

6. MOLECULAR BASIS OF INHERITANCE

- Nucleic acids (DNA & RNA) are the building blocks of genetic material.
- DNA is the genetic material in most of the organisms.
- RNA is the genetic material in some viruses. RNA mostly functions as **messengers**.

THE DNA

STRUCTURE OF POLYNUCLEOTIDE CHAIN

Polynucleotides are the polymer of **nucleotides**. DNA & RNA are polynucleotides. A nucleotide has 3 components:

1. A **nitrogenous base**.
2. A **pentose sugar** (ribose in RNA & deoxyribose in DNA).
3. A **phosphate group**.

Nitrogen bases are 2 types:

Purines: It includes **Adenine (A)** and **Guanine (G)**.

Pyrimidines: It includes **Cytosine (C)**, **Thymine (T)** & **Uracil (U)**. Thymine (5-methyl Uracil) present only in DNA and Uracil only in RNA.

A nitrogenous base is linked to the OH of 1' C pentose sugar through an **N-glycosidic linkage** to form **nucleoside**.

Nucleosides in RNA	Nucleosides in DNA
Adenosine	Deoxyadenosine
Guanosine	Deoxyguanosine
Cytidine	Deoxycytidine
Uridine	Deoxythymidine

A phosphate group is linked to OH of 5' C of a nucleoside through **phosphoester linkage** to form **nucleotide** (or deoxynucleotide).

In RNA, each nucleotide has an additional -OH group at 2' C of the ribose (2'-OH).

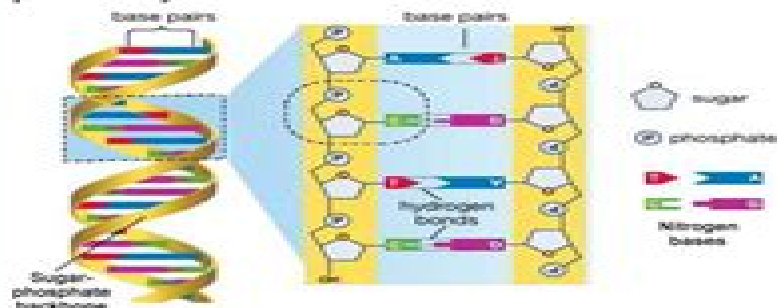
2 nucleotides are linked through **3'-5' phosphodiester bond** to form **dinucleotide**.

When more nucleotides are linked, it forms **polynucleotide**.

STRUCTURE OF THE DNA

Friedrich Meischer (1869): Identified DNA and named it as 'Nuclein'.

James Watson & Francis Crick (1953) proposed **double helix model** of DNA. It was based on X-ray diffraction data produced by **Maurice Wilkins & Rosalind Franklin**.



Pitch of helix = 3.4 nm (34 Å)

Number of base pairs in each turn = 10

Distance between adjacent base pairs = 0.34 nm (3.4 Å)

DNA is made of 2 polynucleotide chains coiled in a right-handed fashion. Its backbone is formed of sugar & phosphates. The bases project inside.

The 2 chains have **anti-parallel polarity**, i.e. one chain has the polarity 5' → 3' and the other has 3' → 5'.

The bases in 2 strands are paired through **H-bonds** forming **base pairs (bp)**.

A=T (2 hydrogen bonds) C=G (3 hydrogen bonds)

Purine comes opposite to a pyrimidine. This generates uniform distance between the 2 strands.

Erwin Chargaff's rule: In DNA, the proportion of A is equal to T and the proportion of G is equal to C.

$$\therefore [A] + [G] = [T] + [C]$$

$$\text{or } [A] + [G] / [T] + [C] = 1$$

- Φ 174 (a bacteriophage) has 5386 nucleotides.
- Bacteriophage lambda has 48502 base pairs (bp).
- *E. coli* has 4.6×10^6 bp.
- Haploid content of human DNA is 3.3×10^9 bp.

Length of DNA = number of base pairs X distance between two adjacent base pairs.

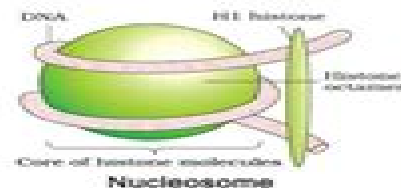
$$\begin{aligned} \text{Number of base pairs in human} &= 6.6 \times 10^9 \\ \text{Hence, the length of DNA} &= 6.6 \times 10^9 \times 0.34 \times 10^{-9} \\ &= 2.2 \text{ m} \end{aligned}$$

$$\text{In } E. coli, \text{ length of DNA} = 1.36 \text{ mm } (1.36 \times 10^{-3} \text{ m})$$

$$\begin{aligned} \therefore \text{The number of base pairs} &= \frac{1.36 \times 10^{-3}}{0.34 \times 10^{-9}} \\ &= 4 \times 10^6 \text{ bp} \end{aligned}$$

PACKAGING OF DNA HELIX

- In prokaryotes (E.g. *E. coli*), the DNA is not scattered throughout the cell. DNA is negatively charged. So it is held with some positively charged proteins to form **nucleoid**.
- In eukaryotes, there is a set of positively charged, basic proteins called **histones**.
- Histones are rich in positively charged basic amino acid residues **lysines** and **arginines**.
- 8 histones form **histone octamer**.
- Negatively charged DNA is wrapped around histone octamer to give **nucleosome**.
- A typical nucleosome contains **200 bp**.



$$\begin{aligned} \text{Therefore, total number of nucleosomes in human} &= \frac{6.6 \times 10^9 \text{ bp}}{200} = 3.3 \times 10^7 \end{aligned}$$

- Nucleosomes constitute the repeating unit to form **chromatin**. Chromatin is the thread-like stained bodies.

The Molecular Basis Of Neuropathology

Eli M. Mizrahi, Frederick Sachs



The Molecular Basis Of Neuropathology:

The Molecular Basis of Neuropathology Alan Nelson Davison, Robert Henry Stewart Thompson, 1981 *Greenfield's Neuropathology, 2-Volume Set, Eighth Edition* Seth Love, David Louis, David W Ellison, 2008-02-29

Greenfield's Neuropathology the worlds leading neuropathology reference provides an authoritative comprehensive account of the pathological findings in neurological disease their biological basis and their clinical manifestations This account is underpinned throughout by a clear description of the molecular and cellular processes and reactions that are relevant to the development and normal and abnormal functioning of the nervous system While this scientific content is of paramount importance however care has been taken to ensure that the information is presented in a way that is accessible to readers working within a range of disciplines in the clinical neurosciences and that also places the neuropathological findings within the context of a broader diagnostic process The new eighth edition incorporates much new information new illustrations and many new authors while retaining the depth breadth and quality of content so praised in previous editions Each chapter opens with an introductory section designed to offer an integrated approach to diagnosis taking account of clinical manifestations neuroradiological and laboratory findings as well as the neuropathological and molecular genetic features of the diseases being considered Strong emphasis has been placed on facilitating the retrieval of neuropathological information by non neuropathologists grappling with differential diagnoses or seeking information on broad categories of neurological disease and boxes and tables are used to present important symptoms and signs patterns of disease and other features for ease of reference High quality line and photographic illustrations the majority in full colour are all available on a companion CD to complete the offering

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Pediatric Neuropathology Dawna Armstrong,William Halliday,Cynthia Hawkings,Sachio Takashima,2008-02-01 At last a much needed route map to pediatric neuropathology Up to now a comprehensive volume covering of pediatric neuropathology simply did not exist This atlas is thus a unique all encompassing reference providing material on the fundamentals of brain disorders of the nervous system that can affect fetuses infants and young children as well as the essentials of diagnosis in developmental brain pathology and neuroimaging Emphasising the characteristic morphology and a concise summary of clinical features pathogenesis and genetics the generously illustrated atlas presents more than 100 disorders This compilation is a valuable resource for pathologists pediatric neurologists and neurosurgeons geneticists neonatologists radiologists and pediatricians

The Neuropathology of Huntington's Disease: Classical Findings, Recent Developments and Correlation to Functional Neuroanatomy Udo Rüb,Jean Paul G. Vonsattel,Helmut Heinsen,Horst-Werner Korf,2015-09-29 This monograph describes the progress in neuropathological HD research made during the last century the neuropathological hallmarks of HD and their pathogenic relevance Starting with the initial descriptions of the progressive degeneration of the striatum as one of the key events in HD the worldwide practiced Vonsattel HD grading system of striatal neurodegeneration will be outlined Correlating neuropathological data with results on the functional neuroanatomy of the human brain subsequent chapters will highlight recent HD findings the neuronal loss in the cerebral neo and allocortex the neurodegeneration of select thalamic nuclei the affection of the cerebellar cortex and nuclei the involvement of select brainstem nuclei as well as the pathophysiological relevance of these pathologies for the clinical picture of HD Finally the potential pathophysiological role of neuronal huntingtin aggregations and the most important and enduring challenges of neuropathological HD research are discussed

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The Behavioral Neurology of Dementia Bruce L. Miller, Bradley F. Boeve, 2016-11-17 This new edition of *The Behavioral Neurology of Dementia* provides clinicians and researchers with the latest research findings written by the leading dementia experts. With chapters ranging from cognitive evaluation to imaging and genetics and pathology to treatment, the detailed clinical descriptions of diseases and symptoms serve not only as an educational tool for trainees but also as an opportunity for experienced clinicians to deepen their knowledge and better serve their patients. After years of little progress, the pace of discovery has been speeding up in the last decade and the authors distill the most valuable discoveries into clear, insightful chapters with applicable information. All the chapters from the first edition have been refreshed with new text and figures. There are new chapters on autoimmune antibody associated encephalopathy, chronic traumatic encephalopathy and sleep issues in dementia.

Mitochondrial Disorders in Neurology Anthony H.V. Schapira, S. Dimauro, 2013-10-22 *Mitochondrial Disorders in Neurology* provides an overview of mitochondrial diseases. This book discusses the effects of mitochondrial dysfunction based on the relevant biochemistry and molecular genetics. The abnormal muscle and mitochondrial morphology in a variety of clinical presentations from isolated ophthalmoplegia to severe encephalopathy are also elaborated. This text likewise deliberates Leber's hereditary optic neuropathy, neurodegenerative disorders and respiratory chain defects. Other topics covered include mitochondrial DNA and the genetics of mitochondrial disease, cytochrome oxidase deficiency, use of tissue culture in the diagnosis of mitochondrial disease and advances in mitochondrial genetics. This publication is a good source for clinicians and students concerned with the defective mitochondrial function.

SPEC - Handbook of Clinical Neurology, Volume 144, Huntington Disease, 12-Month Access, eBook, 2019-05-16 Huntington Disease summarizes the most recent findings related to the disease, providing both cutting edge coverage for clinical research specialists looking to expand their knowledge base of Huntington disease information as well as solid groundwork for advanced students from various backgrounds: neurology, psychiatry.

neuropsychology genetics The volume includes all major areas of Huntington disease clinical care and research whereas many other HD texts focus solely on neurological symptoms This book also addresses behavioral and cognitive symptoms brain imaging and family dynamics and therapeutic alliances in working with individuals affected by HD Clinical trials are covered extensively including design considerations for therapeutic studies The devastating nature of Huntington s disease is well appreciated throughout the neuroscience neurology and psychiatric communities and a great amount of basic and clinical research is currently taking place However much of that occurs in isolated research silos and it is critical that an interdisciplinary resource be developed to provide in depth information to enhance communication and collaboration This volume in the Handbook of Clinical Neurology series is that resource Includes coverage of both basic science and clinical aspects of the disease as well as treatment experimental therapeutics and biomarkers Provides an essential resource for the non neurologist including necessary background for understanding the disease before making a more detailed study proposal Provides an interdisciplinary approach that can be applied in everyday clinic and research efforts Features chapters edited by leaders in the field around the globe the broadest expert coverage available

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