1 TABLE 1 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>Escherichia coli K2</i>	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

The fundamental significance of the A = T and G = C relationships (**Chargaff's rules**) could not emerge, however, until serious attention was given to the three-dimensional structure of DNA.

First parity rule

The first rule holds that a **double-stranded DNA molecule globally has percentage base pair equality**: %A = %T and %G = %C. The rigorous validation of the rule constitutes the basis of Watson-Crick pairs in the DNA double helix model.

Second parity rule

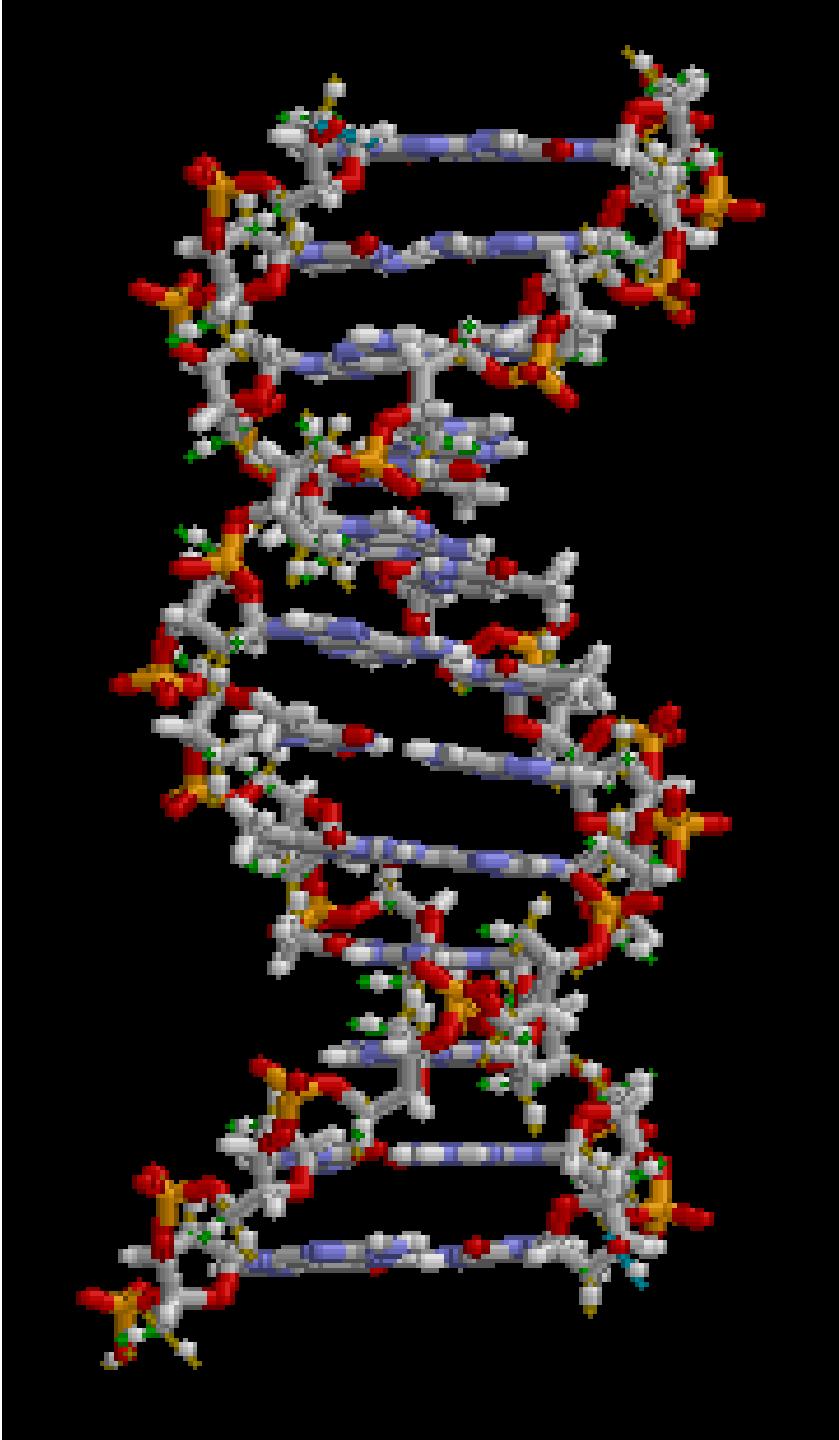
The second rule holds that both %A = %T and %G = %C are **valid for each of the two DNA strands**. This describes only a global feature of the base composition in a single DNA strand.

Serratia marcescens – rod-shaped Gram-negative bacteria (the human pathogen – urinari tract infections, wound infections etc)

Bacillus schatz – medicine against tuberculosis - Albert Israel Schatz, Elizabeth Bugie, and Selman Waksman at Rutgers University isolate streptomycin, the first antibiotic and first bacterial agent effective against tuberculosis (TB) and against other penicillin-resistant bacteria

X-ray crystallography pattern of DNA

<https://www.dnalc.org/view/15874-Franklin-s-X-ray.html>



The structure of part of a DNA double helix



DNA replication

- 1956 Arthur Kornberg demonstrated DNA synthesis in cell-free extracts of bacteria
 - DNA Polymerase I
 - dATP, dGTP, dCTP, dTTP
- Works only in the presence of DNA

TABLE 2-1 A Comparison of the Base Composition of Enzymatically Synthesized DNAs and Their DNA Templates

Source of DNA Template	Base Composition of the Enzymatic Product				$\frac{A + T}{G + C}$	$\frac{A + T}{G + C}$
	Adenine	Thymine	Guanine	Cytosine		
<i>Micrococcus lysodeikticus</i> (a bacterium)	0.15	0.15	0.35	0.35	0.41	0.39
<i>Aerobacter aerogenes</i> (a bacterium)	0.22	0.22	0.28	0.28	0.80	0.82
<i>Escherichia coli</i>	0.25	0.25	0.25	0.25	1.00	0.97
Calf thymus	0.29	0.28	0.21	0.22	1.32	1.35
Phage T2	0.32	0.32	0.18	0.18	1.78	1.84

DNA strands are separated during replication

- 1958 Matthew Meselson and Franklin W. Stahl elegantly showed that the two strands of the double helix separate from each other during replication
- **15N -> 14N** - what it means???
 - After one generation – all DNA is heavy-light
 - After two generations – half the DNA is heavy-light, half is light-light

DNA complementary strands can be separated

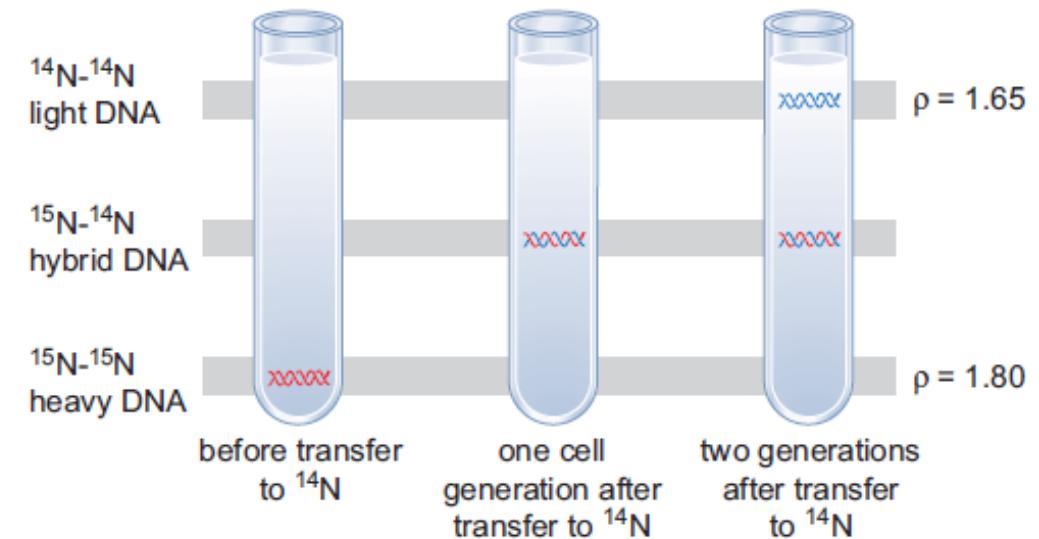
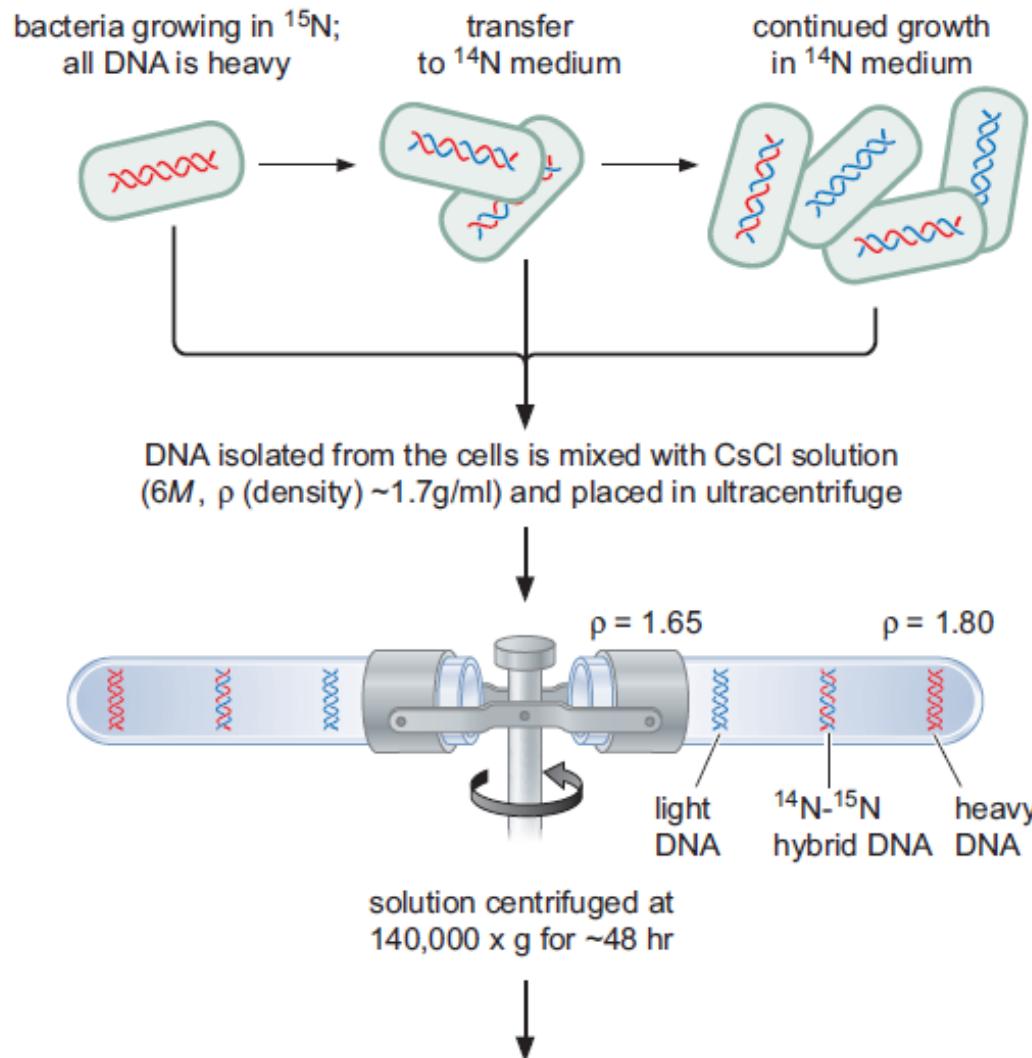


FIGURE 2-9 Use of a cesium chloride (CsCl) density gradient to demonstrate the separation of complementary strands during DNA replication.

DNA replication

In the dispersive model, which was favored by many at the time, the DNA strands were proposed to be broken as frequently as every ten base pairs and used to prime the synthesis of similarly short regions of DNA.

These short DNA fragments would subsequently be joined to form complete DNA strands. In this complex model, all DNA strands would be composed of both old and new DNA (thus nonconservative) and fully light DNA would only be observed after many generations of growth.



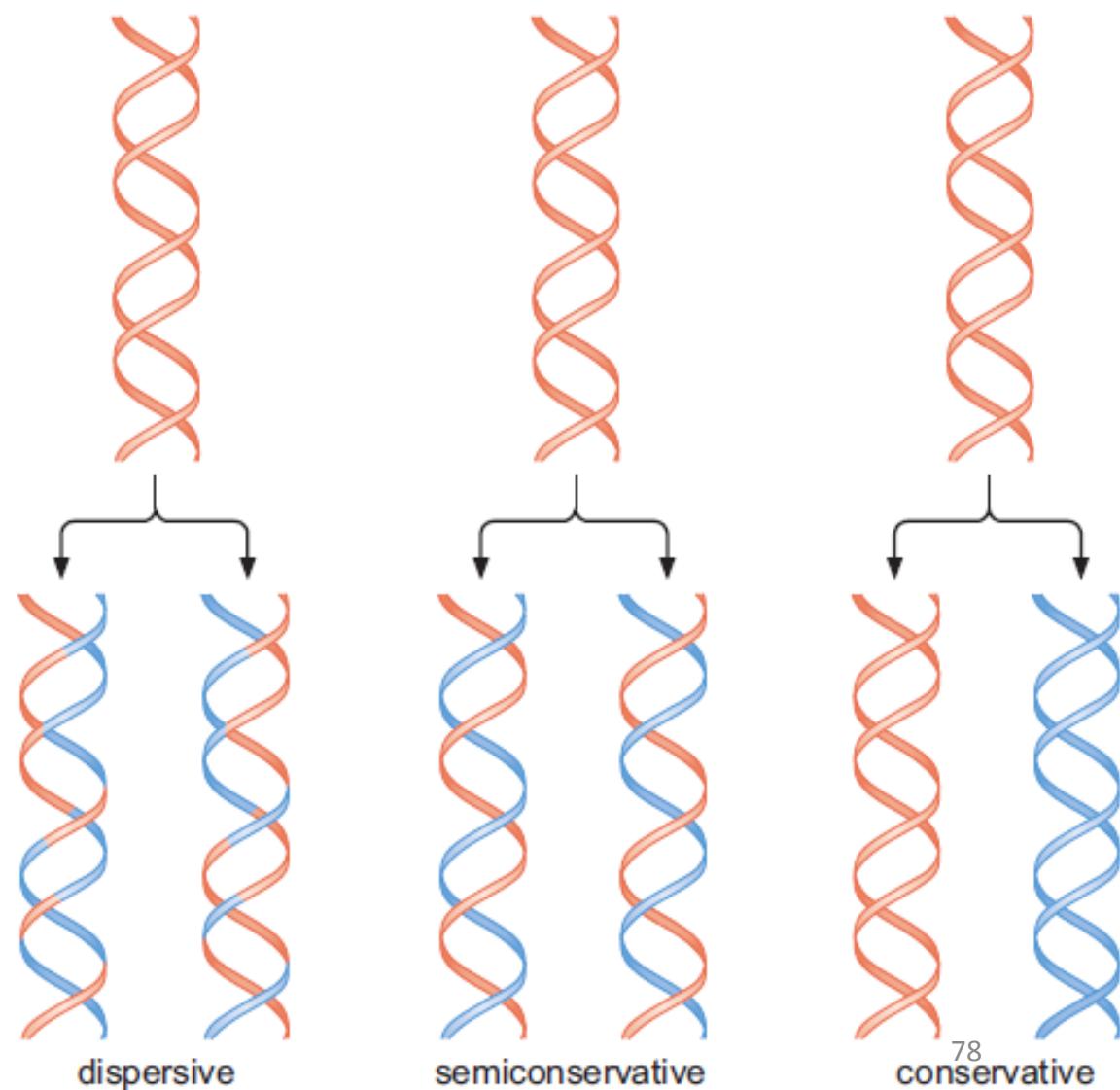
FIGURE 2-6 The replication of DNA. The newly synthesized strands are shown in orange.

What mechanism is used in DNA replication?

In the **dispersive model**, which was favored by many at the time, the DNA strands were proposed to be broken as frequently as every ten base pairs and used to prime the synthesis of similarly short regions of DNA. These short DNA fragments would subsequently be joined to form complete DNA strands. In this complex model, all DNA strands would be composed of both old and new DNA (thus nonconservative) and fully light DNA would only be observed after many generations of growth.

FIGURE 2-10 Three possible mechanisms for DNA replication. When the structure of DNA was discovered, several models were proposed to explain how it was replicated; three are illustrated here. The experiments proposed by Meselson and Stahl clearly distinguished among these models, demonstrating that DNA was replicated semiconservatively.

Which mechanism is used mostly in DNA replication?



What is the template for proteins?

- DNA can not be the template for protein synthesis, even if it carries the information
- Protein synthesis occurs in places where no DNA is present = in the cytoplasmic regions
- RNA?
 - Single-stranded
 - Very similar to DNA

RNA is similar to DNA

1900 YEARS:

RNA was initially known as
"yeast nucleic acid" and

DNA was
"thymus nucleic acid"

The role of RNA in protein synthesis was suspected already in 1939

Caspersson T, Schultz J (1939). "Pentose nucleotides in the cytoplasm of growing tissues". Nature. 143 (3623): 602–03.

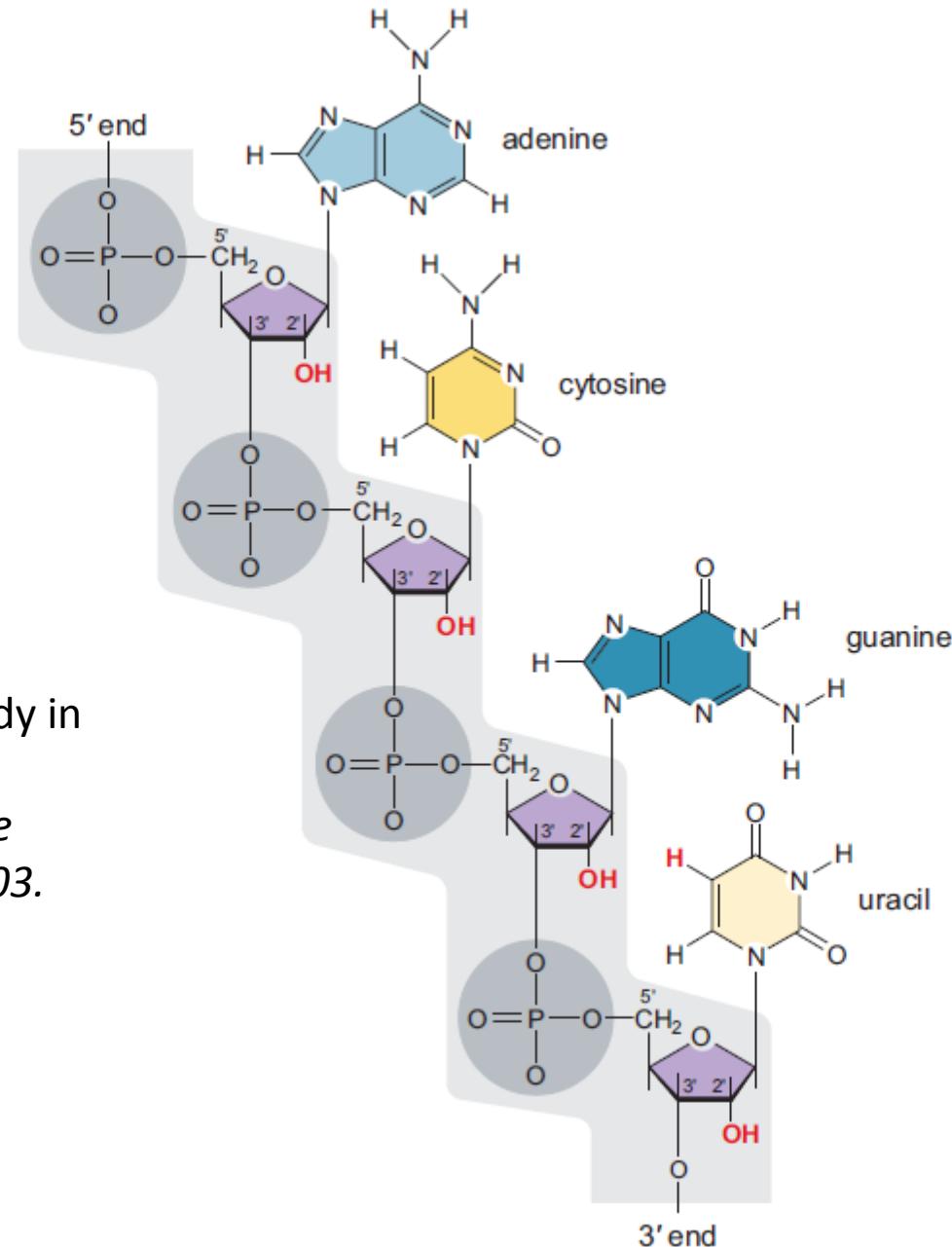


FIGURE 2-11 A portion of a polyribonucleotide (RNA) chain. Elements in red are distinct from DNA.

In 1933, while studying virgin [sea urchin](#) eggs, [Jean Brachet](#) (1909 - 1988) Belgian biochemist suggested that [DNA](#) is found in [cell nucleus](#) and that [RNA](#) is present exclusively in the [cytoplasm](#). He made a key contribution in **understanding the role of RNA**.

At the time, "yeast nucleic acid" (RNA) was thought to occur only in plants, while "thymus nucleic acid" (DNA) only in animals.

The concept of messenger RNA emerged during the late 1950s, and is associated with [Crick](#)'s description of his "Central Dogma of Molecular Biology", which asserted that DNA led to the formation of RNA, which in turn led to the synthesis of [proteins](#). During the early 1960s, sophisticated genetic analysis of mutations in the [lac operon](#) of [E. coli](#) and in the rII locus of [bacteriophage T4](#) were instrumental in defining the nature of both messenger [RNA](#) and the [genetic code](#).

DNA and RNA – what's the difference?

RNA contains no thymine but instead contains the closely related pyrimidine uracil

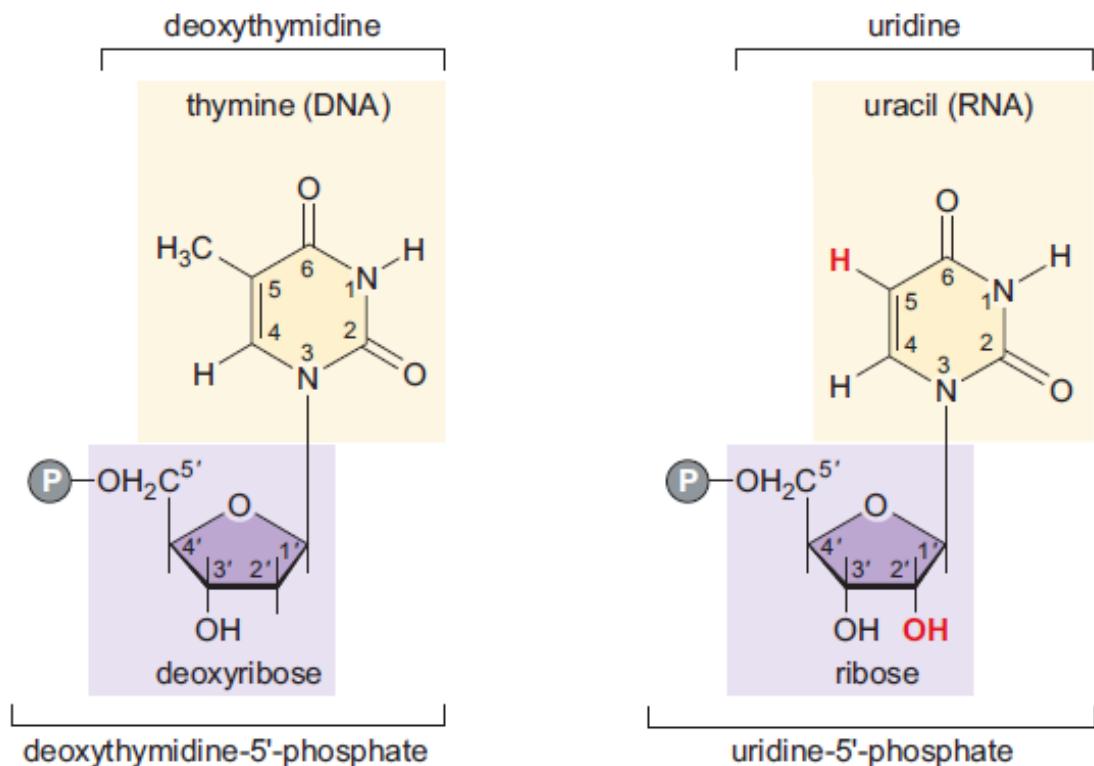


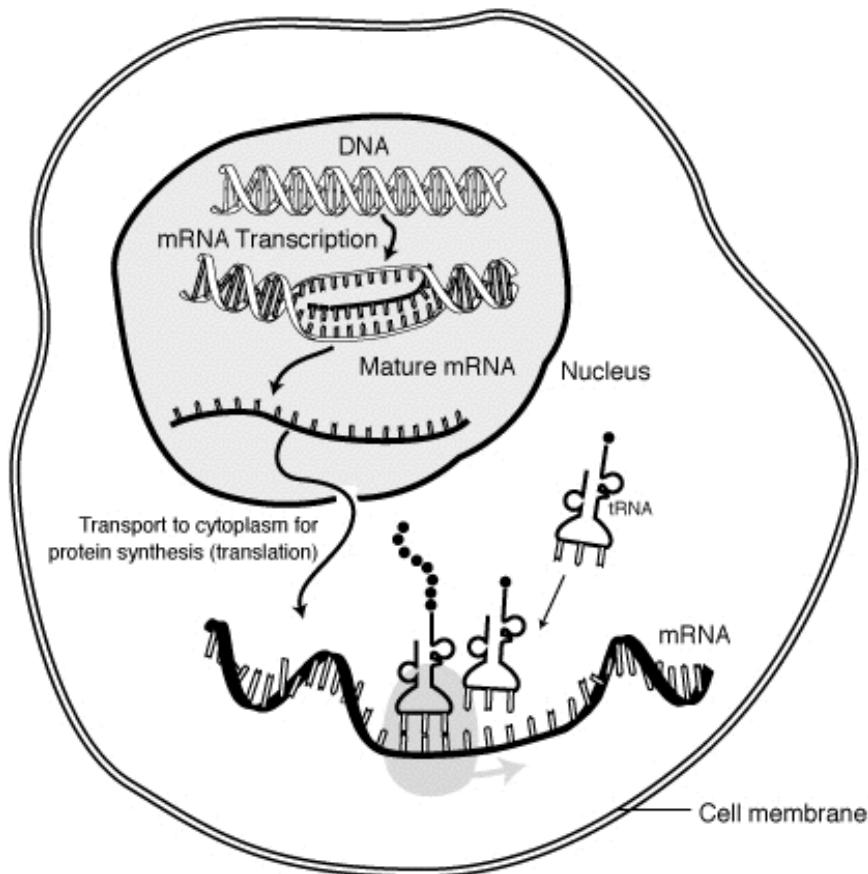
FIGURE 2-12 Distinctions between the nucleotides of RNA and DNA. A nucleotide of DNA is shown next to a nucleotide of RNA. All RNA nucleotides have the sugar ribose (instead of deoxyribose for DNA), which has a hydroxyl group on the 2' carbon (shown in red). In addition, RNA has the pyrimidine base uracil instead of thymine. Uracil has a hydrogen at the 5 position of the pyrimidine ring (shown in red) rather than the methyl group found in that position for thymine. The three other bases that occur in DNA and RNA are identical.

RNA contains ribose

The sugar of DNA is deoxyribose, whereas **RNA contains ribose**, identical to deoxyribose except for the presence of an additional OH (hydroxyl) group on the 2⁰ carbon.

The second difference is that RNA contains no thymine but instead contains the closely related pyrimidine uracil. Despite these differences, however, polyribonucleotides have the potential for forming complementary helices of the DNA type.

The "life cycle" of an mRNA in a eukaryotic cell. [RNA](#) is [transcribed](#) in the [nucleus](#); after [processing](#), it is transported to the [cytoplasm](#) and [translated](#) by the [ribosome](#). Finally, the mRNA is degraded.



The short-lived nature of bacterial RNAs, together with the highly complex nature of the cellular mRNA population, made the biochemical isolation of mRNA very challenging.

This problem was overcome in the 1960s by the use of [reticulocytes](#) in vertebrates, which produce large quantities of mRNA that are highly enriched in RNA encoding alpha- and beta-globin (the two major protein chains of [hemoglobin](#)).

The first direct experimental evidence for the existence of mRNA was provided by such a hemoglobin synthesizing system.

The existence of mRNA was first suggested by [Jacques Monod](#) and [François Jacob](#), and subsequently discovered by Jacob, [Sydney Brenner](#) and [Matthew Meselson](#) at the California Institute of Technology in 1961.

Lamfrom H (1961). "Factors determining the specificity of hemoglobin synthesized in a cell-free system". J. Mol. Biol. 3 (3): 241–52.

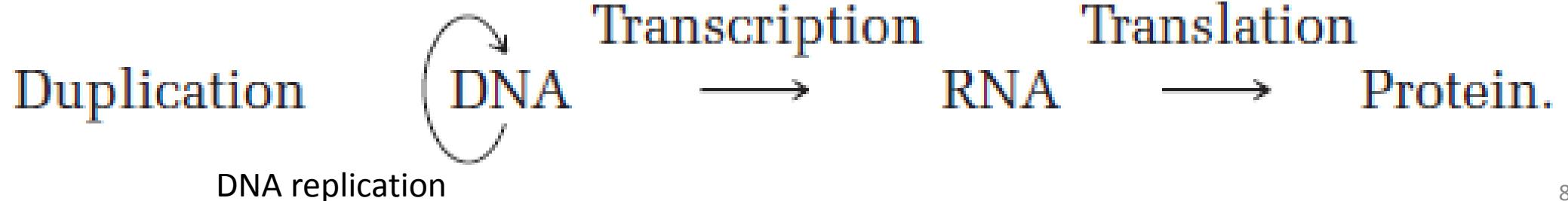
Central dogma in MB

Replication
Transcription
Translation

- 1953 Chromosomal DNA functions as the template for RNA molecules

Francis Crick, 1956

central dogma



Adaptor Hypothesis, discovery of tRNA

The courier between DNA and protein

- RNA templates fold to form cavities specific for 20 amino acids
- Francis Crick proposed the existence of an adaptor molecule
- tRNA was discovered in late 1950s

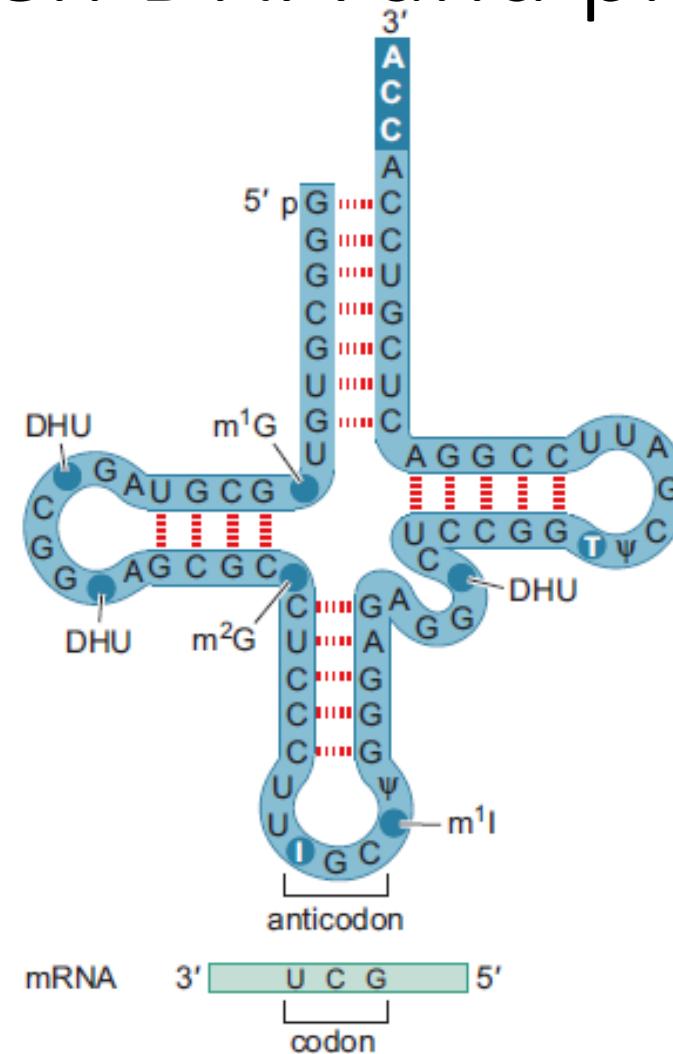


FIGURE 2-14 Yeast alanine tRNA structure, as determined by Robert W. Holley and his associates. The anticodon in this tRNA recognizes the codon for alanine in the mRNA. Several modified nucleosides exist in the structure: ψ = pseudouridine, T = ribothymidine, DHU = 5,6-dihydrouridine, I = inosine, m^1G = 1-methylguanosine, m^1I = 1-methylinosine, and m^2G = N,N-dimethylguanosine.



Where does protein synthesis take place?

- Ribosomes, small RNA-containing particles in the cytoplasm

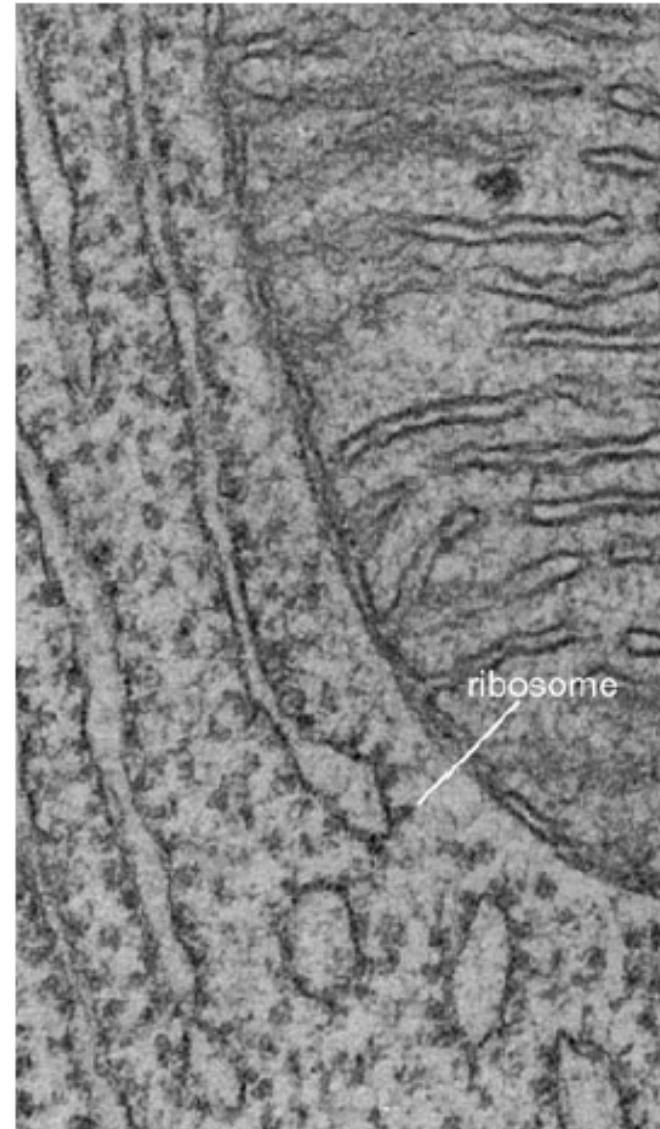
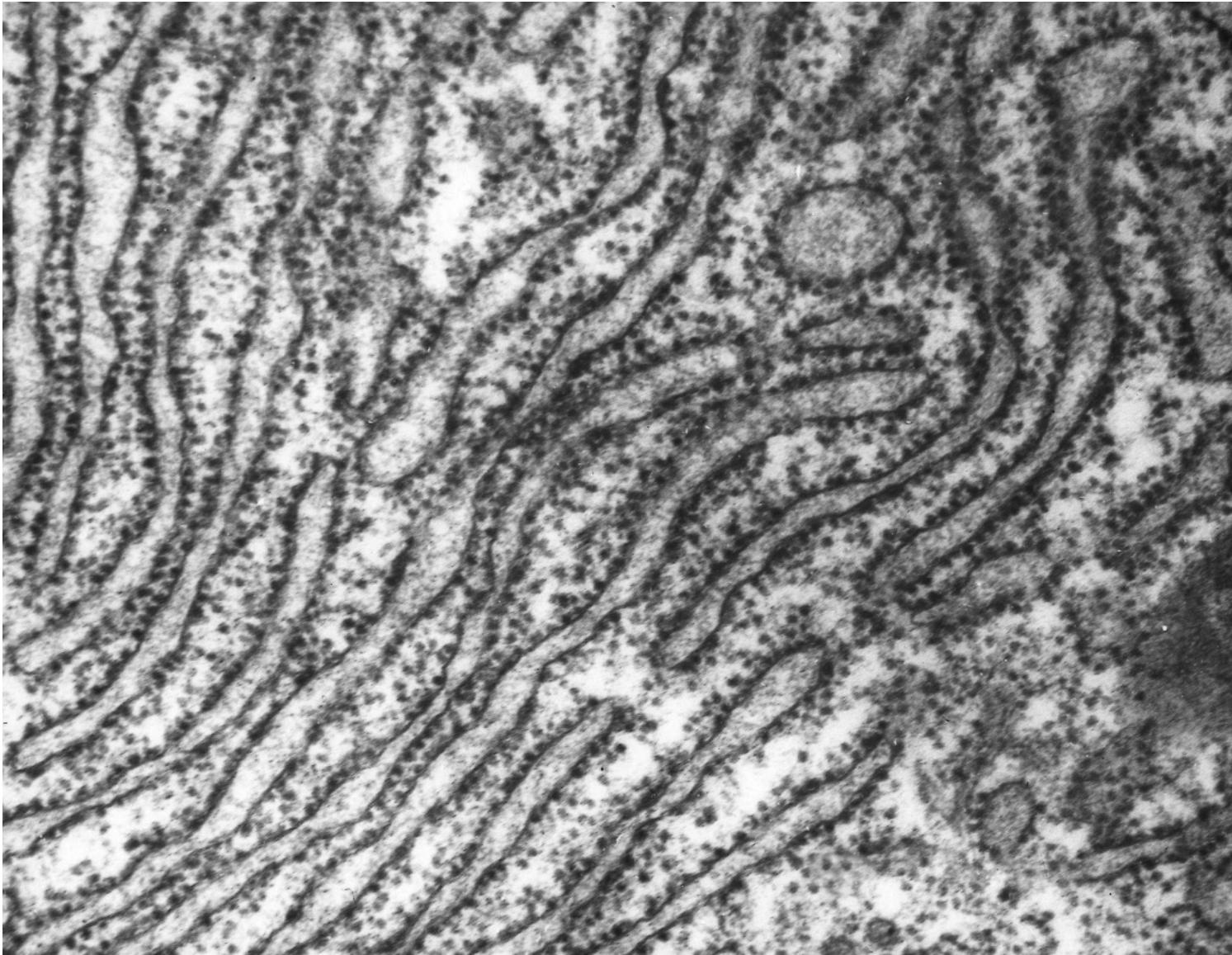


FIGURE 2-13 Electron micrograph of ribosomes attached to the endoplasmic reticulum. This electron micrograph (105,000x) shows a portion of a pancreatic cell. The upper right portion shows a portion of the mitochondrion and the lower left shows a large number of ribosomes (small circles of electron density) attached to the membranous endoplasmic reticulum. Some ribosomes exist free in the cytoplasm; others are attached to the membranous endoplasmic reticulum. (Courtesy of K.R. Porter.)



What acts as a template for protein synthesis?

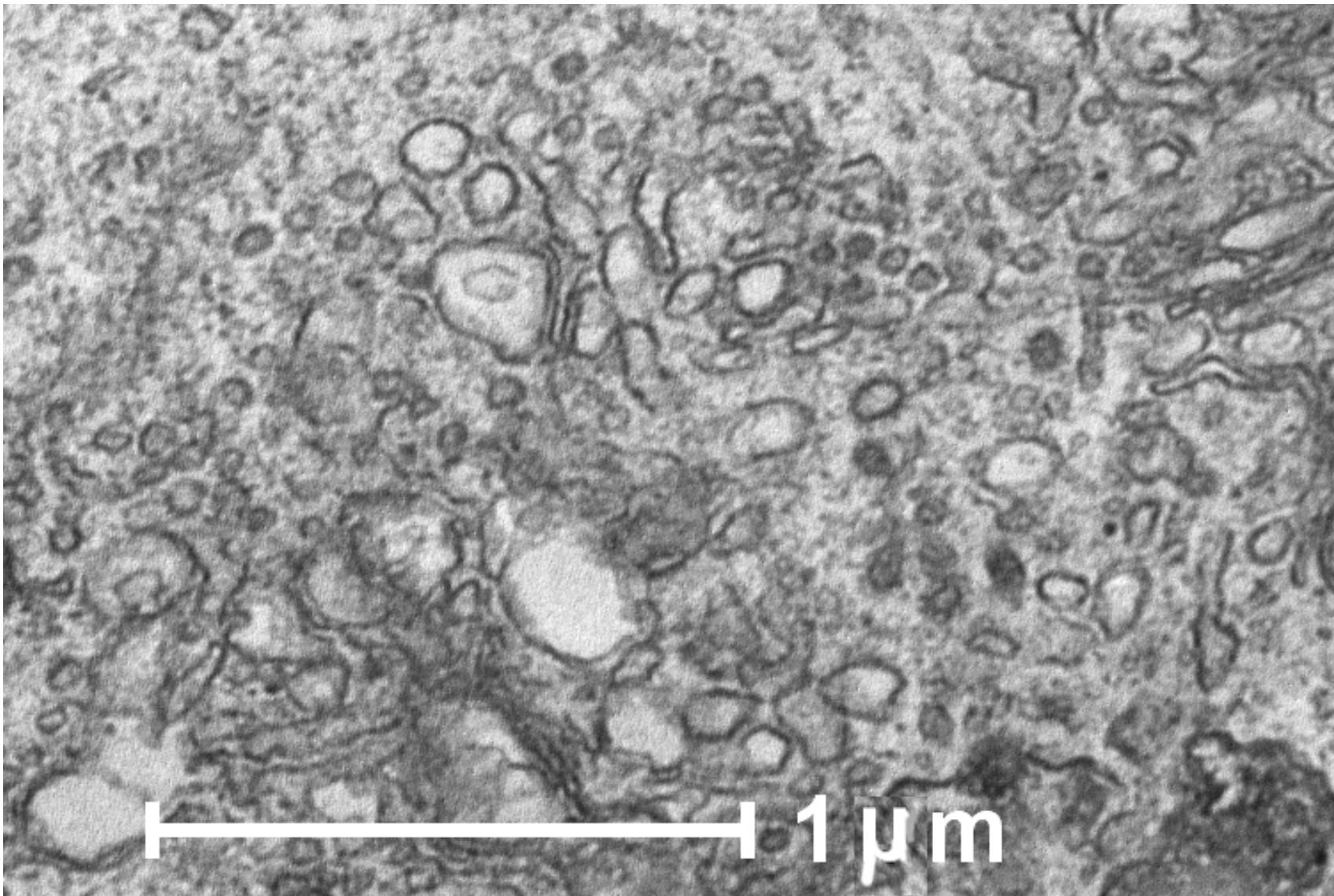
- Initially, ribosomal RNA was thought to be the template
 - 85% of cellular RNA is in ribosomes
 - where is placed the other 15% of RNA?
 - what kind of RNAs do You know more?
 - Two subunits, rRNA length is constant
- mRNA?



EM-photo: Jüri Kärner

Endoplasmic reticulum (ER) + ribosomes =
rough ER

Free ribosomes (polysomes) - they are not
connected with ER and ER named then
smooth ER



1 μ m

Smooth ER without
ribosomes. Mammalian cell.

Combining transcription and translation

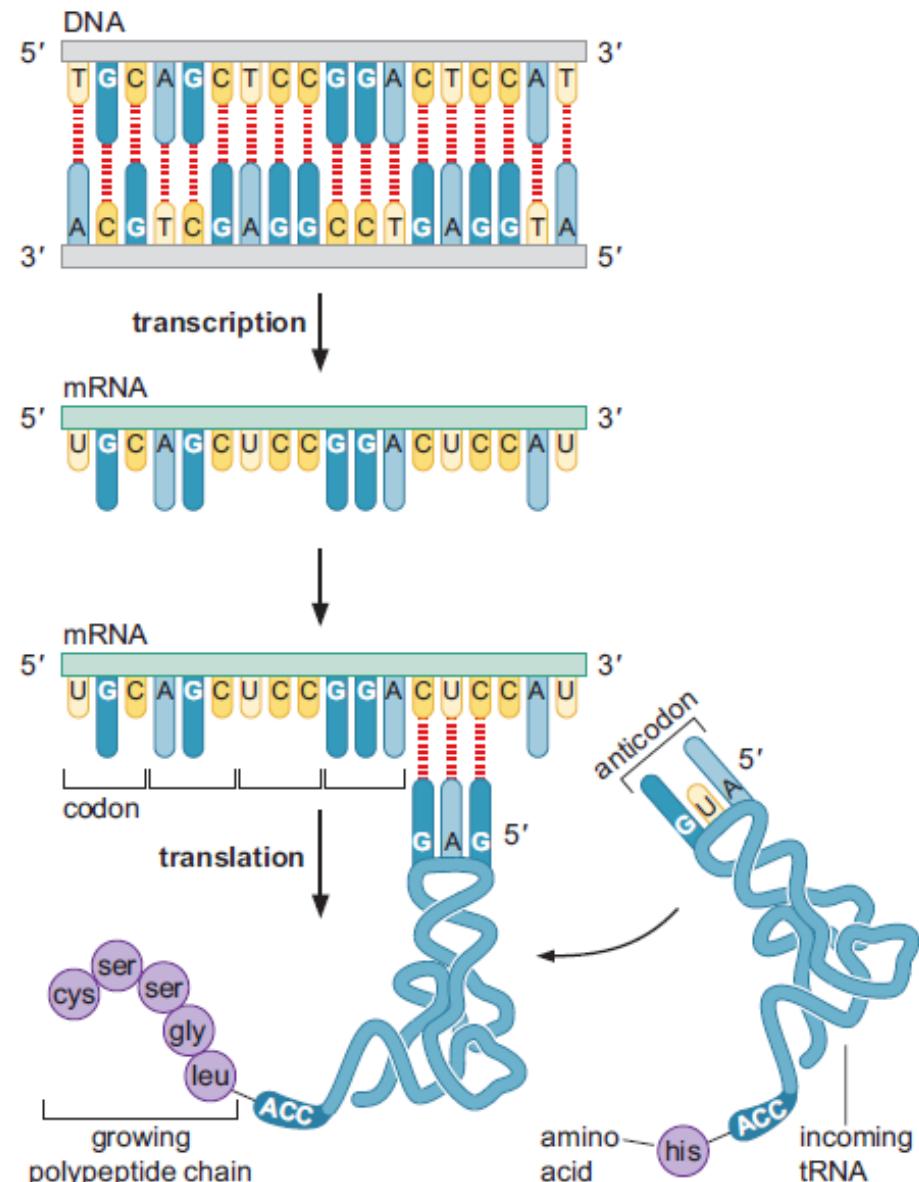


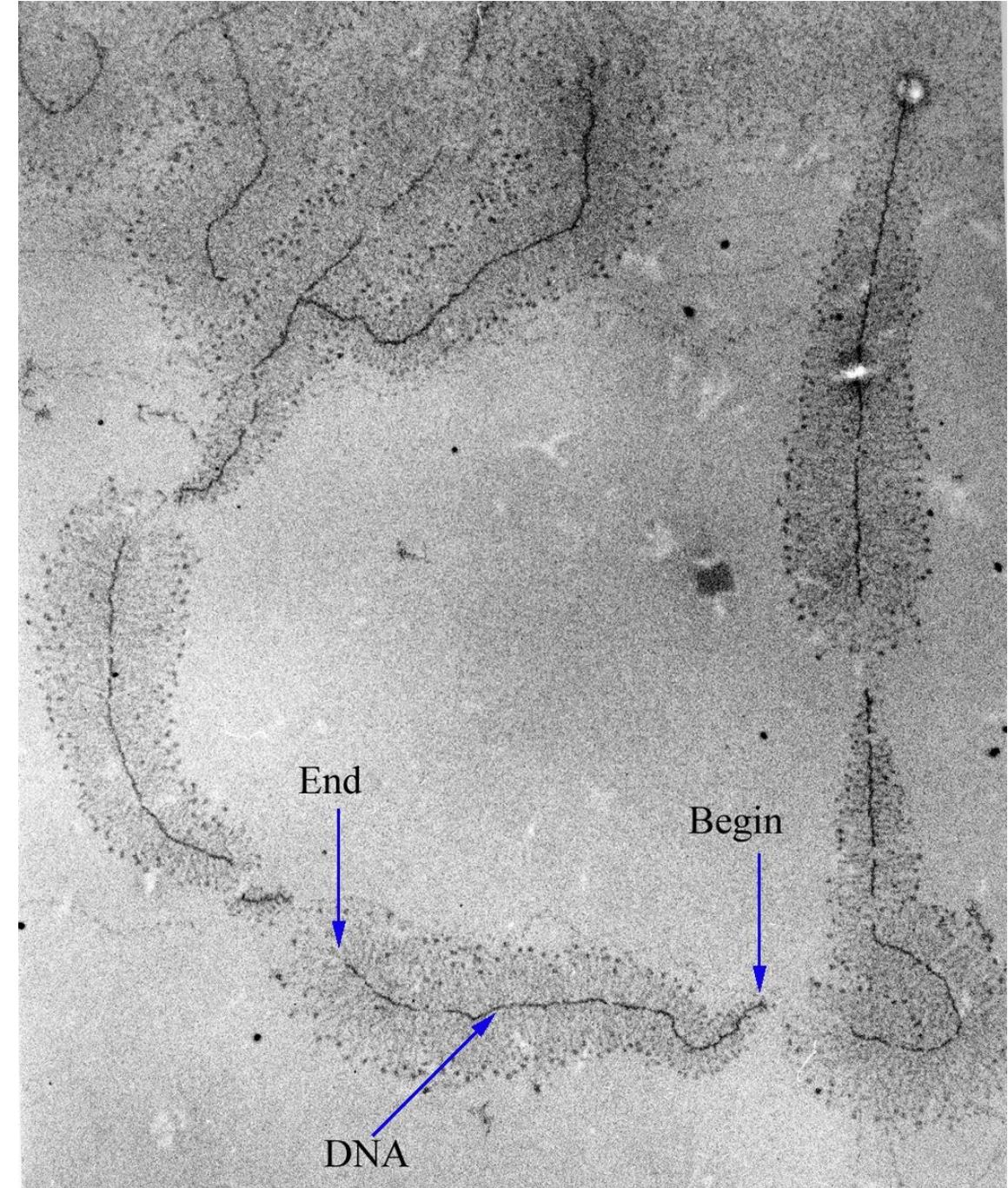
FIGURE 2-15 Transcription and translation. The nucleotides of mRNA are assembled to form a complementary copy of one strand of DNA. Each group of three is a codon that is complementary to a group of three nucleotides in the anticodon region of a specific tRNA molecule. When base pairing occurs, an amino acid carried at the other end of the tRNA molecule is added to the growing protein chain.



Transcription or RNA synthesis (only in the nucleus)

- Jerald Hurwitz and Samuel B. Weiss, RNA polymerases

https://en.wikipedia.org/wiki/RNA_polymerase



Transcription aka (also known as) how to make RNA from DNA template

The Royal Swedish Academy of Science. 1959.

The Nobel Prize in Physiology or Medicine 1959 was awarded jointly to **Severo Ochoa** and **Arthur Kornberg** 'for their discovery of the mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid'.

It's takes place only in the nucleus!

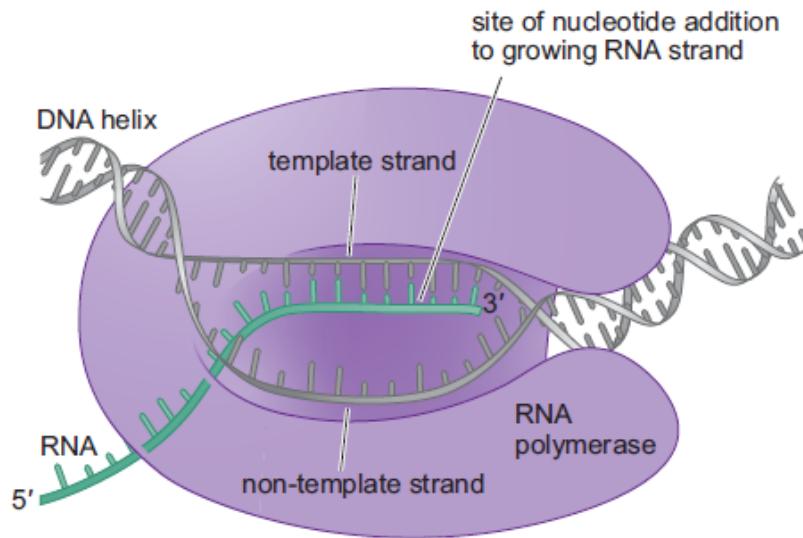


FIGURE 2-17 Enzymatic synthesis of RNA upon a DNA template, catalyzed by RNA polymerase.

TABLE 2-2 Comparison of the Base Composition of Enzymatically Synthesized RNAs with the Base Composition of Their Double-Helical DNA Templates

Source of DNA Template	Composition of the RNA Bases				Observed	$\frac{A + U}{G + C}$	$\frac{A + T}{G + C}$
	Adenine	Uracil	Guanine	Cytosine			
T2	0.31	0.34	0.18	0.17	1.86	1.84	
Calf thymus	0.31	0.29	0.19	0.21	1.50	1.35	
<i>Escherichia coli</i>	0.24	0.24	0.26	0.26	0.92	0.97	
<i>Micrococcus lysodeikticus</i> (a bacterium)	0.17	0.16	0.33	0.34	0.49	0.39	

Protein synthesis or **translation** by (poly)ribosomes (it takes part only in cytoplasm)

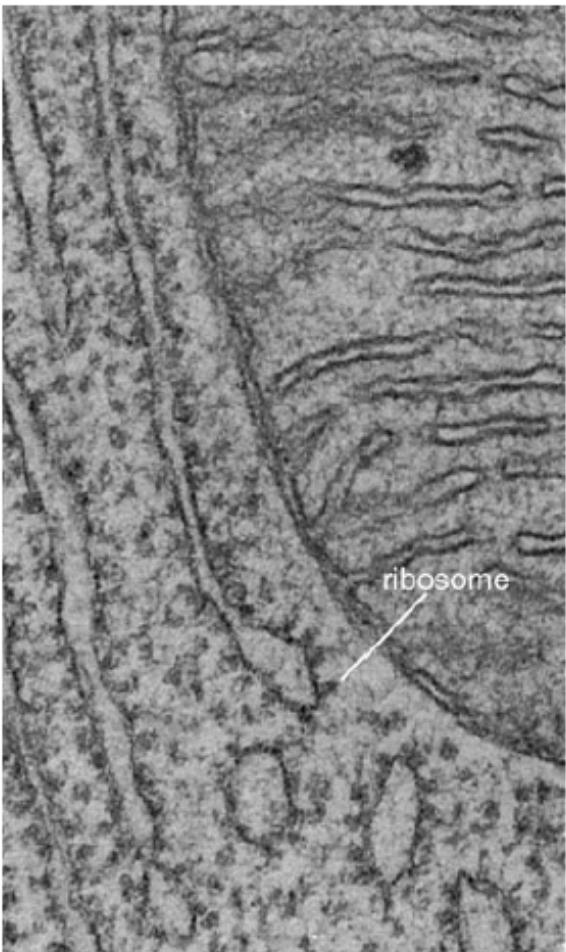


FIGURE 2-13 Electron micrograph of ribosomes attached to the endoplasmic reticulum. This electron micrograph (105,000x) shows a portion of a pancreatic cell. The upper right portion shows a portion of the mitochondrion and the lower left shows a large number of ribosomes (small circles of electron density) attached to the endoplasmic reticulum. Some ribosomes exist free in the cytoplasm; others are attached to the membranous endoplasmic reticulum. (Courtesy of K.R. Porter.)

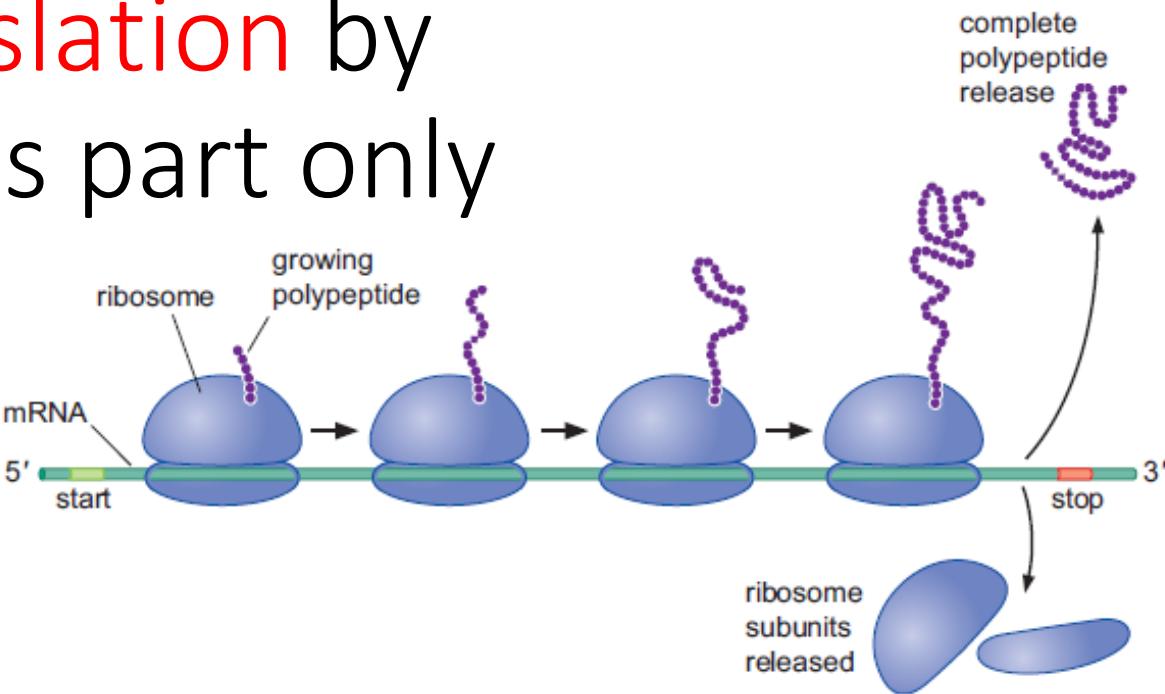


FIGURE 2-16 Diagram of a polyribosome. Each ribosome attaches at a start signal at the 5' end of an mRNA chain and synthesizes a polypeptide as it proceeds along the molecule. Several ribosomes may be attached to one mRNA molecule at one time; the entire assembly is called a polyribosome.

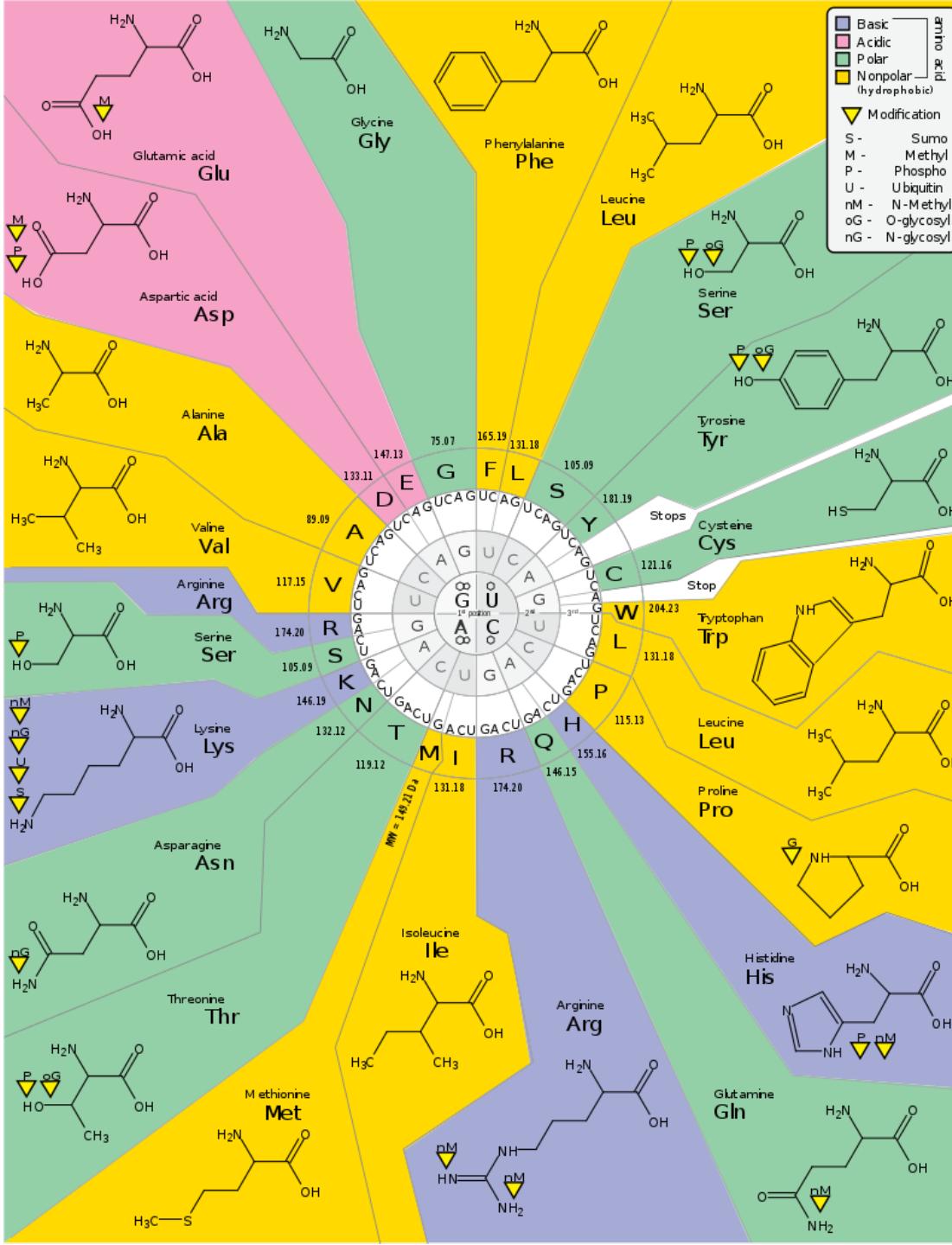
How to translate RNA sequence into protein?

TABLE 2-3 The Genetic Code

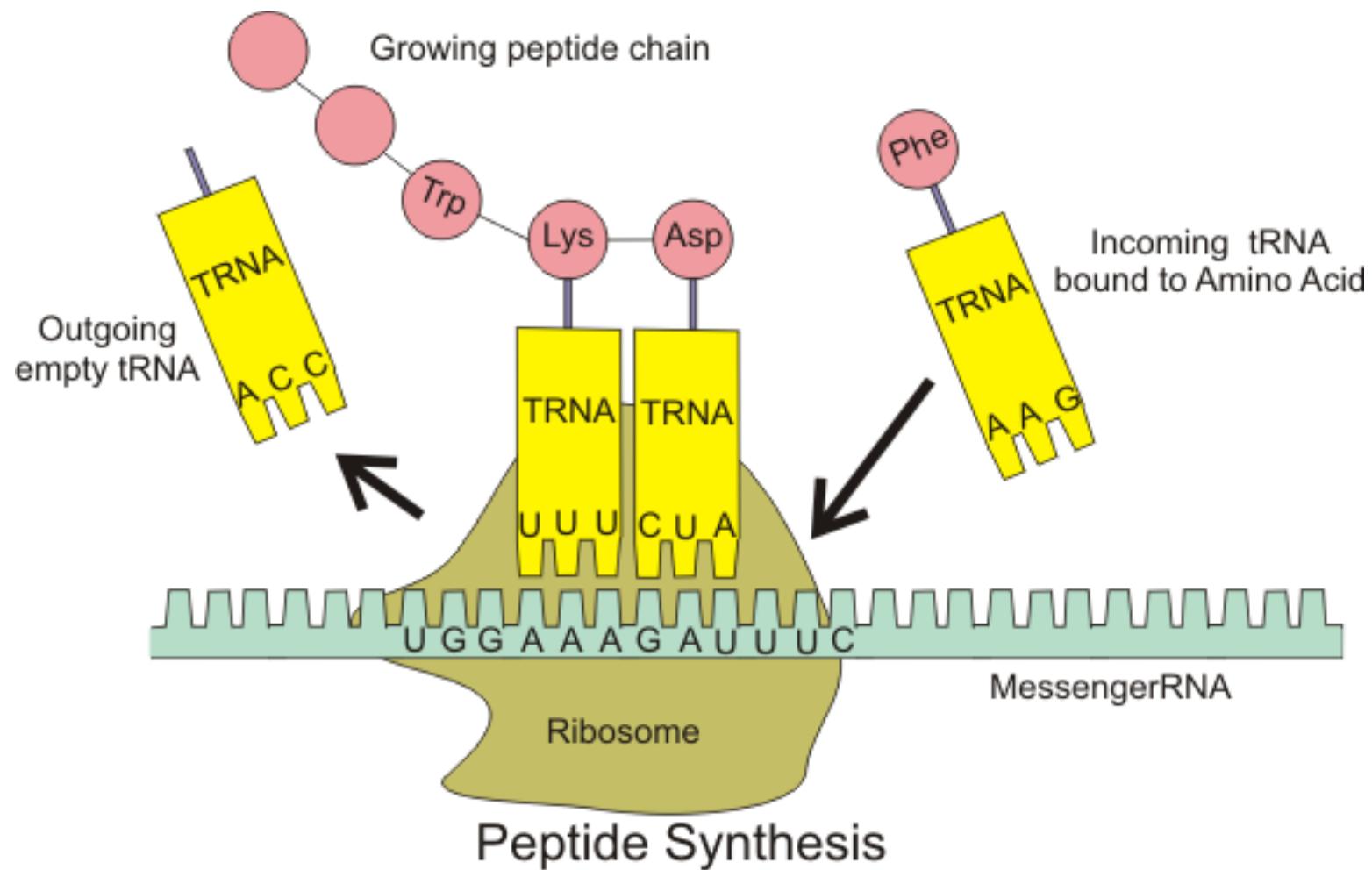
		second position					
		U	C	A	G		
first position	U	UUU UUC UUA UUG	Phe	UCU UCC UCA UCG	Ser	UAU UAC UAA UAG	Tyr stop stop
	C	CUU CUC CUA CUG	Leu	CCU CCC CCA CCG	Pro	CAU CAC CAA CAG	His Gln
	A	AUU AUC AUA AUG	Ile	ACU ACC ACA ACG	Thr	AAU AAC AAA AAG	Asn Lys
	G	GUU GUC GUA GUG	Val	GCU GCC GCA GCG	Ala	GAU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

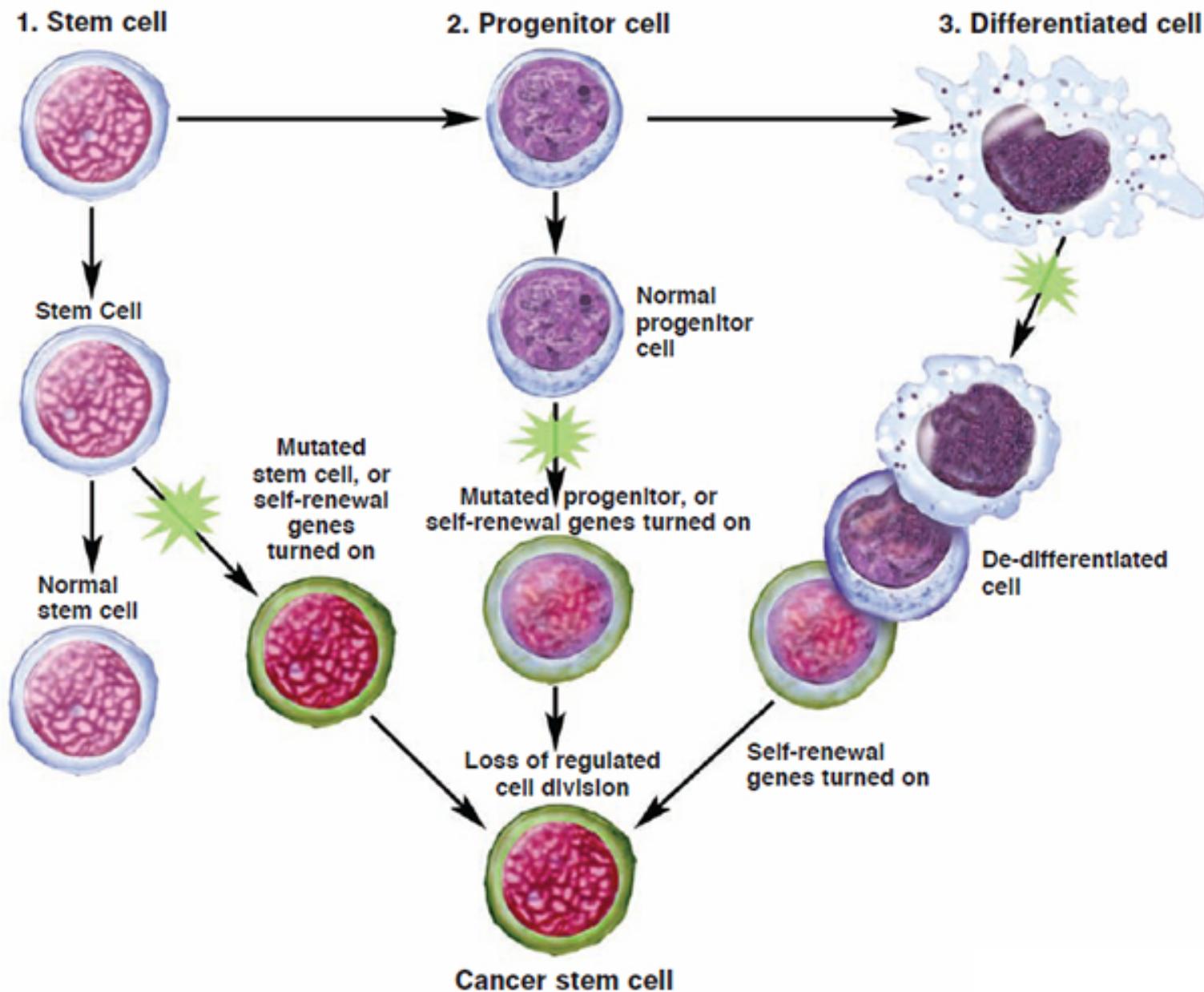
- 1966 complete code

The Fr. Crick, S. Brenner, L Barnett and R. J. Watts-Tobin demonstrated that the genetic code is made up of a series of three base pair codons which code for individual amino acids.



The translation - The interaction of tRNA and mRNA in protein synthesis.



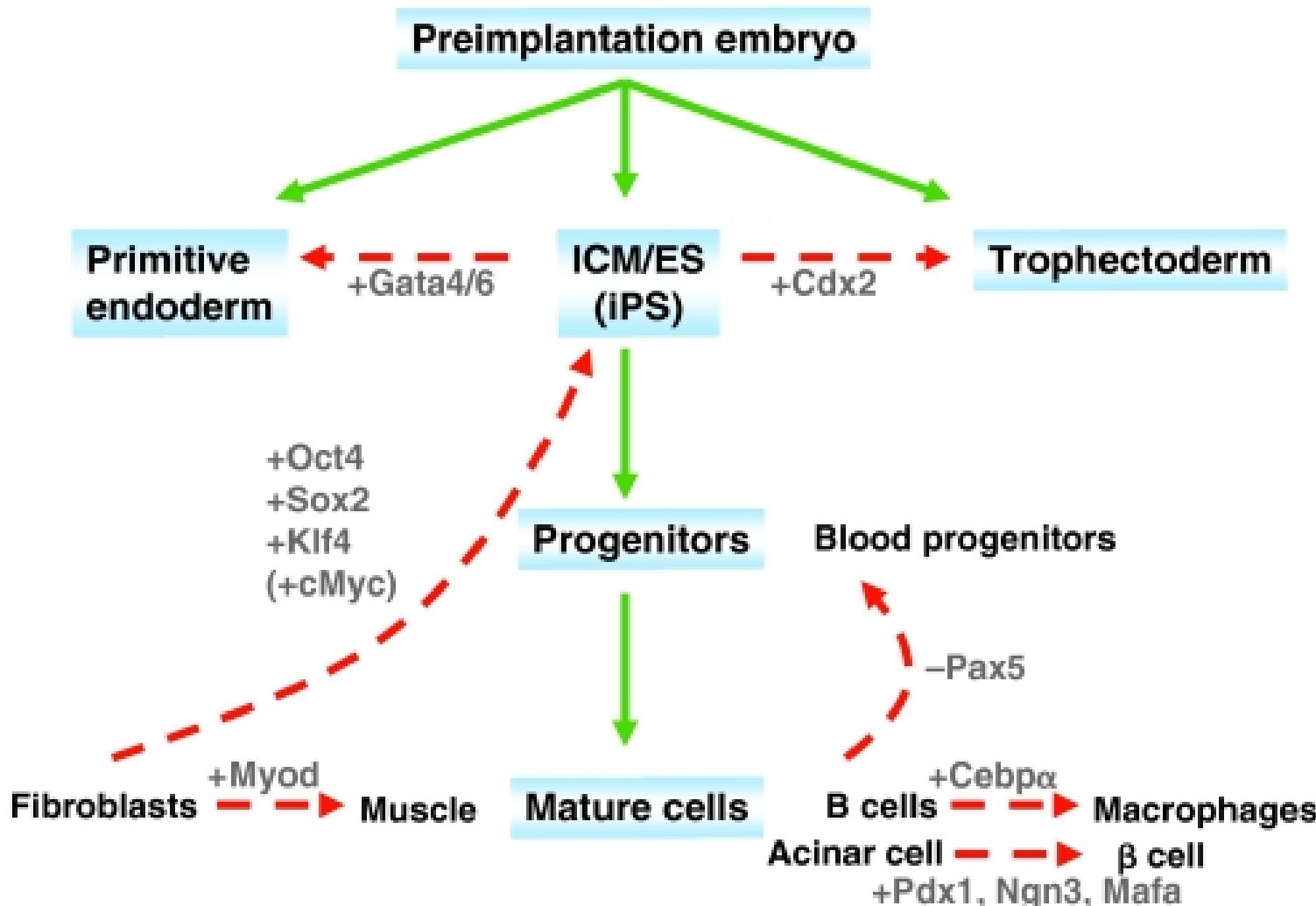


The protein synthesis (translation) is the key to the development

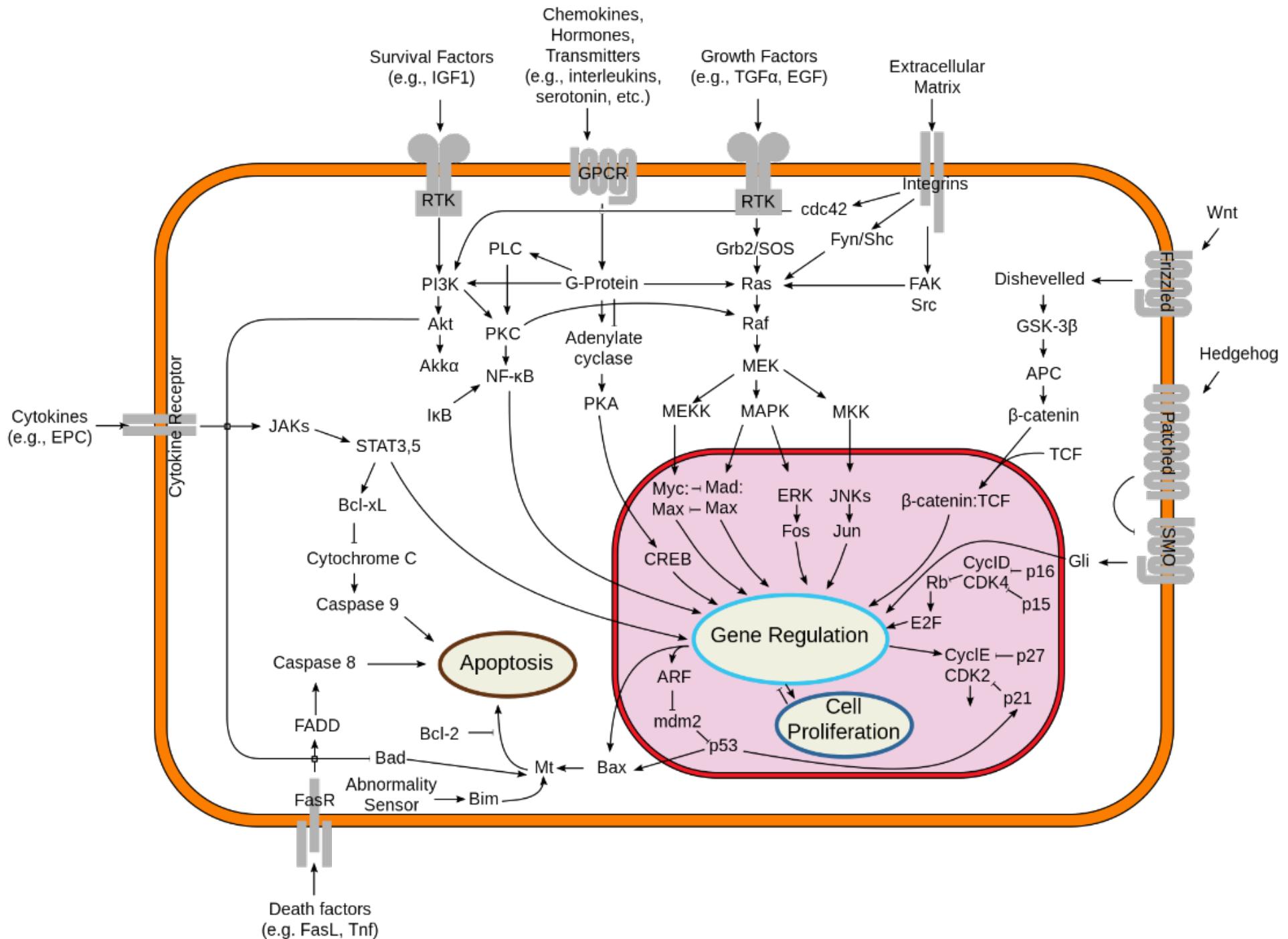
(it must take part at the **right time** and at the **normal amount** - only then the differentiation goes in normal way)

Example:

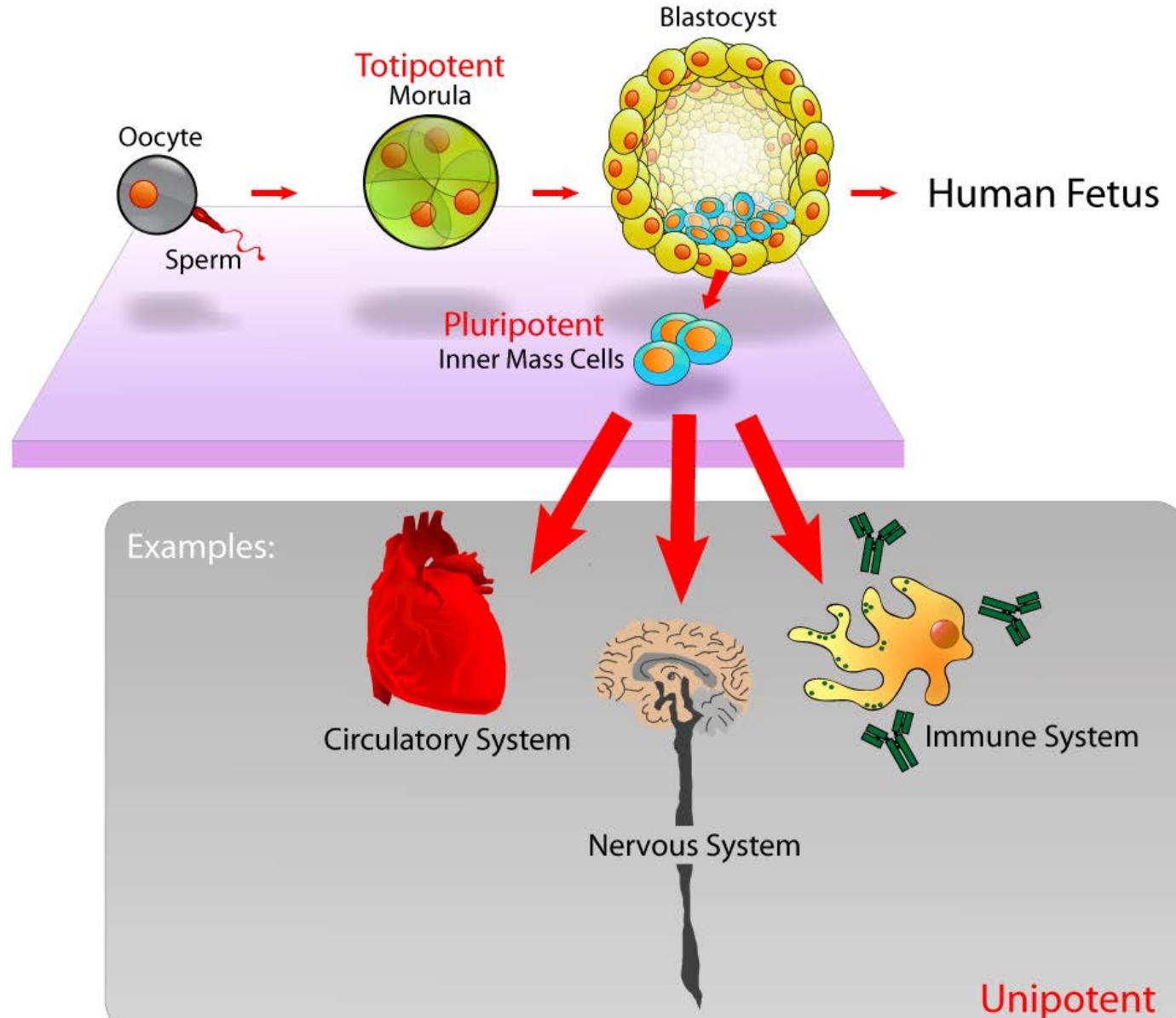
The differentiation of stem cell to the way of progenitor cell and further to the final differentiation; to the direction of normal stem cell (re-newing of stem cells); the cancerous way to the cancer stem cell (non-differentiated cells)



2. The differentiation of early embryo to the several types of cells depends on the activation and deactivation of several genes and transcription factors



3. The signalization machinery of the cell
(the synthesis of signal factors in the nucleus and moving of them to the cytoplasm where they have some specific functions)

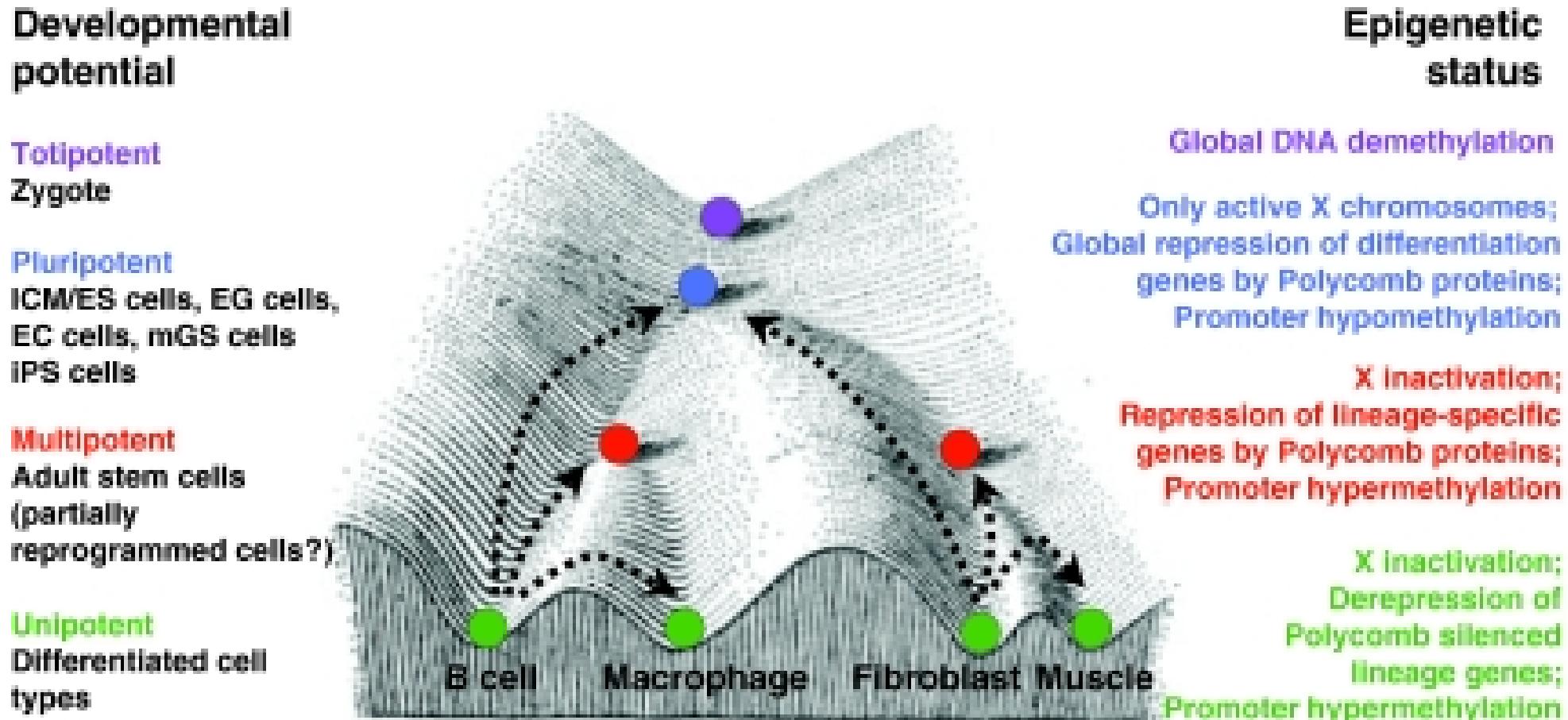


How to get an organism?

When and what kind of genes activation we need?

What is the Gene?

Genes activity – Differentiation – Determination – Development



Next topic

The structure of DNA, topology *etc*
(chapter 4)