Introduction to Molecular Biology

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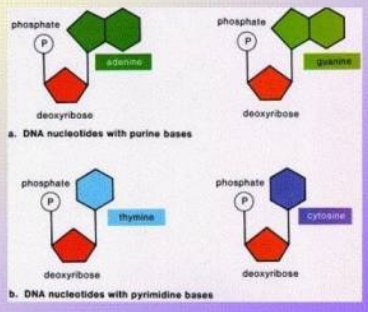
Overview

1.1 Implications of DNA-based genomes
1.2. Flow of genetic information
1.3. Genotype and phenotype
1.4. Molecular basis of two example inherited disorders

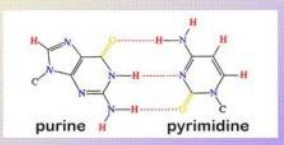
Implications of the Structure of DNA

- DNA as the genetic material
- DNA-based genomes
- RNA-based genomes

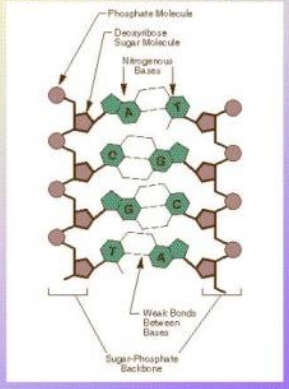
A minimalist viewpoint: bases in DNA



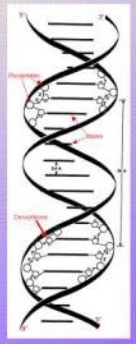
Bases are part of of a larger structure



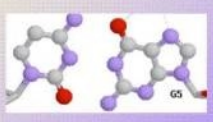
DNA consists of connected bases

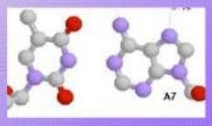


The Watson and Crick model of DNA as a double helix

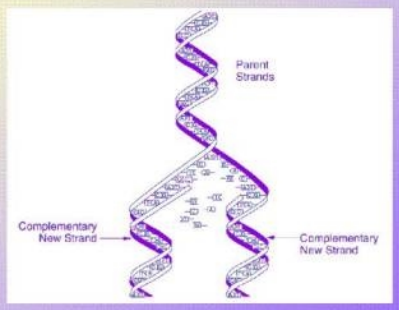


Knowledge of the sequence of one strand allows us to infer the sequence of the other strand.

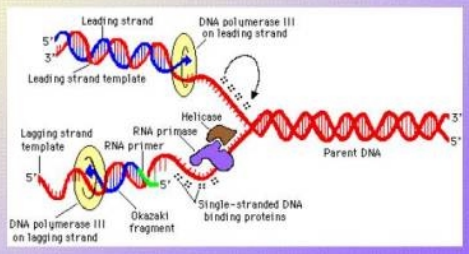




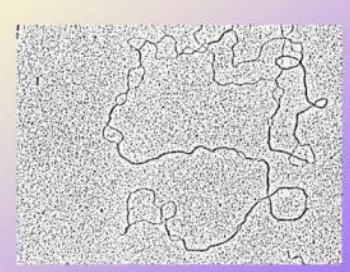
Double-stranded DNA is peeled apart to replicate DNA



DNA replication, like most cellular processes, needs assistance



Base content varies along a strand

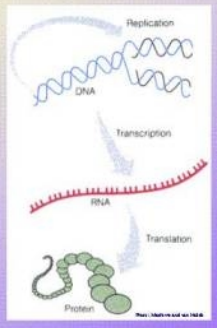


Flow of Genetic information

The central dogma

DNA → RNA → protein

Transcription and translation : a classical viewpoint



The Genetic Code provides a dictionary
(a classical viewpoint, continued)

2nd base in codon

1st base in codon	U	C	A	G	3rd base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Genotype and phenotype

Example 1: From *open reading frame* to *transcript* to *protein*

ATG GCT GGC TTC ...

↓

AUG GCU GGC UUC ...

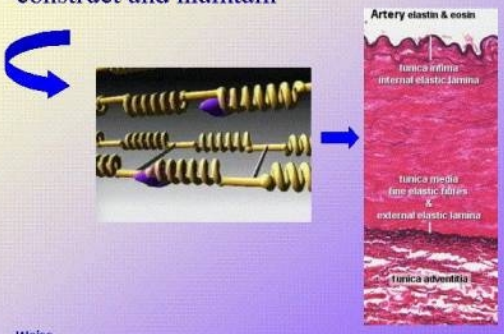
↓

Met Ala Gly Phe ...

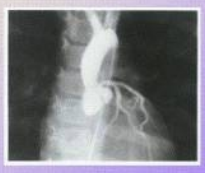
Example 2: A mutation in a coding sequence

ATG GCT GGC TTC ...	**ATG GCT GGC TCC ...**
↓	↓
AUG GCU GGC UUC ...	**AUG GCU GGC UCC ...**
↓	↓
Met Ala Gly Phe ...	**Met Ala Gly Ser ...**

Protein and RNA components work together: construct and maintain



Changes in DNA sequence can lead to changes in molecular architecture and function



We are more than the sum of our parts…

Molecular basis of selected diseases

- Inborn error of metabolism
- Pharmacogenetics

Alkaptonuria

- blackening of urine, degenerative arthritis of spine and large joints
- Archibald Garrod. Predictions from careful observation
- homogentisic acid in large amounts in urine
- blackening on oxidation (urine, cartilage…)

Alkaptonuria *(continued)*

- metabolism. Individual steps affected
- amino acid intake (phenylalanine and tyrosine)
- enriched in first cousins. Mendelian recessive.
- damage to gene resulting in aberrant *homogentisic acid oxidase*

Acute haemolytic anemia

- primaquine (antimalarial prophylaxis)
- secondary anemia (hemolysis) or occasionally severe anemia
- deficiency in *glucose-6-phosphate dehydrogenase (G6PD).*
- Several hundred million people affected
- contributes to redox status. Fava beans, sulfonamides, aspirin, quinine…

Acute haemolytic anemia *(continued)*

- **Glucose-6-phosphate dehydrogenase** : stability, reduced lifetime. Cannot resist oxidative stress.
- Mature red blood cells lack nucleus and are consequently unable to replenish: most affected
- Altered gene on X chromosome: prospect of resistance to malaria in females

Many genes imply diversity

"Genomic changes distinguish us"

Weiss

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