



مقدم من فريق أفق الطبي



Genetic 1 History

BY

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GREGOR MENDEL AND THE LAWS OF INHERITANCE

Early Beginnings

The history of genetics in relation to medicine is one of breathtaking discovery from which patients and families already benefit hugely but in today's world success will be measured by continuing progress in the treatment and prevention of disease.

↑
الجراح اليوم يتم قياسه في علية صنع لموت المرض الجيني ولو صار كيف نعالج

Developments in genetics during the twentieth century have been truly spectacular.

مدهشة

In 1900 Mendel's principles were awaiting rediscovery, chromosomes were barely visible, and the science of molecular genetics did not exist.

مندل على قوانينه قبل ١٩٠٠ ولما بسنة ١٩٠٠ بدأوا يدرسون
قوانينه

- كروموسوم غير واضح
- علم الوراثة الجزيئية لم يكن مستكشف

- By contrast, at this time over 14000 single-
- ① gene disorders or traits have been identified,
 - ② chromosomes can be analyzed to a very high level of sophistication, and the draft
 - ③ sequence of the entire human genome has been reported .

له النسخة الوراثية لكن الجينوم الآن أصبحت معروفة

• اندر اساتح الحديثه لكها تدل على اهمية علم الوراثة بل ان الجراحه
الطبيه

This revolution in scientific knowledge and expertise has led to the realization that genetics is an area of major importance in almost every medical discipline.

Recent discoveries impinge not just on rare and esoteric 'small-print' diseases, but also on many of the common acquired disorders of adult life, such as cardiovascular disease, psychiatric illness and cancer.

• علم الوراثة لا يقتصر على الامراض النادره التي تصيب الانسان ولكن يمتد
الى الامراض الشائعه ايضاً

Consequently genetics is now widely accepted as being at the forefront of medical science and has become an important and integral component of the undergraduate medical curriculum.

أصبح علم الوراثة الآن في مقدمة العلوم الطبية لأهميته
في علوم الطب القصيرة

In order to put the exciting development and growth of genetic science into context we start with a brief overview of some of the most notable milestones in the history of medical genetics.

قبل إضافة أي شيء نكتب يجب فهم تاريخ وعمله
درا. ع. ع. ع.

Early Greek philosophers and physicians such as Aristotle and Hippocrates concluded, with typical masculine modesty, that important human characteristics were determined by semen, utilizing menstrual blood as a culture medium and the uterus as an incubator.

في الآباء بقاء من semen هو واد هواد في البوار حرة عبارة عن وسط زراعي
Semen was thought to be produced by the whole body; hence baldheaded fathers would beget baldheaded sons.

وإنه من semen يتم إنتاجه من كل الجسم
والآباء البلى عندهم صلح أولادهم. وكانوا لا يهتمون عنهم

These ideas prevailed until the seventeenth century, when Dutch scientists such as Leeuwenhoek and de Graaf recognized the existence of sperm and ova, thus explaining how the female could also transmit characteristics to her offspring.

اُنْتُوَا فِي عَرَبِ ١٧١٠ بِإِنِّهٖ صِفَاتِ الْأَبْنَادِ قَدَّرَ مِنَ الْأَبَادِ وَالْأُمَمَاتِ سَاحِلًا
وَالْبِتَوَا وَجُودَ الْبُوصِيَّةِ وَالْحَيَوَانِ الْمُنَوِيَّ

Man of Science, Man of God:

Gregor Johann Mendel



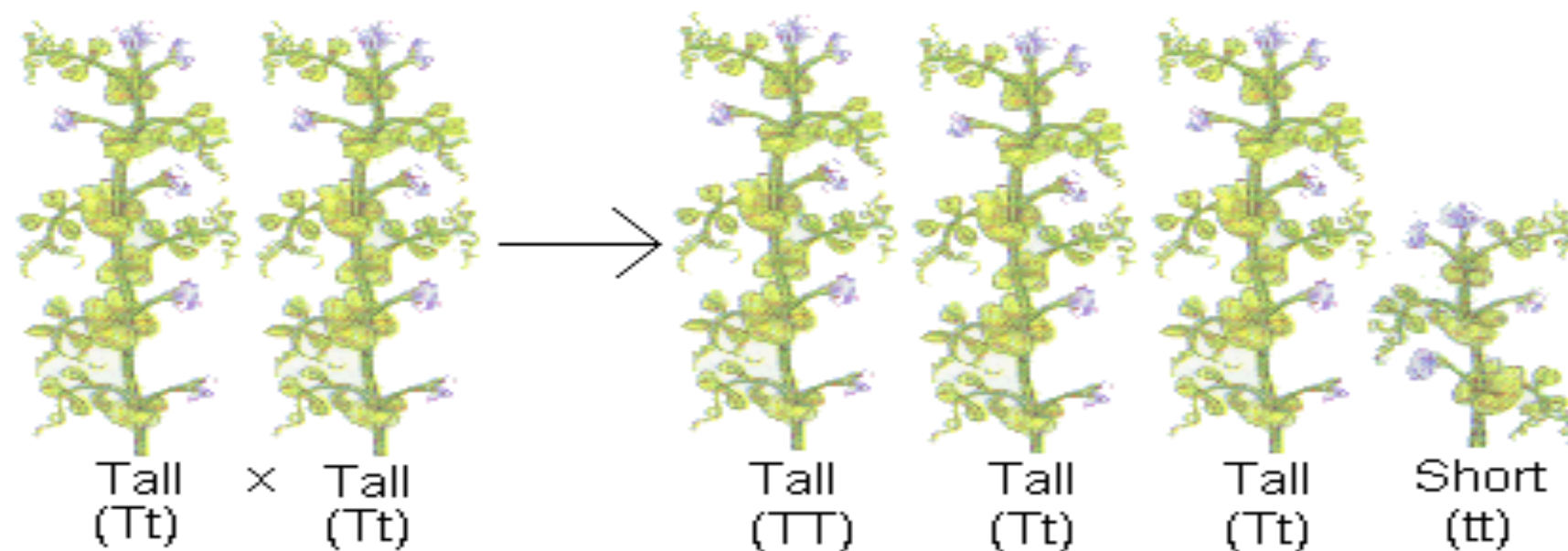
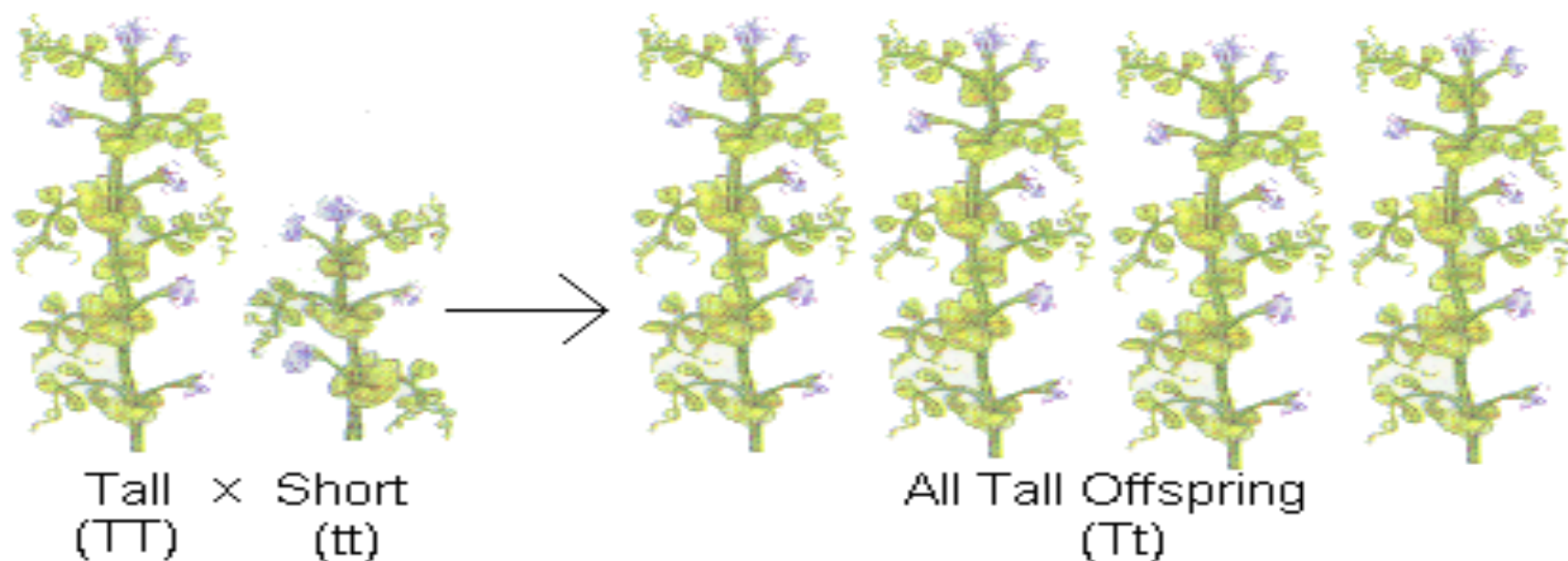
1865

خلال دراسته كان يهتم في صفات متناقضة وكان يجرى تجارب على نبات البازلاء النقية

In his breeding experiments Mendel studied contrasting characters in the garden pea, using for each experiment varieties that differed in only one characteristic.

For example, he noted that when strains that were bred for a feature such as tallness were crossed with plants bred to be short, all the offspring in the first *filial* or F₁ generation were tall. If plants in this F₁ generation were interbred, then this led to both tall and short plants in a ratio of three to one .

لما جرب صنف البازلاء النقية مع صنف البازلاء القصير اكتشف انه الجيل الاول كله كان قصيرا
ولمّا جرب الجيل الاول مع جيل (الجيل الفرعي) طبع معه 3 طمان وواحد قصير



Mendel's proposal was that the plant characteristics being studied were each controlled by a pair of factors, one of which was inherited from each parent.

صفات النبات حتى تظهر بتحكم فيها عاملين، وكل واحد من الأبوين يورث

The pure-bred plants, with two identical genes, used in the initial cross would now be referred to as *homozygous*

الصفة المتجانسة تتلوه نقيية
ex TT, tt

The hybrid F₁ plants, each of which has one gene for tallness and one for shortness, would be referred to as *heterozygous*. The genes responsible for these contrasting characteristics are referred to as *allelomorphs*, or *alleles*.

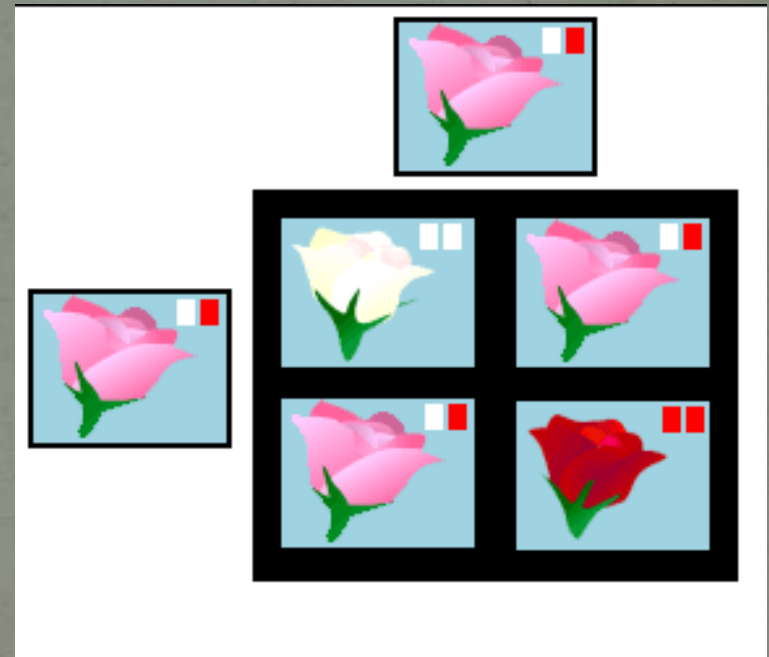
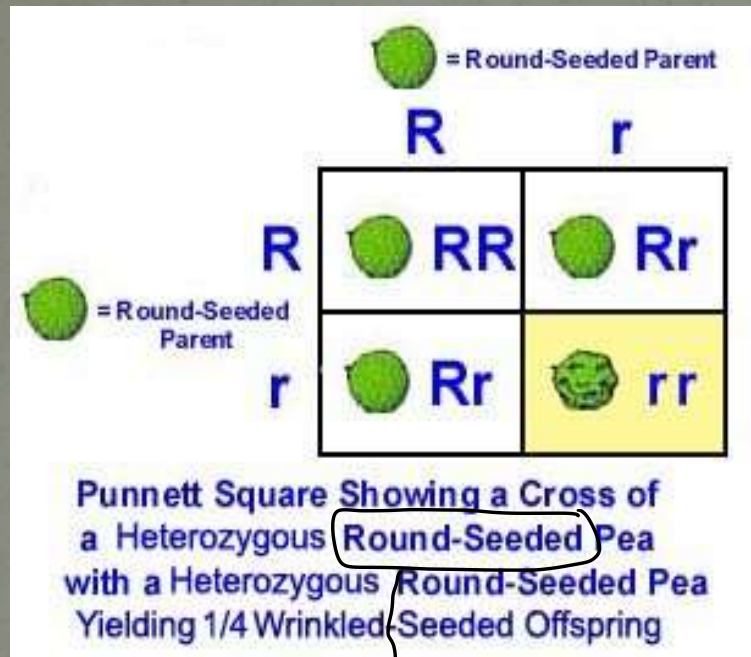
هجين Tt غير متجانس

↑
الكين المتضاد
عن طور الصفات

An alternative method for determining *genotypes* in offspring involves the construction of what is known as a Punnett's square).

↑
علاوة على ذلك، فإن النتائج المتزاوية

PUNNETT'S SQUARE



oishu12121

On the basis of Mendel's plant experiments,
three main principles were established.

①
These are known as the laws of uniformity,
segregation and independent assortment .
② ③

THE LAW OF UNIFORMITY :

كلمة نفسي الشئ

The law of uniformity refers to the fact that when two homozygotes with different alleles are crossed, all the offspring in the F₁ generation are identical and heterozygous.

عند جمع 2 من homozygotes وكله باختلاف الأليل، كل يطول مطابقة مع الآخر
في نفس اللون

In other words, the characteristics do not blend as had been believed previously, and can reappear in later generations .

الصغار لا تخرج وكله هناك صفات سود والآخرى تتدغم في

الجيل الأول وتظهر في الجيل الثاني

THE LAW OF SEGREGATION :

قانون الانقسام

The *law of segregation* refers to the observation that each individual possesses two genes for a particular characteristic, only one of which can be transmitted at any one time.

كل فرد عنه جينين لصفة معينة، لا يمكن نقلهما
خلال وقت طيناً يوحى لها صيت

Rare exceptions to this rule can occur when two allelic genes fail to separate because of chromosome non-disjunction at the first meiotic division.

! في حالة نادرة الجينات ما ينقسم

لا تهاجر في انقسام للانقسام المتساوي لأول، في مثلية (2n)

نقزج الصفا ٢ ٢م باستقلالية

THE LAW OF INDEPENDENT ASSORTMENT:

Refers to the fact that members of different gene pairs segregate to offspring independently of one another.

عن صفة الأول
مستقلة في القوارث
عن صفة آتية

In reality, this is not always true, as genes that are close together on the same chromosome tend to be inherited together, i.e. they are linked.

مستقلا ٢ يكون مستقلة مثلا واحد كسفر وعيون
زهره صان الصفا ٢ خريبة على بعض على نفس الكروموسوم
عياو! لا ٢م نوارهم مع بعض (مرتبطين ببعض)

There are a number of other ways by which the laws of Mendelian inheritance are breached but, overall, they remain foundational to our understanding of the science.

في اختراقها لحدود القوانين
ولكن تبقى قوانين مندل هي الأساس (أساسي)

THE CHROMOSOMAL BASIS OF INHERITANCE

As interest in Mendelian inheritance grew, there was much speculation as to how it actually occurred.

عمر ما اهتموا بتوانين مندل صاروا يفكر في
بنيان صاده في صخر

At that time it was also known that each cell contains a nucleus within which there are several thread-like structures known as *chromosomes*, so called because of their affinity for certain stains

chroma = color, *soma* = body.

ولقد اكد الوقت كانوا
مكتشفين النواة و هي

↓
خضائى الصبغة

سبحه الخيط صوم كروموسوم

In 1903, **Walter Sutton**, an American medical student, and **Theodor Boveri**, a German biologist, independently proposed that chromosomes carry the hereditary factors, or genes.

١٥ سنين قبل منقول لمدى ما عرفنا جفت
فكرنا اننا الكروموسوم هو الذي يحمل الصفات الوراثية

These suggestions were prompted by the realization that the behaviour of chromosomes at cell division could provide an explanation for how genes could segregate.

انفصال الكروموسوم خلال انقسام الخلية
كذلك ففكرنا اننا انما نعرف انقسام الخلية

When the connection between Mendelian inheritance and chromosomes was first made, it was thought that the normal chromosome number in humans was 48; the correct number of 46 was not established until 1956, 3 years after the correct structure of DNA was proposed.

Within a few years it was shown that some disorders in humans could be caused by loss or gain of a whole chromosome as well as an abnormality in a single gene.

صاروا يعتقدوا . ان الامراض التي ينتج عنها
تقصير او زياده في الكروموسومات او بنية
في غير هيكلي في الجينوم

DNA AS THE BASIS OF INHERITANCE

Whilst **James Watson** and **Francis Crick** are justifiably credited with discovering the structure of DNA in 1953, they were only attracted to working on it because its key role as the genetic material was established in the 1940.

Formerly many believed that hereditary characteristics were transmitted by proteins.

كانوا يعتقدوا ان الوراثة تنتقل ببروتينات

The genius of Watson and Crick, at Cambridge, was to hit on a structure for DNA that would explain the very fact of biological reproduction, and their elegant double helix has stood the test of time. Crucial to their discovery was the X-ray crystallography work of Maurice Wilkins and Rosalind Franklin at King's College, London .

↓
کیمیاء،
جینز DNA اور لیپس

السَّابِقُ ثمَّ اتَّعَافَ السَّيْرُ وَجِئَتْهُ
لِغَاظِ الْغُضْبَةِ فِي الْبُرُوسَةِ
السَّابِقِ إِلَى سَابِقِ سَابِقِ

The relationship between the sequence of bases in DNA and the sequence of amino acids in protein, i.e. the genetic code, was unravelled in some very elegant biochemical experiments in the 1960s.

Thus it became possible to predict the base change in DNA that led to the amino acid change in the protein.

هَذَا يَتَوَقَّعُ مَسَلَّةً فِي DNA
وَيُؤَدِّي هَذَا كَوْنُ الْمَرْفُوعِ
إِلَى مَسَلَّةٍ فِي الْغَاظِ الْغُضْبَةِ

However, direct confirmation of that prediction had to wait until DNA sequencing methods became available after the advent of recombinant DNA techniques. أي توقع ذي هذا ما يمكنه يتم استخدام تقنيات الـ DNA المتطورة

Interestingly, however, the first genetic trait to be characterized at the molecular level had already been identified in 1957 by laborious sequencing of the purified proteins.

This was **sickle-cell anemia**, in which the mutation affects the amino-acid sequence of the blood protein hemoglobin. أحد هذه تسمى اكتساف

أثر على الأحمضات الأمينية في الدم و كسر البروتينات

Quiz **THE FRUIT FLY**



Before returning to historical developments in human genetics, it is worth a brief diversion to consider the merits of this unlikely creature that has proved to be of great value in genetic research. The fruit fly , *Drosophila* possesses several distinct advantages for the study of genetics.

الفنا ۲ الوراثة ۱ الوراثة ۱
کفر جوتا ۲ الوراثة ۱
علم الوراثة

THESE ARE AS FOLLOWS :

- It can be bred easily in a laboratory .
تكاثر بسهولة بالمختبر
- It reproduces rapidly and prolifically at a rate of 20-25 generations per annum .
تكاثر سريع
- It has a number of easily recognized characteristics, such as curly wings^① and a yellow body^②, which show Mendelian inheritance^③ .
البشر كل 30 سنة فقط

- *Drosophila melanogaster*, the species most frequently studied, has only four pairs of chromosomes, each of which has a distinct appearance so that they can be identified easily.

۱۶۴ و ۴ کروموسومات مختلفه
در اصطلاح

- The chromosomes in the salivary glands of *Drosophila* larvae are among the largest known in nature, being at least 100 times bigger than those in other body cells.

کروموسومها از نظر اندازه بزرگتر ۱۰۰ مرتبه

In view of these unique properties, fruit flies were used extensively in early breeding experiments.

Today their study is still proving of great value in fields such as developmental biology, where knowledge of gene homology throughout the animal kingdom has enabled scientists to identify families of genes that are very important in human embryogenesis .



Multiple-Choice Questions (MCQs) on Medical Genetics

1. 1. Which concept was first theorized by early Greek philosophers like Aristotle regarding heredity?

- A. Mendelian inheritance
- B. Genetic traits from both parents
- ☒ C. Semen determines human characteristics
- D. Chromosomes as carriers of traits

2. 2. What did Mendel's breeding experiments focus on?

- A. Genetic mutations
- ☒ B. Contrasting characters in pea plants
- C. Reproduction in fruit flies
- D. Chromosome abnormalities

3. 3. What term refers to an organism with identical genes for a trait?

- A. Heterozygous
- ☒ B. Homozygous
- C. Hybrid
- D. Dominant

4. 4. Which of the following is a principle established by Mendel's experiments?

- A. Chromosomal crossover
- ☒ B. Law of segregation
- C. Genetic drift
- D. Law of mutation

5. 5. Who independently proposed that chromosomes carry hereditary factors?

- A. Watson and Crick
- B. Mendel
- ☒ C. Sutton and Boveri
- D. Rosalind Franklin

6. 6. The structure of DNA was discovered in:

- A. 1865
- B. 1940
- ☒ C. 1953
- D. 1960

7. 7. What is the correct number of chromosomes in humans?

- ☒ A. 46
- B. 48
- C. 23
- D. 50

8. 8. What technique confirmed Watson and Crick's DNA model?

- A. Punnett square analysis
- ☒ B. X-ray crystallography
- C. Recombinant DNA sequencing
- D. Protein structure modeling

9. 9. What does the genetic code specify?

- A. Chromosomal arrangement
- ☒ B. Amino acid sequences in proteins
- C. Gene silencing
- D. RNA synthesis

10. 10. What was the first genetic disorder characterized at the molecular level?

- A. Cystic fibrosis
- ☒ B. Sickle-cell anemia
- C. Down syndrome
- D. Hemophilia

11. 11. Why is *Drosophila melanogaster* used in genetic studies?

- ☒ A. Large chromosomes in salivary glands
- B. High resistance to mutations
- C. Lack of Mendelian inheritance
- D. Short lifespan only

12. 12. How many chromosome pairs does *Drosophila melanogaster* have?

- A. 2
- B. 3
- ☒ C. 4
- D. 6

13. 13. What makes *Drosophila* chromosomes unique?

- A. Similarity to human chromosomes
- ☒ B. 100x larger size in salivary glands
- C. Rapid mutation rates
- D. Multicellular structure

14. 14. What happens during chromosome non-disjunction?

- A. Genes replicate incorrectly
- ☒ B. Chromosomes fail to separate during meiosis
- C. DNA fails to code for proteins
- D. Traits blend during inheritance

15. 15. What type of inheritance occurs with linked genes?

- A. Independent assortment
- B. Mutations
- ☒ C. Chromosomal linkage
- D. Polygenic traits

16. 16. What does 'heterozygous' mean in Mendelian genetics?

- A. Identical genes for a characteristic
- ☒ B. Different genes for a characteristic
- C. Absence of a dominant gene
- D. Presence of only one allele

17. 17. What does 'allelomorph' refer to in genetics?

- A. A dominant trait
- B. A type of chromosome
- ☒ C. Alternative forms of a gene (alleles)

D. A mutant gene

18. 18. The process of constructing a Punnett square helps determine:

A. DNA mutations

☒ B. Genotypes of offspring

C. Chromosomal disorders

D. Genetic diseases

19. 19. Which discipline studies inherited traits affecting common adult disorders like cancer?

A. Molecular biology

☒ B. Medical genetics

C. Biochemistry

D. Embryology

20. 20. Which principle explains how genes are inherited independently?

A. Genetic linkage

☒ B. Law of independent assortment

C. Chromosome non-disjunction

D. Genetic imprinting

Answers:

1. C

2. B

3. B

4. B

5. C

6. C

7. A

8. B

9. B

10. B

11. A

12. C

13. B

14. B

15. C

16. B

17. C

18. B

19. B

20. B

GENITICS 2

The Origin & Impacts Of Medical Genitrics

By: Dr. Sawsan Shurrab



THE ORIGINS OF MEDICAL GENETICS

- John Dalton of atomic theory fame, observed that some conditions, notably color blindness and hemophilia, show what is now referred to as sex- or X-linked inheritance, and to this day color blindness is still sometimes referred to as daltonism.

- Inevitably, these founders of human and medical genetics could only speculate as to the nature of the mechanisms underlying their observations.

هـ خطوا ملاحظاً حـرّيةً
وكلوا نفكروا بآلية هـو

- In 1900 Mendel's work resurfaced.
- His papers were quoted almost simultaneously by three European botanists - De Vries (Holland), Correns (Germany) and Von Tschermak (Austria) - and this marked the real beginning of medical genetics, providing an enormous impetus for the study of inherited disease .

كان علمهم بداية في علم الوراثة الطبية
وساعد في دراسة الأمراض الوراثية

- During the course of the twentieth century it gradually became clear that hereditary factors are implicated in many conditions and that different genetic mechanisms are involved.

أخذ عوامل جينية وهرثية

- Traditionally, hereditary conditions have been considered under the headings of *single gene*, *chromosomal* and *multifactorial*. Increasingly, it is becoming clear that the interplay of different genes (polygenic inheritance) is important in disease and a further category - *acquired somatic genetic disease* - should also be included.

جيبه او عامل فيه مشكله

مع ذلك مشكله هارت والله العراة الها دقد
من حذن مشكله في اكر من جيبه بيزم تناسه

its number
for deletion

SINGLE-GENE DISORDERS

- Credit for the first recognition of a single gene trait is shared by William Bateson and Archibald Garrod, who together proposed that alkaptonuria was a rare recessive disorder. هذا الهم موروثا ينتقل عبر جزيء
عامل متنحي
- In this relatively benign condition urine turns dark on standing or on exposure to alkali because of an inability on the part of the patient to metabolize homogentisic acid . موروثا خفيف
البول يصير قاعدي لونه يتغير في مشيئة عند التعرض
وما يكون مقدار انزيم ناقصا
بصير لونه اسود

يَعْمَدُ عَلَى تَفَاعُلِ وَتَلَعُّبِ الْأَنْزِعِيَا ۚ

- Realizing that this was an inherited disorder involving a chemical process, Garrod ^{مُسْتَلَقٌ لَدَى تَقْلَابِ الْوَحْدَانِي} coined the term inborn error of metabolism. Several hundred such disorders have now been identified, giving rise to the field of study known as biochemical genetics.

أَنَّ الْإِنْسَانَ لَقَدْ مَرَّ بِدُرُوسٍ عَجَابٍ طَائِفَةٍ

By 1966 almost 1500 single-gene disorders or traits had been identified, prompting the publication by an American physician, Victor McKusick of a catalog of all known single-gene conditions ..



- By late 2003 OMIM

(Online Mendelian Inheritance of Man) contained 11031 established gene loci and 8784 gene map loci (fewer than the established gene loci) because many genes are associated with more than one phenotype.

موقع بطور کی اد
mutations + clinical symptoms
الہی تم ایکنسٹا

العدر اقل ڈیجینی
اکثر من جیم اسٹرل
م بنفس الوادہ

مشاكل في الكروموسوم منه الذي يتولى على عدد كبير من الجينات

CHROMOSOME ABNORMALITIES

- Improved techniques for studying chromosomes led to the demonstration in 1959 that the presence of an additional number 21 chromosome results in Down syndrome.
Other similar discoveries followed rapidly.
- The identification of chromosome abnormalities was further aided by the development of banding techniques.

يصنف الكروموسوم وفي مناطق تظهر غامقة

ومناطق غامقة منسجمة Banding
فأرى منسجمة به منسجمة له منسجمة له منسجمة له منسجمة له

- These enabled reliable identification of individual chromosomes and helped confirm that loss or gain of even a very small segment of a chromosome can have major effects.

هذه الدراسات هي
بأنه أي زيادة أو نقصان في أي قطعة
بالتكرار أو النقصان

- Most recently it has been shown that several rare conditions featuring learning difficulties and abnormal physical features are due to loss of such a tiny amount of chromosome material that no abnormality can be detected using even the most high-powered light microscope.
- These conditions are referred to as **microdeletion syndrome**.



حذف جزء بسيط من

الكروموسوم

١- تلف عقلي
٢- مشاكل فيزيائية (جسدية)

- They are diagnosed using a technique known as **FISH** *fluorescent in-situ hybridization* which combines conventional chromosome analysis *cytogenetics* with much newer DNA diagnostic technology *molecular genetics*.

علم دراهه ال DNA

علم دراهه
الکروسوسوم

MULTIFACTORIAL DISORDERS

دراثمیک

- This model of quantitative inheritance is now widely accepted and has been adapted to explain the pattern of inheritance observed for many relatively common conditions.

صالح! نه كثير امراضه. بغيره من الامراض

- These include congenital malformations such as cleft lip and palate, and late-onset conditions such as hypertension, diabetes mellitus and Alzheimer disease.

له هذه الامراض. بسببها عوامل وراثية وبيئية مع بعض

- The prevailing view is that genes at several loci interact to generate a susceptibility to the effects of adverse environmental trigger factors.

أكثر من جين يتحدوا بعض وكفها الشخص أكثر عرضة لأنه يتأثر بالعوامل البيئية
حتى يذنبه اعرفها

- Recent research has confirmed that many genes are involved in most of these adult-onset disorders, although progress in identifying specific susceptibility loci has been disappointingly slow.

مشدني مرض السكري لا يخلو وجبوا وأنه لو كان في جين معين عند الإنسان
يعلمه من أكثر حتى ينصاب بالمرض ولعله أنه نسبة معينة ، أما ما لهذه الجين
بأنه أقل عرضة

- It has also emerged that in some conditions, such as type I diabetes mellitus, different genes can exert major or minor effects in determining susceptibility .

هذا الجين ليس المسؤول الوحيد عن حدوث المرض
ولكنه عند تواجده الظروف البيئية مثلًا السمنة
نرى تزايد نسبة حدوث المرض

ACQUIRED SOMATIC GENETIC DISEASE

- Not all genetic errors are present from conception. Many billions of cell divisions (mitoses) occur in the course of an average human lifetime.
- During each *mitosis* there is an opportunity for both single-gene mutations to occur, because of DNA copy errors, and for numerical chromosome abnormalities to arise as a result of errors in chromosome separation.

خلل في الـ DNA
أو الكروموسوم

- Accumulating somatic mutations and chromosome abnormalities are now known to play a major role in causing cancer.
- They probably also explain the rising incidence with age of many other serious illnesses, as well as the aging process itself.
- It is, therefore, necessary to appreciate that not all disease with a genetic basis is hereditary.

مصابين بالسرطان في وقت لاحق من الحياة

لأن ما تقدمه الوراثة للإنسان أكثر عدداً
من العوامل البيئية

بعض مريضين مع الأساس الجيني
عندما يولد أولادهم لديهم

DEFINITIONS

معدل حدوث

Incidence

معدل تدرّس في صلات. حدوث

- *Incidence* refers to the rate at which new cases occur.
- Thus, if the birth incidence of a particular condition equals 1 in 1000, then on average 1 in every 1000 newborn infants is affected .

معدل الانتشار

Prevalence

↓
number of cases

↓
number of all newborn infants

- This refers to the proportion of a population affected at any one time.
نسبة السكان المصابين في منطقة خلال وقت معين
- The prevalence of a genetic disease will usually be less than its birth incidence, either because life expectancy is reduced or because the condition shows a delayed age of onset .

لأنه في منجم بلونوا لا خوف
وفي لساخو عندهم اطرخ
على مكر متأخر

عدد الحالات
عدد السكان

incidence

الاسم الغير علمي لا



Frequency

- Is a general term that lacks scientific specificity, although the word is often taken as being synonymous with incidence when calculating gene frequencies.

منذ الولادة

Congenital

- *Congenital* means that a condition is present at birth. Thus, cleft palate represents an example of a congenital malformation. Not all genetic disorders are congenital in terms of age of onset (for example, Huntington disease), nor are all congenital abnormalities are genetic in origin.

ليس كل genetic disorder عبارة عن congenital

وكل congenital عبارة عن genetic

THE IMPACT OF GENETIC DISEASE

- For some parameters, such as perinatal mortality, the actual numbers of cases with exclusively genetic causes have probably remained constant but their *relative* contribution to overall figures has increased as other causes, such as infection, have declined.
- During the twentieth century improvements in all areas of medicine, most notably public health and therapeutics, resulted in changing patterns of disease, with increasing recognition of the role of genetic factors in causing illness at all ages.

عدد الحالات التي سببها جين ثابته

ولكن الأسباب الأخرى التي لها علاقة زادت، وهذا يفسر كيف نستطيع عليها

الصحة العامة أدركت وبشكل واضح أن الوراثة تعتبر سبب
مهم في حدوث الموت والعجز

- For other conditions, such as the chronic diseases of adult life, the overall contribution of genetics has almost certainly increased as greater life expectancy has provided more opportunity for adverse genetic and environmental interaction to manifest itself, for example in coronary heart disease and diabetes .

حتى في الأمراض التي يتبعي للبار السن الجينات الهادئة
نتيجة لتحسن جودة الحياة بالتالي العمر يزيد للاشخاص ضيق أكثر عرضة
للعوامل الوراثية والبيئية تأتهم يتلوا ذلك في الجينات وعبر عرضة لهم معية

Spontaneous miscarriages :

- Chromosome abnormality is present in 40-50% of all recognized first-trimester pregnancy loss.

دجوا ، انه الاجهاض في اول ٣ شهور حمل سببه يعود لـ ٤٠-٥٠٪ وجوا مسئلة بالكرموسوم

- This figure would be much higher if unrecognized pregnancies could also be included and it is likely that a significant proportion of miscarriages with normal chromosomes do in fact have catastrophic submicroscopic genetic errors.

هذه النسبة غير دقيقة لان في نساء الجوهوا بروس مايرفوا ، انه في
مسئلة بالكرموسوم ، وانه البعض يلعبه غير دقيقة ولودققوا اكثر
يلقوا انه في لغوا واصباب اخرى ادى الى حدوثها عند عي الكرموسوم

Newborn infants

- Of all neonates, 2-3% have at least one major congenital abnormality, at least 50% of which are caused exclusively or partially by genetic factors .

من كل ١٥٥ طفل ينولد في 2-3 طفل عندهم مشاكل جينية وراثية كبيرة
ونصفهم بسبب أسباب وراثية

Childhood

Genetic disorders account for 50% of all childhood blindness, 50% of all childhood deafness and 50% of all cases of severe learning difficulty.

In developed countries genetic disorders and congenital malformations together also account for 30% of all childhood hospital admissions and 40-50% of all childhood deaths.

↓
الأطفال التي مبرهنوا
و بدخلوا الى مستشفى
هنا بسبب إصابات عارضة

Adult life

١٪ نزاعون الوراثي يولدون مع مشكلة جينية مزمنة

- Approximately 1% of all malignancy is caused by single-gene inheritance, and between 5% and 10% of common cancers such as breast, colon and ovary have a strong hereditary component.

١٪ نزاعون الوراثي يولدون مع مشكلة جينية مزمنة
٥-١٠٪ عراري

- By the age of 25, 5% of the population will have a disorder in which genetic factors play an important role.

- Taking into account the genetic contribution to cancer and cardiovascular diseases, such as coronary artery occlusion and hypertension, it has been estimated that over 50% of the older adult population in developed countries will have a genetically determined medical problem.

MAJOR NEW DEVELOPMENTS

- The study of genetics and its role in causing human disease is now widely acknowledged as being among the most exciting and influential areas of medical research.
- Since 1962 when Francis Crick, James Watson and Maurice Wilkins gained acclaim for their elucidation of the structure of DNA, the Nobel Prize for Medicine and/or Physiology has been won on 18 occasions by scientists working in human and molecular genetics or related fields .

1962: Nobel Prize in Physiology and Medicine

Watson, J.D. and F.H. Crick, "Molecular Structure of Nucleic Acids: A Structure for Deoxynucleic Acids". *Nature* 171 (1953), p. 738.



James D.
Watson



Francis H.
Crick



Maurice H. F.
Wilkins



What about?
Rosalind Franklin



ما كانوا يعرفون انهم جينت! ولا حتى
double helix

- With DNA technology rapidly progressing, a group of visionary scientists in the USA persuaded Congress in 1988 to fund a coordinated international program to sequence the entire human genome.
- The program would run from 1990 to 2005 and 3 billion US dollars were initially allocated to the project, including 5% allocated to the study of the ethical and social implications of the new knowledge.

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

- The draft DNA sequence of 3 billion base pairs was successfully completed in 2000.
- Prior to the closing stages of the project it was believed that there might be approximately 100000 coding genes that provide the blueprint for human life. 
- It has come as a surprise to many that the number is much lower, with current estimates at around 30000 .

بعض جينات جينوم الانسان اكثر من وظيفة

- However, many genes have the capacity to perform multiple functions, which in some cases is challenging traditional concepts of disease classification.
- The immediate benefits of the sequence data are being realized in research that is leading to better diagnosis and counseling for families with a genetic disease .

معرفة الجينوم كامل للإنسان لا يساهم في تشخيص
في حال بومهن

- In the longer term an improved understanding of how genes are expressed will hopefully lead to the development of new strategies for the prevention and treatment of both single-gene and polygenic disorders. *طاعاً منجواً او mutation هاءه اقدار يهنا نه يهنا الاستلاء*

- Rapid DNA sequencing technologies currently under development will in due course greatly extend the range and ease of genetic testing, though the application has important ethical and social implications .

*في عالمنا ترغص نحل ال genom
ولم حاليًا اذ جزء تطور هاءه نحل بوقت اقصير*

GENE THERAPY

- Most genetic disease is resistant to conventional treatment so that the prospect of successfully modifying the genetic code in a patient's cells is extremely attractive. Despite major investment and extensive research success in humans has so far been limited to a few very rare immunological disorders .

الأمراض الجينية صعب معالجتها بالأساليب العادية لذلك
تفكير في كود الجين الذي عليه سلسلة راع على مشاكل جينية كثيرة ونحو الام بياها انزلها عليه

٣- كيف نأمن الفيروس الذي يدخل الجسم ما يستفز الجهاز المناعي

- For more common conditions, such as cystic fibrosis, major problems have been encountered, such as targeting the correct cell populations, overcoming the body's natural defense barriers and identifying suitably non-immunogenic vectors.
①
②
③

١- كيف نوصّلنا الخلايا معينة التي فيها المرض
٢- ما نأمن في جسم الإنسان فيروسات حتى تدخل الجسم ولا يحفز الجهاز المناعي

- There is universal optimism that in the short-to-medium term the prospects for successful gene therapy are good.

THE INTERNET

- The availability of information in genetics has been greatly enhanced by the development of several excellent online databases. $OMIM : ex$
- These are updated regularly and provide instant access to a vast amount of contemporary information.
- For the basic scientist facilities such as the Genome Database and GenBank enable rapid determination of whether a particular gene has been cloned, together with details of its sequence, location and pattern of expression.

x-linked / صفتي / سائد

له كيفيه نقل الجين

- For the clinician OMIM offers a full account of the important genetic aspects of all Mendelian disorders, together with pertinent clinical details and extensive references.
- It is clear that only electronic technology can hope to match the explosive pace of developments in all areas of genetic research .



GENITICS 3

The Cell & The Hereditary Material

By

Dr. Sawsan Salem Shurrab

- ◉ The hereditary material is present in the nucleus of the cell, while protein synthesis takes place in the cytoplasm. What is the chain of events that leads from the gene to the final product.

المادة الوراثية توجد في النواة
ويتم تصنيع البروتين في السيتوبلازم

- To answer ,we should know basic cellular biology outlining the structure of DNA, the process of DNA replication, the types of DNA sequences, gene structure, the genetic code, the processes of transcription and translation.

THE CELL

- ◉ Within each cell of the body, visible with the light microscope, is the cytoplasm and a darkly staining body, the nucleus, the latter containing the hereditary material in the form of chromosomes.

تحتوي الخلية على مادة عريضة على شكل كروموسوم

- ◉ The phospholipid bilayer of the plasma membrane protects the interior of the cell but remains selectively permeable and has integral proteins involved in recognition and signaling between cells.

● The nucleus has a darkly staining area, the **nucleolus**. النوية

● The nucleus is surrounded by a membrane, the *nuclear envelope* , which separates it from the cytoplasm but still allows communication through nuclear pores .

في ثغوب في الغشاء الذي يحد النواة حتى تسمح
للنواة بالتواصل مع مسافات السيتوبلازم

- The cytoplasm contains the cytosol, which is semifluid in consistency containing both soluble elements and cytoskeletal structural elements.
- In addition, in the cytoplasm there is a complex arrangement of very fine, highly convoluted interconnecting channels, the endoplasmic reticulum.
→ smooth
→ rough
- The endoplasmic reticulum, in association with the ribosomes, is involved in the biosynthesis of proteins and lipids.

الخلايا ← مسؤولة عن تصنيع البروتين والدهون

- ◉ the **Golgi apparatus**, which is responsible for the secretion of cellular products.

أي بروتيين يتم تصنيعه بداخل الخلية ، جهاز جولجي يجهده على تقديرات

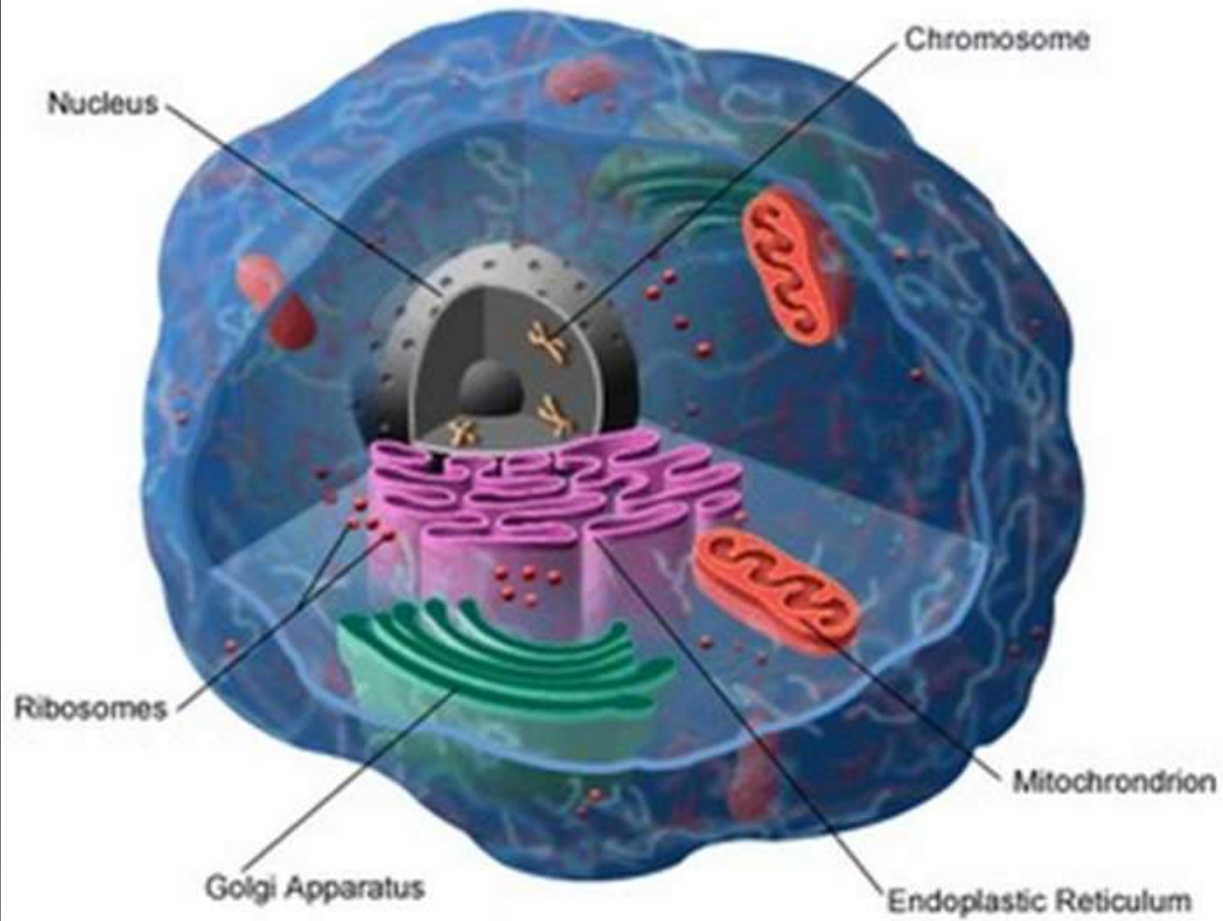
- ◉ The **mitochondria** , which are involved in energy production and metabolic pathways through the oxidative phosphorylation .

→ organelle

- ◉ **lysozomes** , and **peroxisomes** both of which are involved in the degradation and disposal of cellular waste material and toxic molecule.

visceral من جهاز جولجي

Anatomy of a Cell



DNA: THE HEREDITARY MATERIAL

COMPOSITION

- Nucleic acid is composed of a long polymer of individual molecules called nucleotides. Each nucleotide is composed of a nitrogenous base,^①
^② a sugar molecule and a phosphate molecule.^③

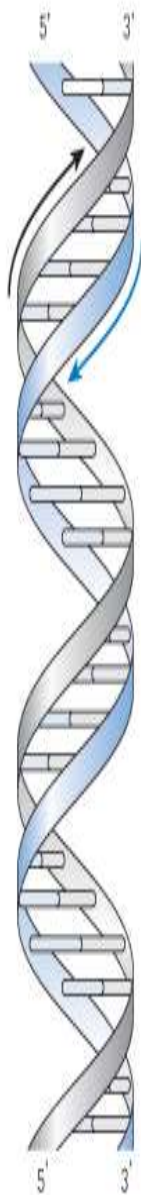
- The nitrogenous bases fall into two types, purines and pyrimidines.

- The purines include adenine and guanine; the pyrimidines include cytosine, thymine and uracil.
(Ag)
(UTC)
c T

↓
RNA only

Purine adenine, guanine

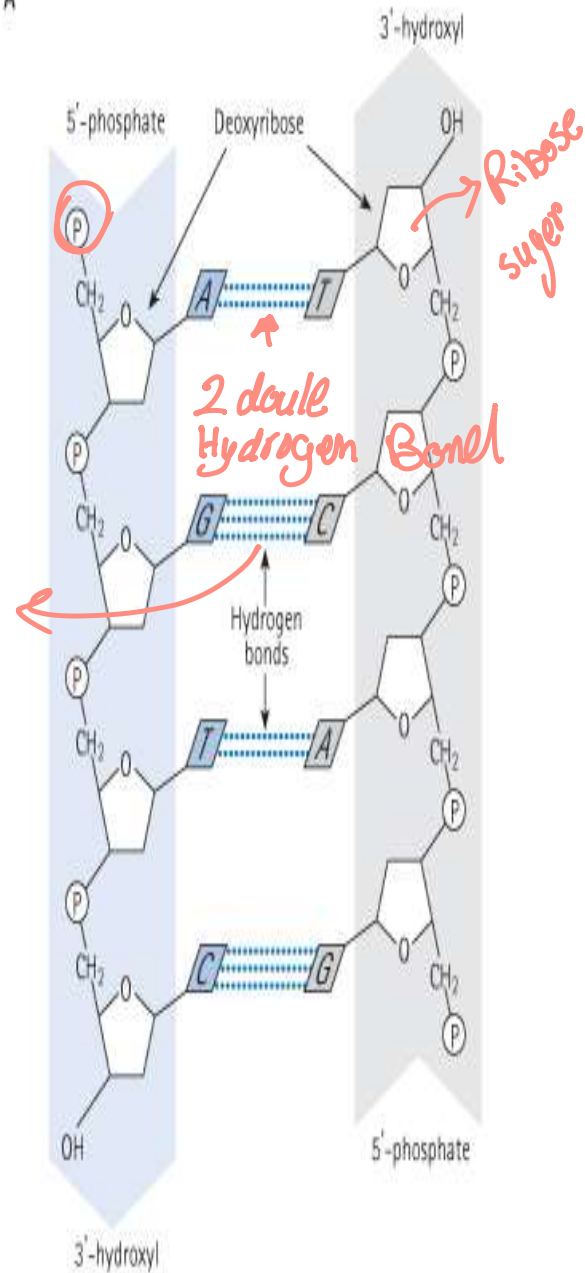
B



A

Phosphate group

$C \equiv G$
↑
triple Bond



- ◉ RNA is present in the cytoplasm and in particularly high concentrations in the nucleolus of the nucleus.
- ◉ DNA, on the other hand, is found mainly in the chromosomes .

STRUCTURE

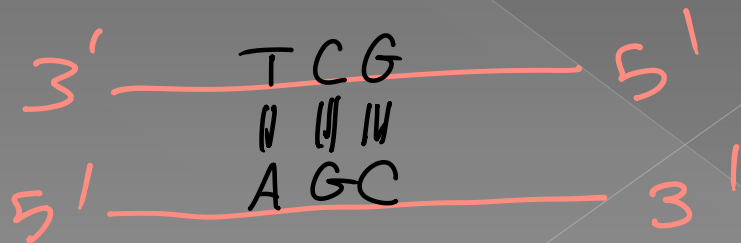
- For genes to be composed of DNA it is necessary that the latter should have a structure sufficiently versatile to account for the great variety of different genes and yet, at the same time, be able to reproduce itself in such a manner that an identical replica is formed at each cell division.

یعنی مرکب از DNA و پروتین بوده و این ماده قادر
بر تغییرات بی‌شمار است و این تغییرات بسیار
بزرگ است و این تغییرات در هر سلول یکسان است

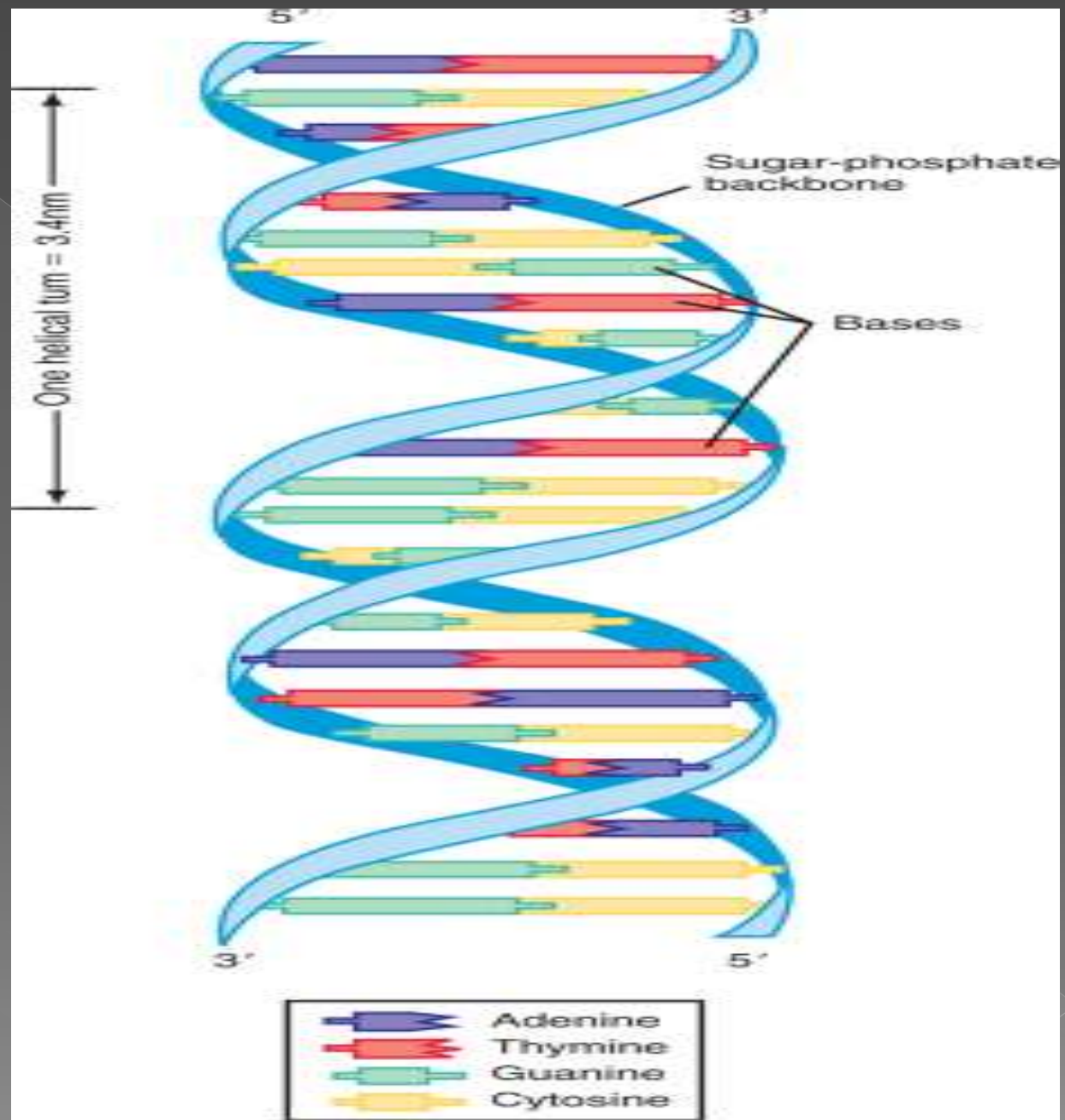
- ◉ DNA molecule is composed of two chains of nucleotides arranged in a double helix.
- ◉ The backbone of each chain is formed by phosphodiester bonds between the 3' and 5' carbons of adjacent sugars,
- ◉ The two chains being held together by hydrogen bonds between the nitrogenous bases which point in towards the centre of the helix.
- ◉ Each DNA chain has a polarity determined by the orientation of the sugar-phosphate backbone.

- The chain end terminated by the 5' carbon atom of the sugar molecule is referred to as the 5' end, and the end terminated by the 3' carbon atom is called the 3' end.
- In the DNA duplex the 5' end of one strand is opposite the 3' end of the other, i.e. they have opposite orientations and are said to be antiparallel.

مضاد التوازي



- ◉ The arrangement of the bases in the DNA molecule is not random: a purine in one chain always pairs with a pyrimidine in the other chain, with specific pairing of the base pairs:
- ◉ Guanine in one chain always pairs with cytosine in the other chain and adenine always pairs with thymine, i.e. this base pairing forms complementary strands.



REPLICATION

- The process of *DNA replication* provides an answer to the question of how genetic information is transmitted from one generation to the next.

لماذا الخلية تحتفظ بنفس
الخطاب بعد ما صار في انقسام وتضاعف

①

- During nuclear division the two strands of the DNA double helix separate through the action of enzyme DNA helicase,

- Each DNA strand directing the synthesis of a complementary DNA strand through specific base pairing, resulting in two daughter DNA duplexes that are identical to the original parent molecule.

في كل انقسام راح ينتج [2] من السلاسل مطابقين للأب (2 من أمي و 2 من أبي)

- In this way, when cells divide, the genetic information is conserved and transmitted unchanged to each daughter cell.
- The process of DNA replication is termed semiconservative, as only one strand of each resultant daughter molecule is newly synthesized.

لا نقول عنه إنه conservative لأنه لو هيك المفروض ال Parent strand فيه زي ما هو بيكون تقيس وتا مفروض يرجع مرة ثانية يتحدوا ال strands 2 وبنه الي صار وبنه مت 2 daughter strands واحد قديم والآخر جديده

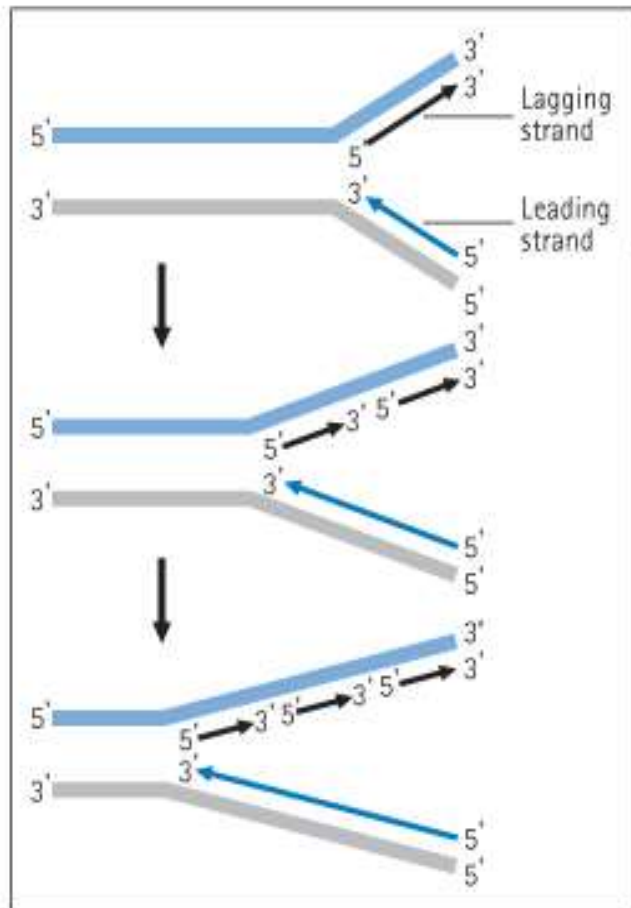
- DNA replication, through the action of the enzyme DNA polymerase, takes place at multiple points known as origins of replication, forming bifurcated Y-shaped structures known as replication forks.

في ال form replication ياح تبفتح جميع ال ال ال مسؤولة عن عمل ال

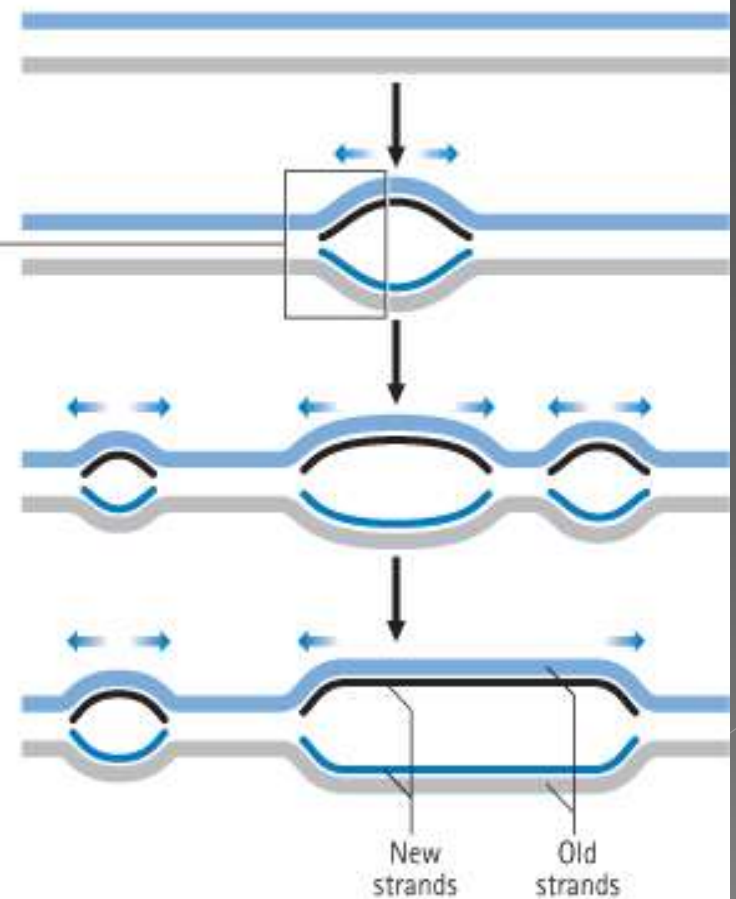
- The synthesis of both complementary antiparallel DNA strands occurs in the 5' to 3' direction. One strand, known as the *leading strand*, is synthesized as a continuous process.

ال ال Polymerase سيقراً ال strand 5' → 3' حتى يفتح ال ال ال Polymerase ال ال ال ال

A



B



يتم تصنيعها على شكل مقاطع

- The other strand, known as the lagging strand, is synthesized in pieces called Okazaki fragments^{أقسام القطع}, which are then joined together as a continuous strand by the enzyme DNA ligase. (3)

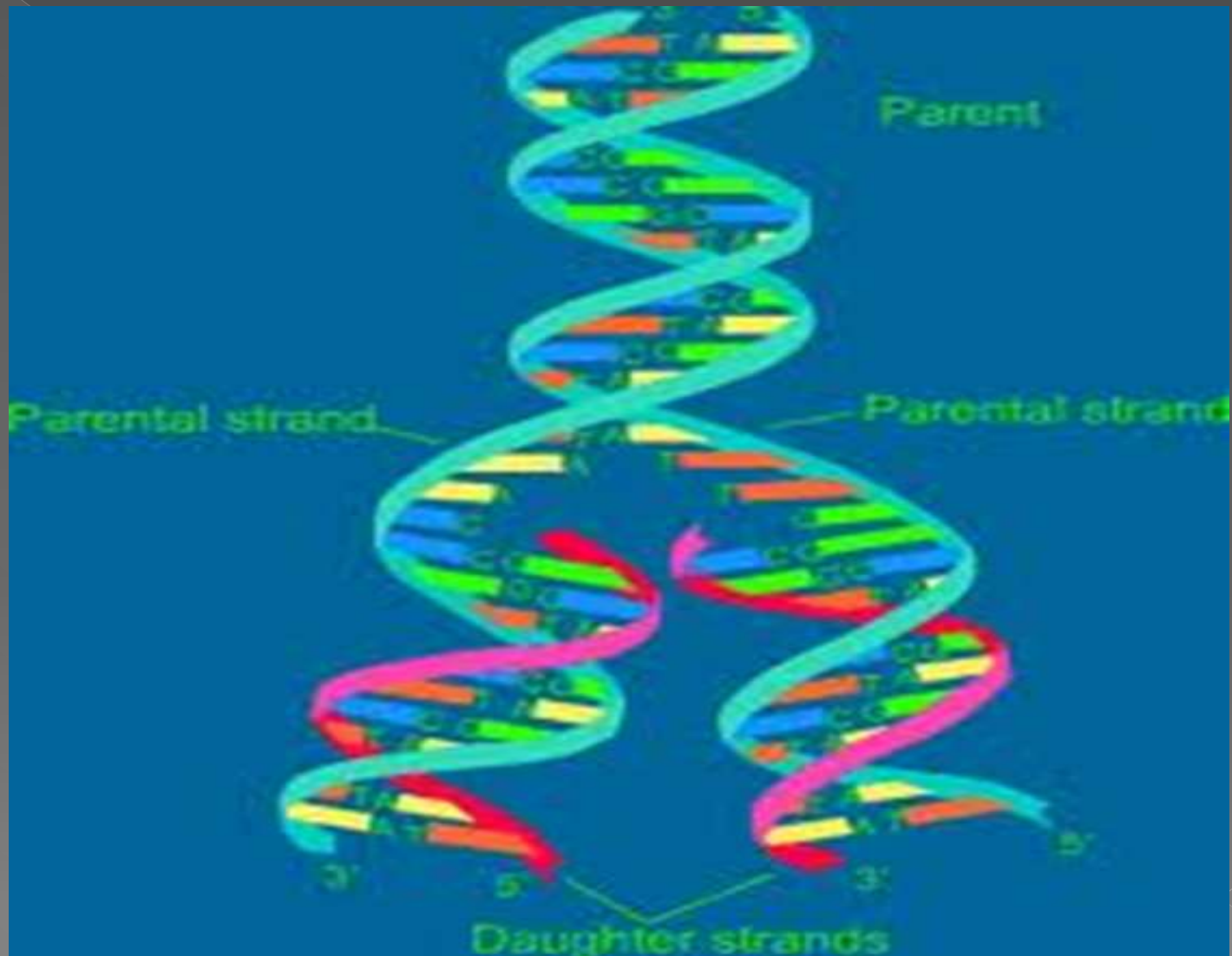
- ◉ DNA replication progresses in both directions from these points of origin, forming bubble-shaped structures, or replication bubbles.

سنتبع الاتجاهين

- ◉ DNA replication in individual replication units takes place at different times in the S-phase of the cell cycle.

مرحلة تضاعف الـ DNA

- ◉ Adjacent replication units fuse until all the DNA is copied, forming two complete identical daughter molecules.



CHROMOSOME STRUCTURE

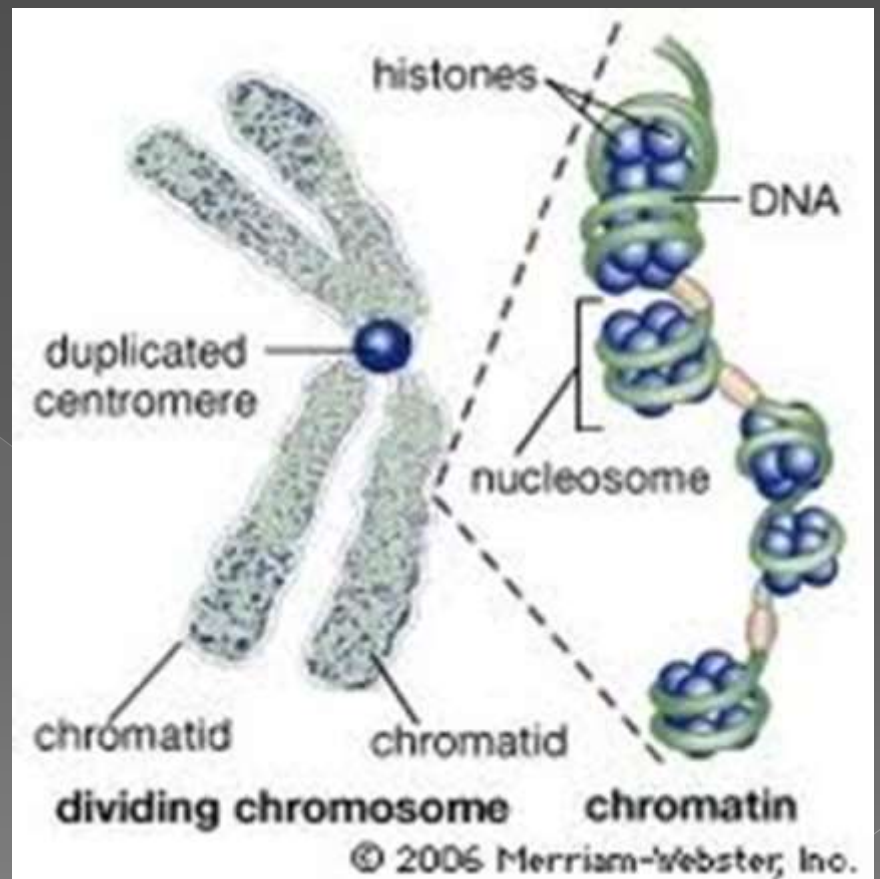
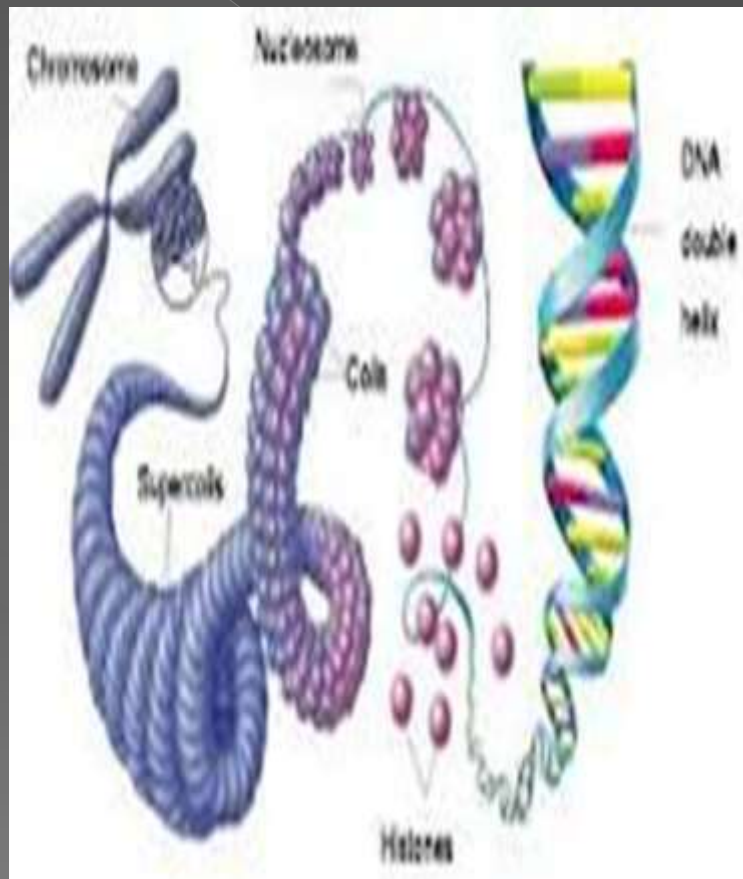
- The idea that each chromosome is composed of a single DNA double helix is an oversimplification.
- A chromosome is very much wider than the diameter of a DNA double helix.

- In addition, the amount of DNA in the nucleus of each cell in humans means that the total length of DNA contained in the chromosomes, if fully extended, would be several meters long! لو غردنا اى DNA الموجود في اكر وموسم حاليه نلحقو اى حيطه حوله اعمار

- In fact, the total length of the human chromosome complement is less than half a millimeter .

- The packaging of DNA into chromosomes involves several orders of DNA coiling and folding.
- In addition to the primary coiling of the DNA double helix, there is secondary coiling around spherical *histone* 'beads', forming what are called *nucleosomes*.

اولی لفافہ ہی کوہ ال DNA اہلا double helix یعنی لاففہ حوالین حالہ
ثانی لفافہ بتلوہ حوالیہ خزانہ برہیتہ ال histone وتلوہ ال
nucleosomes

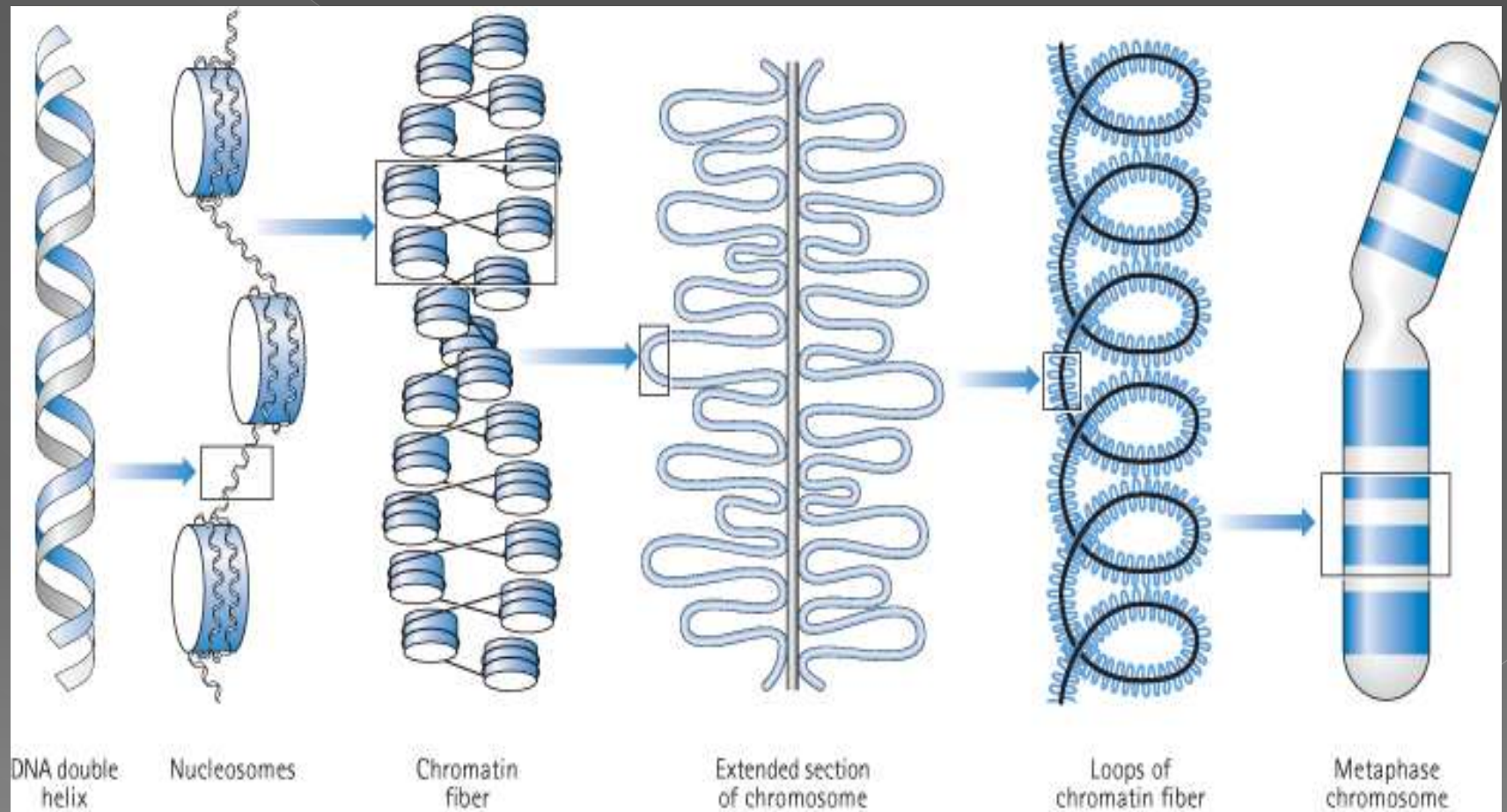


- There is a tertiary coiling of the nucleosomes to form the *chromatin fibres* that form long loops on a scaffold of non-histone acidic proteins, which are further wound in a tight coil to make up the chromosome as visualized under the light microscope .

واللفة الثالثة هي الـ *nucleosomes* تتلف حوالية حبالها كثير حتى تكوّن الـ *chromatin*

واللفة الرابعة هي الـ *chromatin* راجع تلف حوالية بروتينات الـ *non histamine acidic protein*

واللفة الخامسة هي الـ *chromosome* بعد ذلك مع يلف لفاك محكم حتى تكوّن الـ *chromosome* التي تقدر نشاهدها في الميكروسكوب



GENITICS 4

Gene Structure & Classes Of DNA

Dr. Sawsan Salem Shurrah

TYPES OF DNA SEQUENCES

DNA, if denatured, will reassociate as a duplex at a rate that is dependent on the proportion of unique and repeat sequences present, the latter occurring more rapidly.

NUCLEAR GENES

- It is estimated that there are approximately 30 000 genes in the nuclear genome.
- The distribution of these genes varies greatly between chromosomal regions.

- For example, heterochromatic and centromeric regions are mostly non-coding, with the highest gene density observed in sub-telomeric regions .

یعنی سائپلر ال Hetero والیاں الی العامة وحوالہ ال-centro
الوجہ فیہا جبہ ولسہ الی تحت ال telomere کلا جینا 2

لذا سے آجا خلا فہم راج ہوئی! بی نرہفہ کثیرہ

- Chromosomes 19 and 22 are gene rich, whereas 4 and 18 are relatively gene poor.
- The size of genes also shows great variability from small genes with single exons to genes with up to 79 exons e.g. dystrophin.

Unique single-copy genes

- Most human genes are unique single-copy genes coding for polypeptides that are involved in or carry out a variety of cellular functions.
 - These include enzymes, hormones, receptors, and structural and regulatory proteins.
- 

Multigene families

Many genes have similar functions
They are known as multigene families.

Some are found physically close together in clusters, e.g. the α - and β -globin gene clusters on chromosomes 16 and 11 whereas others are widely dispersed throughout the genome occurring on different chromosomes.

دربعض عائلات الجينات تجمع مع بعضها

والبعض عائلات متناثرة في الجينوم

Multigene families can be split into two types :

- **Classic gene families** that show a high degree of sequence homology .
تشابه في التركيب والوظيفة
- **Gene superfamilies** that have limited sequence homology but are functionally related, having similar structural domains.

في domains متشابهة ولدت من الداخل مختلفين
عن بعض

Classic gene families

Examples of classic gene families include :

- ① The numerous copies of genes coding for the various ribosomal RNAs, which are clustered as tandem arrays on the short arms of the five acrocentric chromosomes (13,14,15,21,22).
موجود علویا جینات مسؤوۃ
↑
tandem arrays
بغیر از centromere علاقہ یابی
short arm دیرینہ علاقہ ب
long arm دماغی
الکروموسوم مظہر
- ② The different transfer RNA gene families, which are dispersed in numerous clusters throughout the human genome.

Gene superfamilies

- Examples of gene superfamilies include the HLA genes on chromosome 6 and the T-cell receptor genes, which have structural homology with the immunoglobulin (Ig) genes.

في تناغم بين الhuman و cellular

immune system حيث لازم يتبعوا Gene superfamilies

موا الجينات المسؤولة عن انتاج و Ig, مواد الجينات المسؤولة عن الreceptor
في T-cell

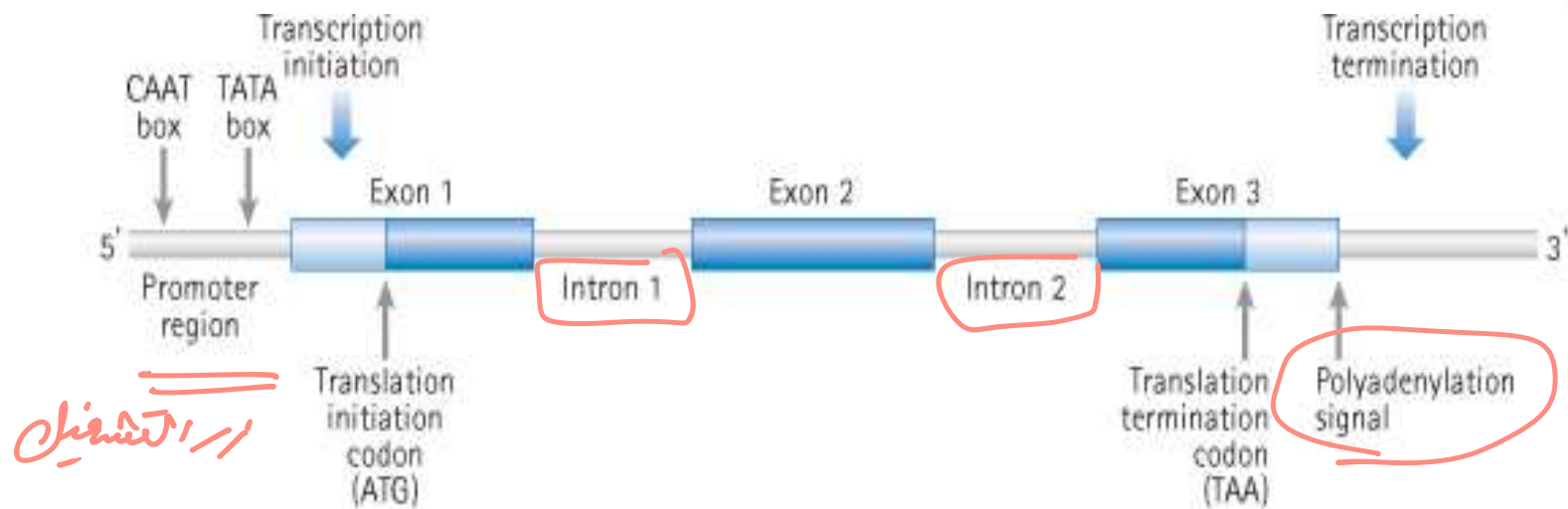
GENE STRUCTURE

- The gene was much longer than necessary to code for the β -globin protein, containing non-coding intervening sequences or introns, which separate the coding sequences or exons.

وحددوا أن الجين أطول من المطلوب لـ code
الـ B. و هو يتكون من قطع C. التي تنقطع (exons)
C. التي تنقطع

- It appears to be the exception for genes in humans to consist of uninterrupted coding sequences.

من المصير ألاتي جيني الإنسان هو introns



The number and size of introns in various genes in humans are extremely variable, although there is a general trend that the larger the gene, the greater the number and size of the exons.



عدد و حجم introns في تلاف وفي قاعدة ؛ انه كلما كان الجين اكبر
كلما زعم و حجم و exons يتبعه اكبر

exons in introns

- Individual introns can be far larger than the coding sequences and some have been found to contain coding sequences for other genes, i.e. genes occurring within genes.

يعني ان intron في هذا الجين قد يكون

exon لجين آخر يعني عبارة عن overlapping genes

- Genes in humans do not usually overlap,
being separated from each other although
some of the genes in the HLA complex have
been shown to be overlapping.

Pseudogenes

- Particularly fascinating is the occurrence of genes that closely resemble known structural genes but which, in general, are not functionally expressed: so-called *pseudogen*.

نفس الجين له بنية وظيفية بالوظيفة

These are thought to have arisen in two main ways:

1. Genes undergoing duplication events that are rendered silent through the acquisition of mutations in coding or regulatory elements.

صار ذلك مضافاً على توقف
بسبب طفرة أو حذف جزئي
فأصبح الجين صامتاً

2. As the result of the insertion of complementary DNA sequences, produced by the action of the enzyme reverse transcriptase on a naturally occurring mRNA transcript, which lack the promoter sequences necessary for expression.

هذا الانزيم سينسخ mRNA transcript
ولكنه يفتقر الى promoter sequences (التي تحتاج)
لذلك فهو inactive

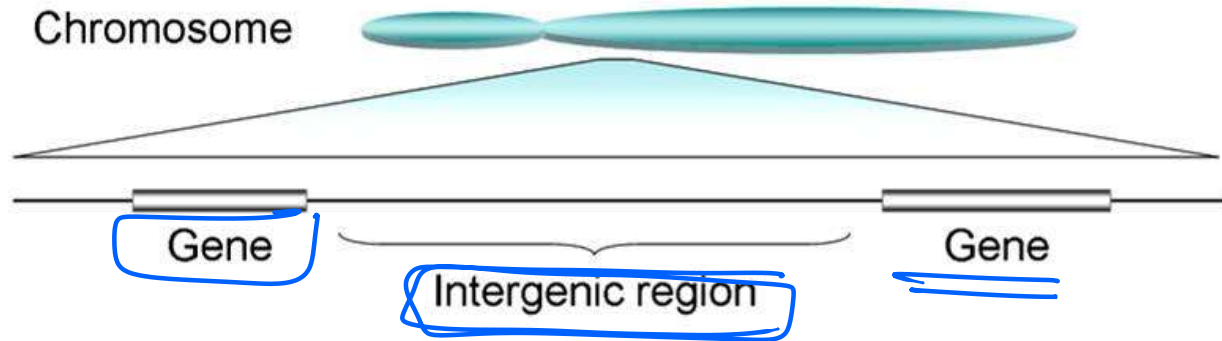
EXTRAGENIC DNA

- The estimated 30 000 unique single-copy genes in humans represent less than 2% of the genome.

98%

- The remainder of the human genome is made up of repetitive DNA sequences that are predominantly transcriptionally inactive.

protein synthesis لا يتم ولا التعبير عن الجين

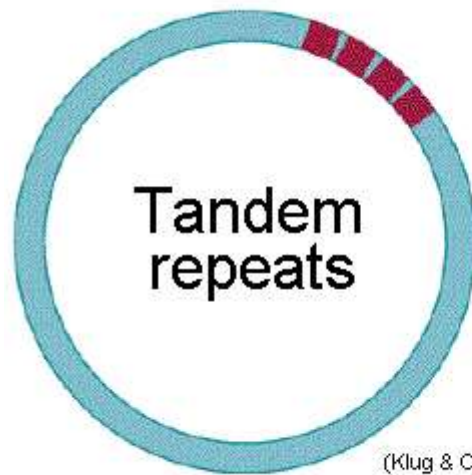


دوره ژنتیک
بهره

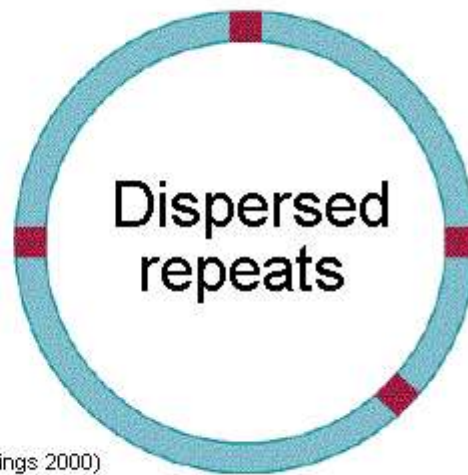
ما هي لزوم

- It has been described as junk DNA, but some regions may play a role in the regulation of gene expression .

له النظام كثير من عناصره واجبة ما تنظم عنه الإنسان



تکرار متوالی



تکرار پراکنده

(Klug & Cummings 2000)

Tandemly repeated DNA sequences

- *Tandemly repeated DNA sequences* consist of blocks of tandem repeats of non-coding DNA that can be either highly dispersed or restricted in their location in the genome.

تنوع جرمی است مرتبہ قوی جفت

- Tandemly repeated DNA sequences can be divided into three subgroups: satellite⁽¹⁾, minisatellite⁽²⁾ and microsatellite⁽³⁾ DNA .

حیثیت اور block ای بنیادی

Satellite DNA

Accounts for approximately 10-15% of the repetitive DNA sequences of the human genome and consists of very large series of short tandemly repeated DNA sequences that are transcriptionally inactive and are clustered around the centromeres of certain chromosomes.

۱) block جویہ و التکرار ایضاً جویہ ہوتا
غیر نشانی ہے اس transcript و جویہ حول ۱) centromere

لما جملوا لـ DNA فصل مرکزي المنطقه Satellite راج تنفصل
جزئیاتی ار shoulder از انقضت تماماً Satellite کا تقرابا طیفی

- This class of DNA sequences can be separated on density-gradient centrifugation as a shoulder, or 'satellite', to the main peak of genomic DNA, and has therefore been referred to as satellite DNA.

Minisatellite DNA

Minisatellite DNA consists of two families of tandemly repeated short DNA sequences, telomeric and hypervariable. ②

- **Telomeric DNA** ; The terminal portions of the telomeres of the chromosomes are necessary for chromosomal integrity in replication and are added to the chromosome by a specialized enzyme known as telomerase .

منطقة الـ telomere كشيروعة كإنزيم معروف بآلة انقسام يغير طولها أحياناً كما يحصل في حالة: انقسام
ما يقدر يصير أقصر من قبله (موتة الشيخوخة) و لذلك تدخل في عملية انتحار (apoptosis)
وعشائر الكروموسوم ما يقصر من بدري في انقسام الـ telomerase ولأنه هذا الانزيم ما يكثر بشكل جيد إن شاء الله
division ما يتوقف ويغير في cancer ولا إنه يلاصه بآلة غير نشطة والـ division يتوقف بدري يصير aging

صم في الدّهب السّريّ رابّات الأبوّة

- **Hypervariable minisatellite DNA**

is made up of highly polymorphic DNA sequences consisting of short tandem repeat of a common core sequence forming the basis of DNA fingerprinting used in forensic and paternity testing .

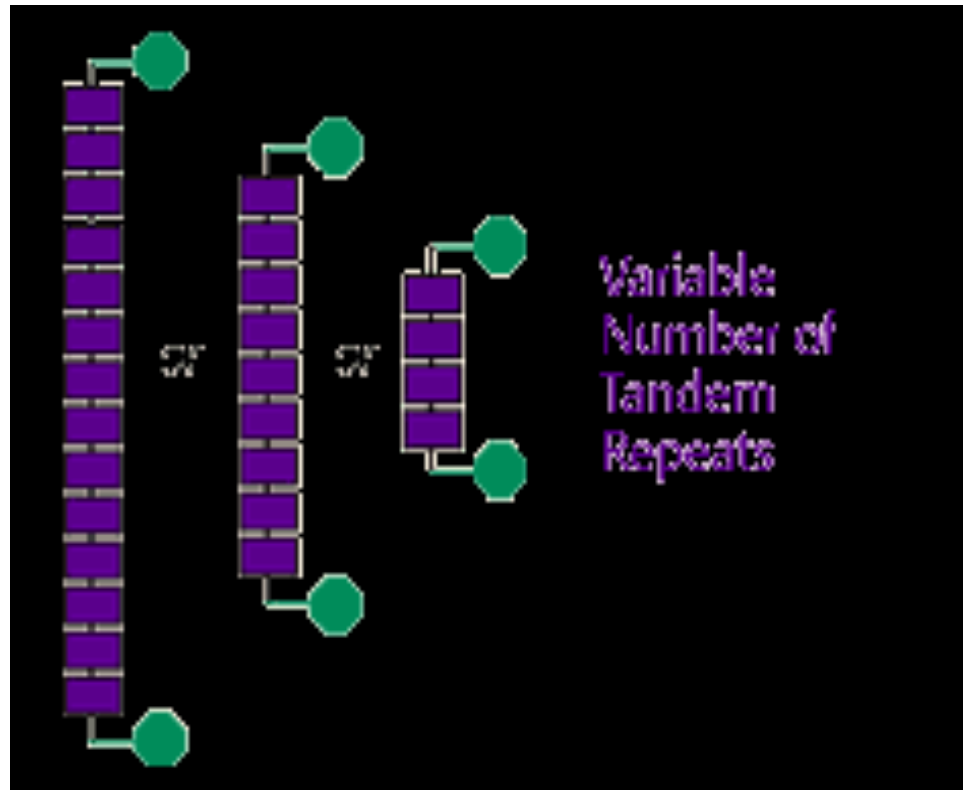
صمّية ال DNA لآلّ نأجوا مختلف من شخص إلى آخر

Although often located near the telomeres, hypervariable minisatellite DNA also occurs at other locations in the chromosomes.

Satellite

minisatellite

microsatellite



Microsatellite DNA

- consists of tandem single, di-, tri- and tetranucleotide repeat base pair sequences located throughout the genome.
- Microsatellite repeats rarely occur within coding sequences but trinucleotide repeats in or near genes are associated with certain inherited disorder.
- DNA microsatellites are highly polymorphic.

ما يسمى الـ repeating في الجين والـ coding sequences وهو يقع في المناطق المشفرة

Interspersed repetitive DNA sequences

Approximately one-third of the human genome is made up of two main classes of short^① and long^② repetitive DNA sequences that are interspersed throughout the genome .

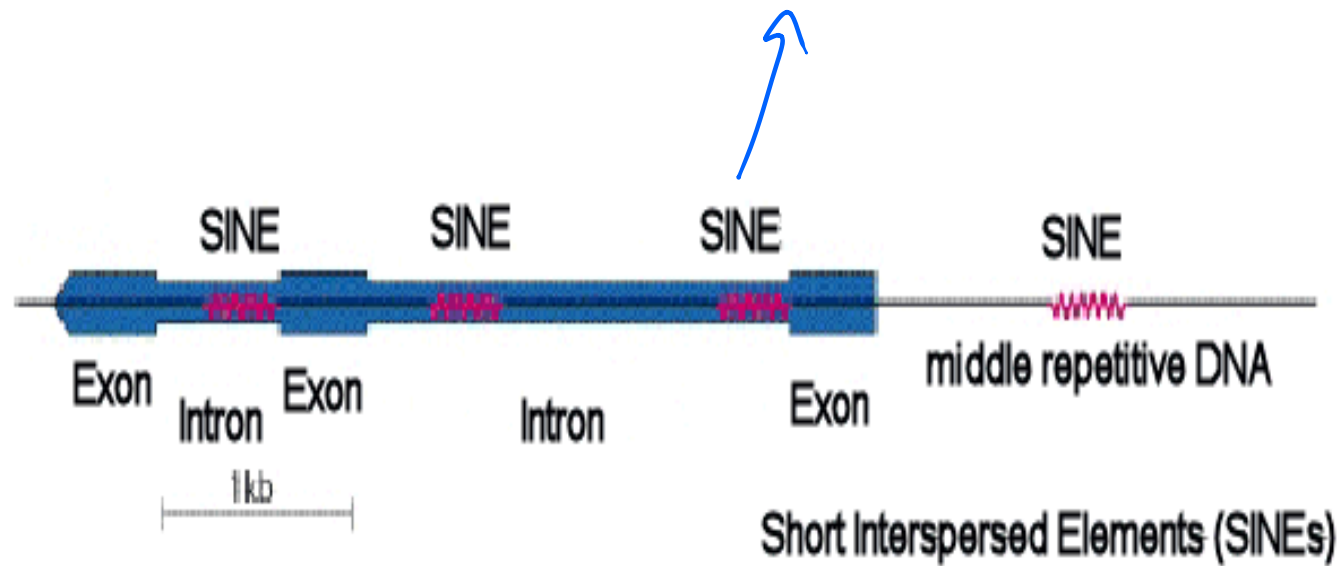
Short interspersed nuclear elements

- About 5% of the human genome consists of some 750000 copies of *short interspersed nuclear elements* or SINEs.
- The most common are DNA sequences that have sequence similarity to a signal recognition particle involved in protein synthesis.
- They are called Alu repeats because they contain an Alu restriction enzyme recognition site.

SINEs

عنصر متكرر في الجينوم البشري
يحتوي على تسلسل مشابه لتسلسل
جزيء إشارة للبروتين
مشارك في تخليق البروتين
تسمى هذه العناصر
SINEs
تحتوي على موقع
اعتراف إنزيم
Alu

میشرفی کس ۱۵ genome



(Klug & Cummings 2000)

Long interspersed nuclear elements

About 5% of the DNA of the human genome is made up of *long interspersed nuclear elements* or *LINEs* .

The most commonly occurring LINE, known as LINE-1 or an L1 element, consists of over 100 000 copies of a DNA sequence that encodes a reverse transcriptase.

↓
Q1.1.9

- The function of these interspersed repeat sequences is not clear at present.
- Members of the *Alu* repeat family are called transposable elements or *transposons* .

تغيير الموقع
A

يعتبر PNA من ثابت ولله في قطع منه
بنتحرك و تنتقل وتسبب الطفرات

- Transposition can create significant mutations and alter the cell's genome size

Transposons are of two types according to their mechanism, which can be either "copy and paste" (class I) or "cut and paste" (class II).

- Class I (Retrotransposons): They copy themselves in two stages, first from DNA to RNA by transcription, then from RNA back to DNA by reverse transcription.
reverse transcriptase enzyme
- The DNA copy is then inserted into the genome in a new position.

وہاں اچھے طریقے سے تفسیر ہے

- Class II (DNA transposons):

By contrast, the cut-and-paste transposition mechanisms of class II transposons do not involve an RNA intermediate.

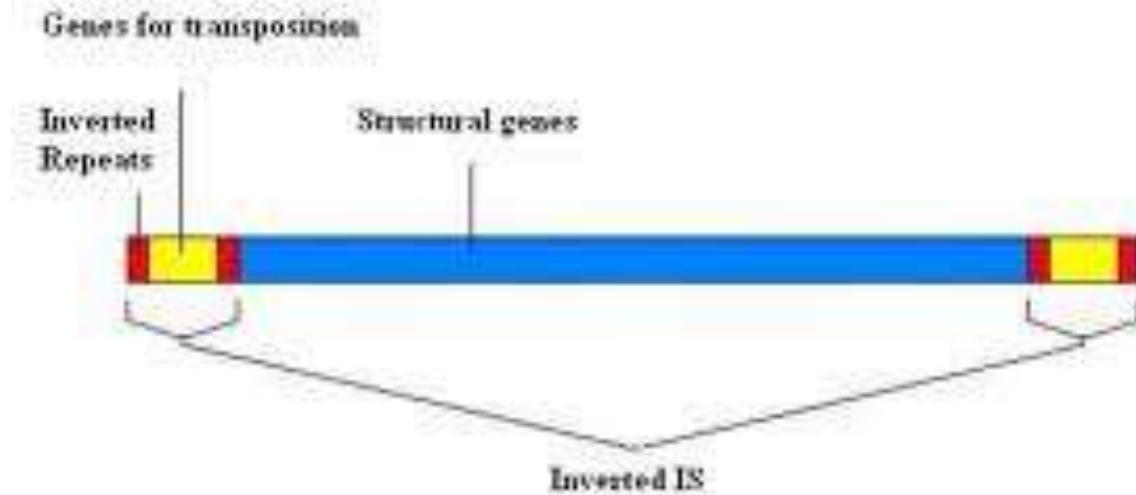
٥١ DNA في (non-replicative) أي ما هو و يذهب في منطقة أخرى

They can damage the genome of their host cell in different ways:

- A transposon or a retroposon that inserts itself into a functional gene will most likely disable that gene.
يوقفوا ونهضه
- After a transposon leaves a gene, the resulting gap will probably not be repaired correctly.

الفراغ الذي تركه مكانه ما يتصلح مع التالي
بصرفي mutation في هذه المنطقة

Bacterial composite transposon



copy and past

لأنه الانعكاسي وله تكرار متساوي
متساوي غائب



- It is postulated that *Alu* repeats could promote unequal recombination, which could lead to pathogenic mutations or provide selective advantage in evolution by gene duplication.

زی البتیر یا ای کانت سensitive

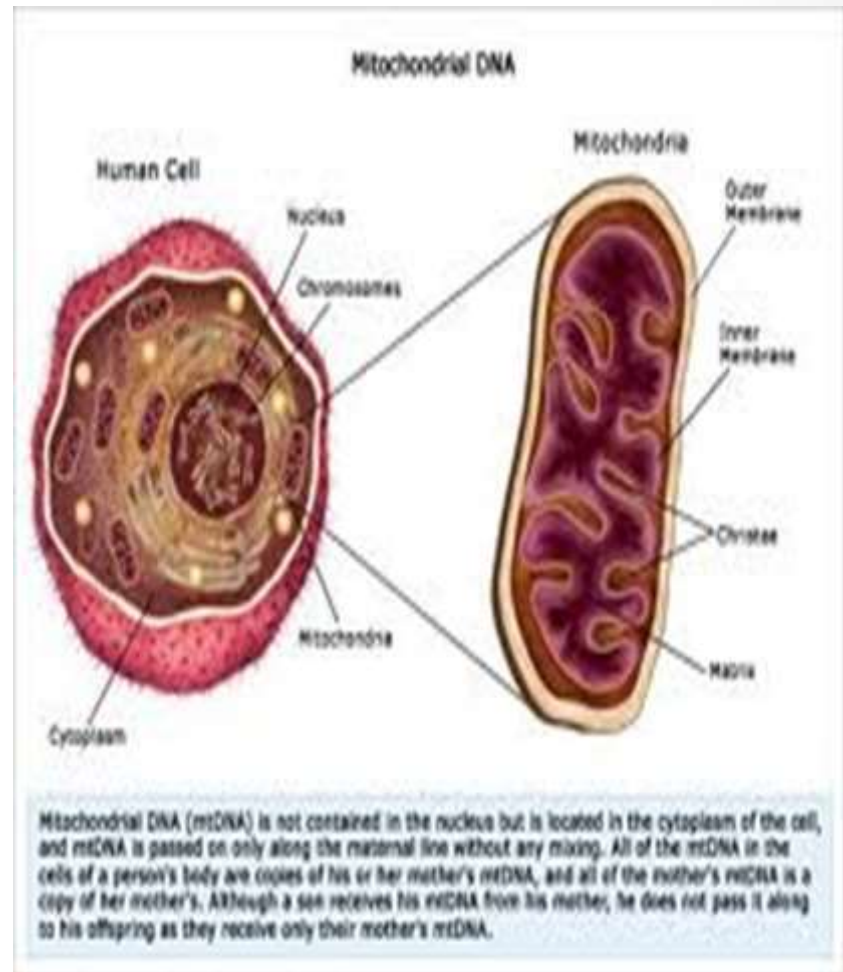
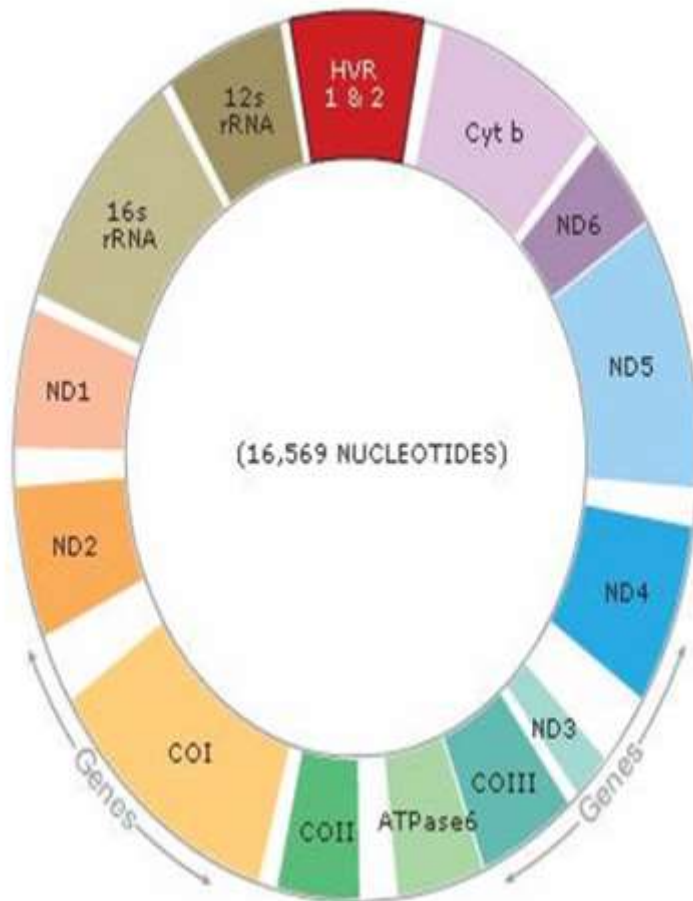
antibiotic resistant لا antibiotic و هذا الانفیل mutation و بتصر antibiotic بعد حارفا و

- Both *Alu* and LINE-1 repeat elements have been implicated as a cause of mutation in inherited human diseases.

نظا encode reverse transcriptase حاذی يساع و copy and past mechanism

MITOCHONDRIAL DNA

- In addition to nuclear DNA, the several thousand mitochondria of each cell possess their own circular double-stranded DNA mitochondrial DNA or mtDNA .



Like ring

• The mitochondrial DNA genome

فیسٹ ہے

is very compact, containing little repetitive DNA, and codes for 37 genes which include :

- ❖ two types of ribosomal RNA.
- ❖ 22 transfer RNA.
- ❖ 13 protein subunits for enzymes, such as cytochrome b and cytochrome oxidase, which are involved in the energy-producing oxidative phosphorylation pathways.

لیسو
للمیتو کونڈریا

اطلا

24 لیسو للمیتو کونڈریا

13 یہا لیسو للمیتو کونڈریا

mtDNA کل انسانی متشابہ

وہا یقیناً فیسٹ mtDNA کریں ← وصیتم افرہ منہ الام فقط یعنی حواوی مطرط الانسانی

والتابع لا يوجد له دور فيه ، لأنه الميتوكوندريا يتصل بـ sperm من حوت الإخصاب

- The genetic code of the mtDNA differs slightly from that of nuclear DNA .
- The mitochondria of the fertilized zygote are inherited almost exclusively from the oocyte, leading to the maternal pattern of inheritance of mitochondrially inherited disorders .

من الأم فقط

لأنها مسئلة راجع عن هذه المسألة لا بها

بنسبة 1:100



GENITICS 6

Chromosomes

Dr.Sawsan Salem Shurrah

- At the molecular or submicroscopic level DNA can be regarded as the basic template that provides a blueprint for the formation and maintenance of an organism.

وجود المعلومات على الـ PNA يحافظ على بنية الحياة
ويحافظ على أن الصفات في الإنسان تبقى كما هي في الإنسان في
الإنسان

- DNA is packaged into chromosomes and at a very simple level these can be considered as being made up of tightly coiled long chains of genes.

تعريفه

لوفودنا كرموسوم الى لولا اقل من 1 ML
لوعيطع معنا امتار عديدة لـ 10¹² DNA يكون
مكتف فيه بيشن كبير

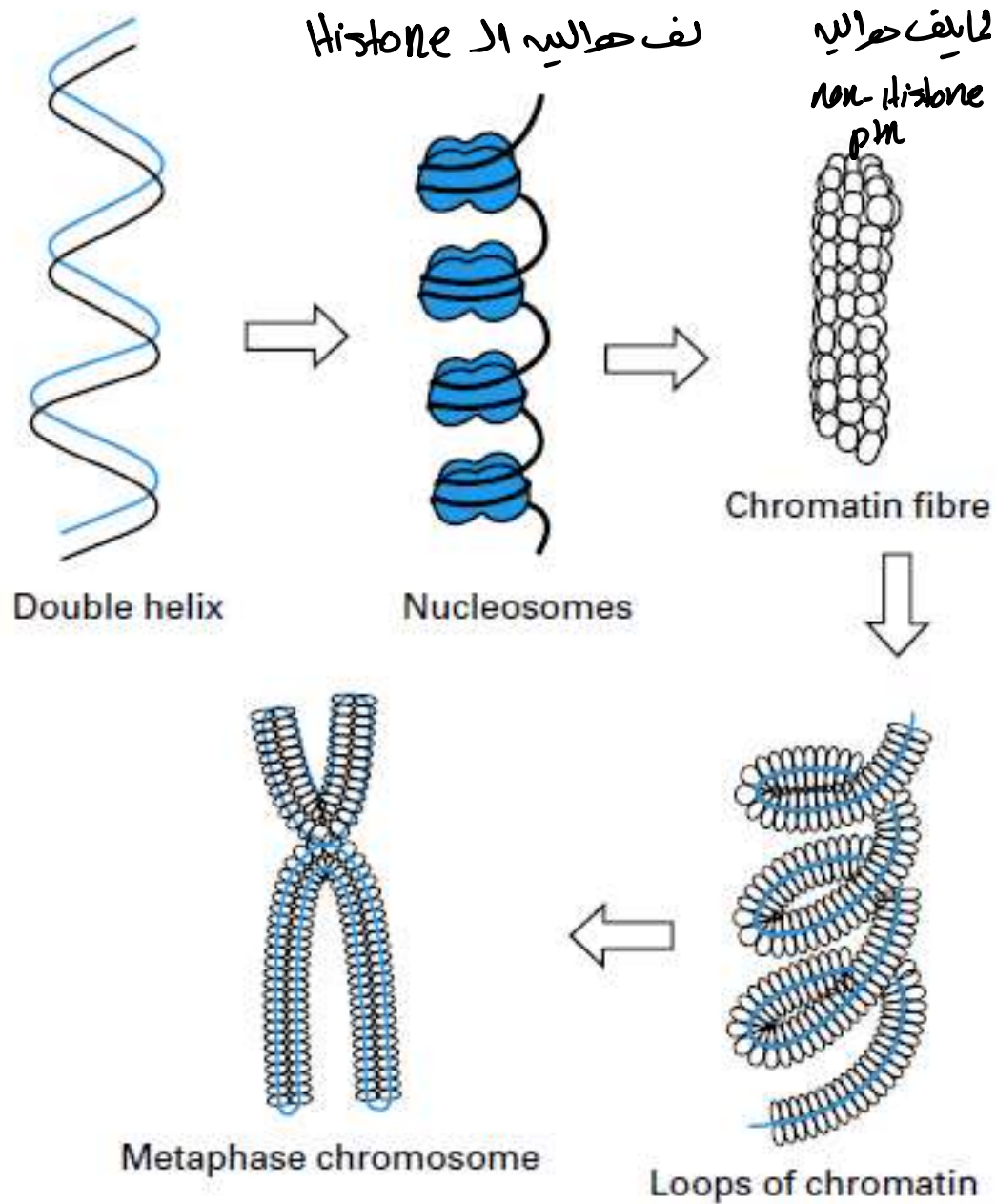


Figure 15.8 Packaging of DNA into chromosomes

- 
- Unlike DNA, chromosomes can be visualized during cell division using a light microscope, under which they appear as thread-like structures or 'colored bodies'.

يشبه الخيط

- The word chromosome is derived from the Greek chroma (= color) and soma (= body).

الجمع الذي - لـ أ ~ يصبغ

- Chromosomes are the factors that distinguish one species from another and that enable transmission of genetic information from one generation to the next.

هي العوامل التي يميز كل species عن الأخرى
وتسمح بنقل المعلومات الوراثية

- Their behavior at somatic cell division in mitosis provides a means of ensuring that each daughter cell retains its own complete genetic complement.

ما يحدث في انقسام جسدي في daughter cell يضمن في المعلومات الوراثية
عن الأم

- 
- Similarly, their behavior during gamete formation in meiosis enables each mature ovum and sperm to contain a unique single set of parental genes.

ہر ذریعہ تولید و انقسام کے ذریعہ ہر خلیہ کی ایک منفرد اور واحد جین کی مجموعہ ہوتی ہے۔

- Chromosomes are quite literally the vehicles that facilitate reproduction and the maintenance of a species.

ان کروموسوم عبارتہ عن وسطیہ تسلسلہ جینیاتی و انسانی و حیوانی
علاوہ السلسلہ ۲

while the study of DNA called ² molecular genetics

- The study of chromosomes and cell division is referred to as cytogenetics.
- The correct chromosome number in humans is 46 and that maleness is determined by the presence of a Y chromosome regardless of the number of X chromosomes present in each cell.

حتى هو في XX وواحد Y يعني male

- It was also realized that abnormalities of chromosome number and structure could seriously disrupt normal growth and development.

■ HUMAN CHROMOSOMES

■ MORPHOLOGY

- At the submicroscopic level chromosomes consist of an extremely elaborate complex, made up of supercoils of DNA.
- Under the electron microscope chromosomes can be seen to have a rounded and rather irregular morphology.

electron

ما بعد را شوقی

- However, most of our knowledge of chromosome structure has been gained using light microscopy. Special stains selectively taken up by DNA have enabled each individual chromosome to be identified.

لن المعلومات عن التركيبات التي يتم إحصاؤها بواسطة light
وقد واصلت نفسا أن DNA من طرف صبغات معينة فيسبب بها بشعرا كذا التركيبات

- These are best seen during cell division, when the chromosomes are maximally contracted and the constituent genes can no longer be transcribed.

وقت على الانقسام ، التركيبات تكون كثر منغصة
وما يقدر على على النسخ
وهناك تلك التركيبات أوفض امشي

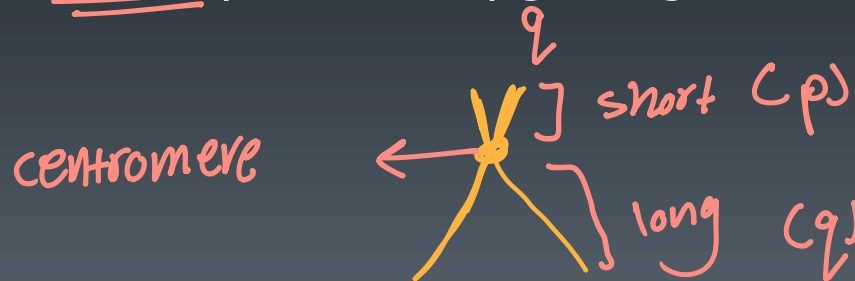
في مرحلة G₂ DNA يتضاعف مرة أخرى ويكوّن جزيئين متطابقين. *double stranded*
وتكوّن *2 sister chromatids* (سواء كان جزيء DNA واحدًا أو زوجًا من الجزيئات).
الجزء الذي يربط بين السمتين يسمى *centromere*.

- At this time each chromosome can be seen to consist of two identical strands known as *chromatids*, or *sister chromatids*, which are the result of DNA replication having taken place during the S (synthesis) phase of the cell cycle
- These sister chromatids can be seen to be joined at a primary constriction known as the *centromere*.

not transcript
not translated
↑

- Centromeres consist of repetitive DNA and are responsible for the movement of chromosomes at cell division.

- Each centromere divides the chromosome into short and long arms, designated p (= petite) and q ('g' = grande), respectively.



- The tip of each chromosome arm is known as the telomere.

طرف الكروموسوم

- Telomeres play a crucial role in sealing the ends of chromosomes and maintaining their structural integrity.

في انزيم telomerase نشاطه سرع بكونه هبان زيادة وده بالنقصان
حتى يحافظ على شدة الكروموسوم

- Telomeres have been highly conserved throughout evolution and in humans they consist of many tandem repeats of a TTAGGG sequence.



maintenance integrity

- During DNA replication an enzyme known as telomerase replaces the 5' end of the long strand, which would otherwise become progressively shorter until a critical length is reached when the cell can no longer divide and thus becomes ^{aging} senescent.

يكون في نهاية الـ 5' جزيء الخلية قصير أقصر مع الوقت
لما توصل لمرحلة إنه ما بقدر يقصر أكثر وصار يكون وصل
مرحلة الشيخوخة

- 
- This is in fact part of the normal cellular aging process, with most cells being unable to undergo more than 50-60 divisions.

عدم زادت الانقسام الخلوي قدر تقسيم

- However, in some tumors increased telomerase activity has been implicated as a cause of abnormally prolonged cell survival.

- Morphologically chromosomes are classified according to the position of the centromere.

- If this is located centrally, the chromosome is *metacentric*, if terminal it is *acrocentric*, and if the centromere is in an intermediate position the chromosome is *submetacentric*.

عاطرف

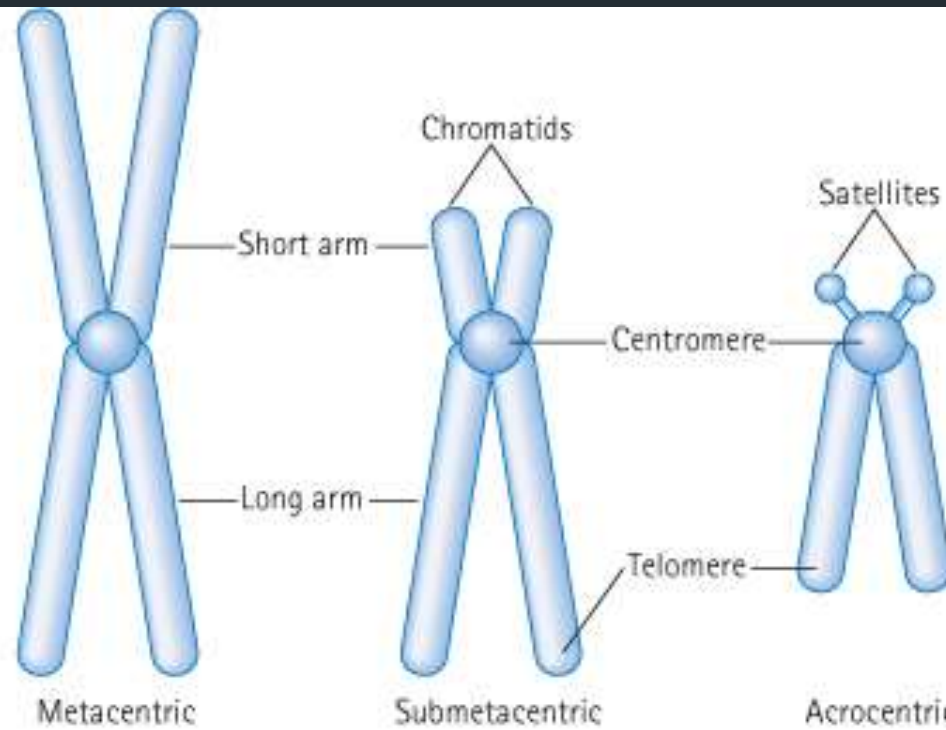
صنّف

ما قبل الطرف

موجود ہیں repetitive DNA سے تعلق رکھتی ہیں ribosomal RNA

- Acrocentric chromosomes sometimes have stalk-like appendages called satellites that form the nucleolus of the resting interphase cell and contain multiple repeat copies of the genes for ribosomal RNA.

اسی



CLASSIFICATION

- Individual chromosomes differ not only in the position of the centromere but also in their overall length.

- Based on the three parameters of ^①length, ^②position of the centromere and the ^③presence or absence of satellites, early pioneers of cytogenetics were able to identify most individual chromosomes, or at least subdivide them into groups labelled A-G on the basis of overall morphology .

حسب الخواص 1، 2، 3 قدروا العلماء انهم يقسموا
الكروموسومات في جروبات من A-G على حسب شكلهم

- 
- In humans the normal cell nucleus contains 46 chromosomes, made up of 22 pairs of *autosomes* and a single pair of sex chromosomes - XX in the female and XY in the male.

- One member of each of these pairs is derived from each parent.

مطلبي نصف عدد الكروموسومات عند الانقسام

- Somatic cells are said to have a diploid complement of 46 chromosomes, whereas gametes (i.e. ova and sperm) have a haploid complement of 23 chromosomes.

مطلبي نصف العدد من الكروموسومات عند الانقسام

- Members of a pair of chromosomes are known as homologs.

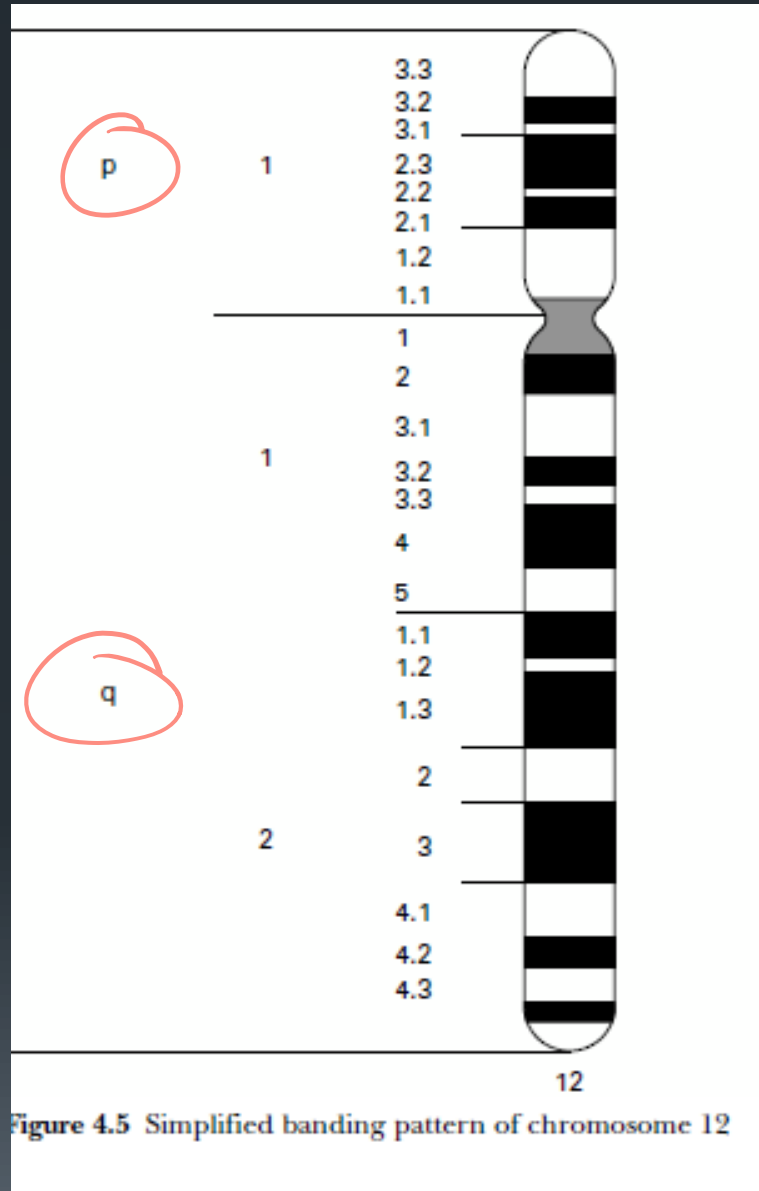
مثلاً كروموسوم 1 جاي من الاب والام

- The development of chromosome banding enabled very precise recognition of individual chromosomes and the detection of subtle chromosome abnormalities.

تطوّر طرق الـ banding والصبغات الكروموسومية قدروا يشوّنوا
الذائعي لطفة زواي نفكي في الكروموسوم

چوکر

کیر



چنداد

Bands

اللو الفاص

وافاق

بقدر اقرار

ای کروموسوم

رقم 12 وانشاف

انا صیغها زولا

- 
- This technique also revealed that *chromatin*, the combination of DNA and histone proteins of which chromosomes are made, exists in two main forms.
 1. *Euchromatin* stains lightly and consists of genes that are actively expressed.
 2. *Heterochromatin* stains darkly and is made up largely of inactive unexpressed repetitive DNA.

THE SEX CHROMOSOMES

- The X and Y chromosomes are known as the sex chromosomes because of their crucial role in sex determination.
طريقه الجيني
- The X chromosome was originally labeled as such because of uncertainty as to its function .
- In humans, and in most mammals, both the male and the female have two sex chromosomes - XX in the female and XY in the male .



Y



X

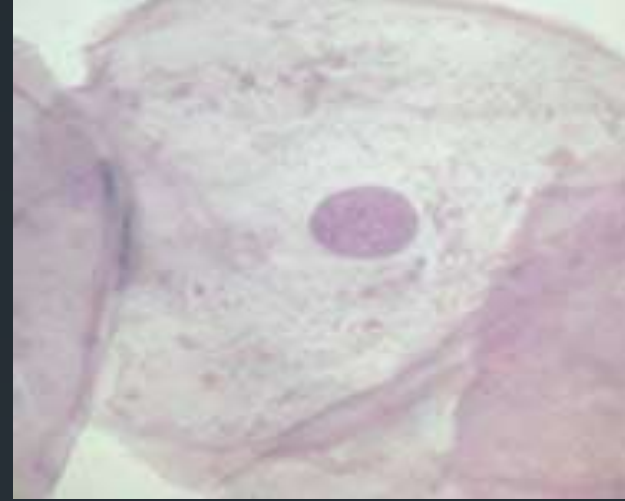
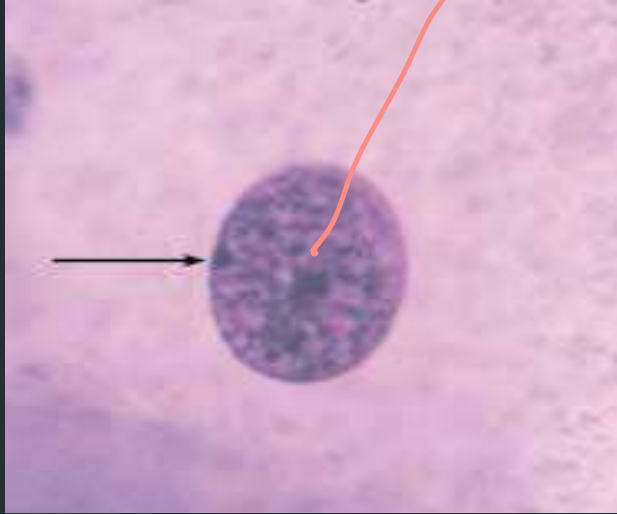
- The Y chromosome is much smaller than the X and carries only a few genes of functional importance, most notably the testis-determining factor, known as SRY. sex regulating Y

وجود راجع خللي او gonad cell نامل testis وليس ovary في او fetus

- Other genes on the Y chromosome are known to be important in maintaining spermatogenesis.

- In the female each ovum carries an X chromosome, whereas in the male each sperm carries either an X or a Y chromosome.

X لون غامق في النواة



A Barr body is an inactivated X chromosome.

(a) Female cell with a Barr body (indicated by arrow).

(b) Male cell without a Barr body.

زما v ما بهم خردوا جنس البشري خاصة لو كانت الحالة atypical

ومشي عارفين ولدوا بنتي فتاها ياهوا buccal smear ^{مسري} وبشوخا طابقه اسوا Barr body

ال Barr Body عبارة عن inactivated ^{موتري} chromosome 6 الانثى عندها 2X كدوموهم ولد عتاف ما

بنفع بلونه في [2] مع عيني فخي واحد قنص ويبقى inactive وهذا اسمه Barr Body

Table 4.2

Number of Barr bodies in human cells with different complements of sex chromosomes

Sex Chromosomes	Syndrome	Number of Barr Bodies
XX	None	1
XY	None	0
XO	Turner	0
XXY	Klinefelter	1
XXYY	Klinefelter	1
XXXY	Klinefelter	2
XXXXY	Klinefelter	3
XXX	Triplo-X	2
XXXX	Poly-X female	3
XXXXX	Poly-X female	4

$1 - \text{X} \text{ pair} = \text{Barr body}$

- As there is a roughly equal chance of either an X-bearing sperm or a Y-bearing sperm fertilizing an ovum, the numbers of male and female conceptions are approximately equal .

لأنه عدد السرم الذي عندهم X
وعدد السرم الذي عندهم Y نفس العدد واحتمالية حدوث الحمل لتلكه نبتة أو ولد
مع البويضة تكونان متساويتين.

- In fact, slightly more male babies are born than females, although during childhood and adult life the sex ratio evens out at 1:1.

لأنه إحصائياً نسبة الذكور الذين تمتصوا دتوهم متساوية أكبر من نسبة
نساء الطغوة بتوهم النسبة 1:1 لأن نسبة وفيات الأخوة أكبر