Lecture 2: Introduction to the Structure of the Genome

Review the chemical composition and structure of DNA

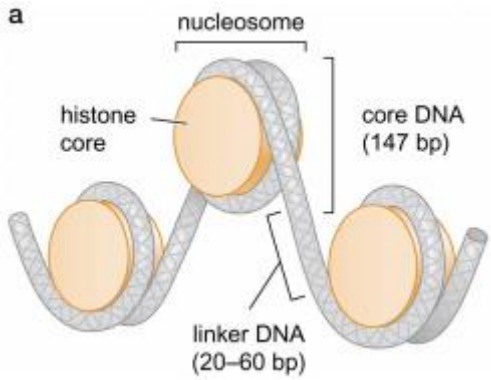
- DNA is a biopolymer made up of nucleotides (sugar, phosphate and base)
- Nucleotides are joined together by phosphodiester bonds
- DNA is double stranded and nucleotides form base pairs
  - Purines (2 rings) pair with pyrimidines (1 ring)
  - AT and GC – complementary "Watson and Crick base pairs"

Appreciate the need for DNA compaction

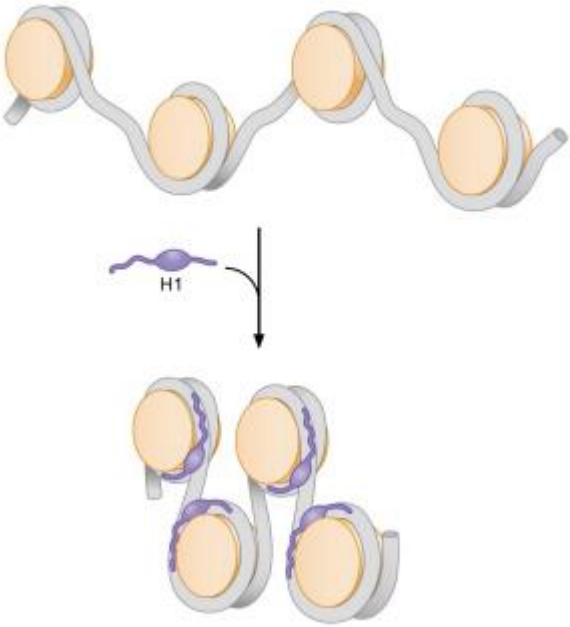
- Prokaryotic example
  - *E. coli* has one long DNA molecule that is 1.3 mm in length
  - Bacterium has diameter ~1um
  - i.e. bacterial dimensions ~1/1000th that of the DNA
- Eukaryotic example
  - Human cell has 6 X 10^9 bp of DNA
  - Each base pair has a "thickness" of 3.4 A
  - Total length of the DNA ~2m
  - Typical human nucleus has diameter 10-15um

Understand at the molecular level the packaging of DNA into c'somes

- In prokaryotes like *E. coli*
  - DNA organised into 50-100 domains/loops
  - Independently supercoiled
  - RNA and protein contribute to folded structure
    - ➔ "folded genome"
- In eukaryotes
  - Packaging begins with formation of <u>nucleosome</u>
  - DNA wound around small proteins called <u>histones</u>
    - 5 classes of histones (1, 2A, 2B, 3 and 4)
    - Core histones = H2A, H2B, H3 and H4
      - ✓ Dimers of each of these together form an <u>octamer</u> that makes up the protein "core" of the nucleosome
    - Core DNA = ~147 bp of DNA that wrap around the core histones
    - Histone octamer + core DNA = nucleosome
  - Histones have lots of lysine and arginine residues, making them very positively charged at pH7



- Linking nucleosomes and H1
  - Adjacent nucleosomes are linked by 20-60 bp DNA = <u>linker DNA</u>
  - Histone H1 interacts with linker DNA and a part of the core DNA = <u>linker histone</u>
  - Induces tighter wrapping of DNA in nucleosome
  - Formation of 30nm fibre



SUMMARY

- Each c'some contains a single molecule of DNA
- DNA wrapped around histone core octamer to form nucleosomes
- Nucleosomes compacted in 30nm fibre by histone H1
- High order packaging not completely understood – loops of DNA held together by nuclear scaffold

<u>Learn about the feature of c'somes</u>

- C'some = complex of DNA, histones and non-histone proteins
- Several features allow their maintenance and transmission to next generation:

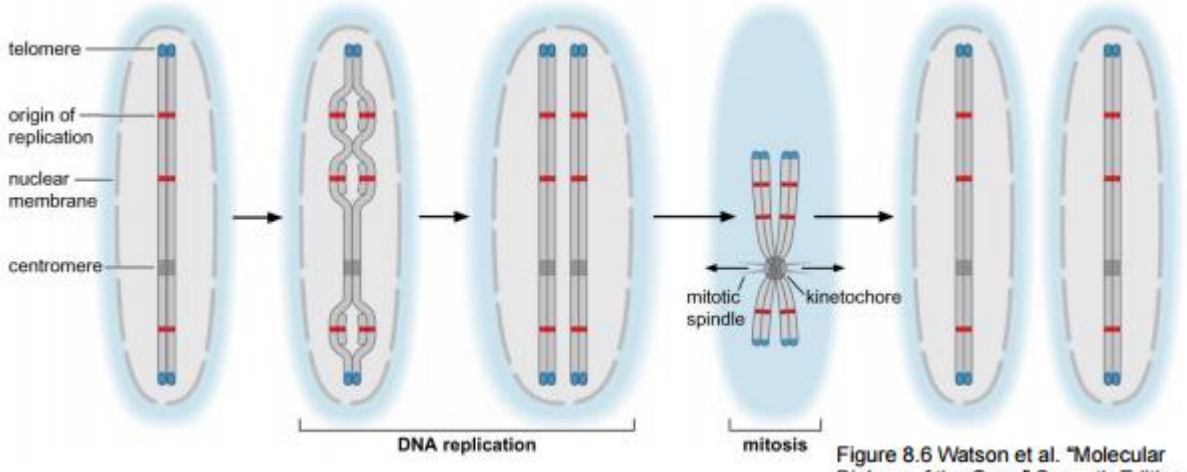


Figure 8.6 Watson et al. "Molecular Biology of the Gene" Seventh Edition