

Chapter 16- The Molecular Basis of Inheritance

(Key Concepts are Underlined)

DNA as the Genetic Material

The search for the genetic material led to DNA: *science as a process*

Transformation- change in genotype and phenotype due to the assimilation of external DNA by a cell

- in 1944, Avery, McCarty, and MacLeod deduced DNA was the transforming agent in the *Transformation of Bacteria Experiment* (first designed by Griffith in 1928)

Bacteriophages- viruses that infect bacteria

- in 1952, Hershey and Chase discovered DNA is the genetic material of a phage called T2 in the *Hershey-Chase Experiment*

- 1) T2 phage's proteins labeled with radioactive Sulfur
- 2) T2 phage's DNA labeled with radioactive Phosphorus
- 3) Both phages were allowed to infect separate samples of *E. coli* cells
- 4) The separate cultures were blended and centrifuged to get a pellet (cells) and supernatant (virus fragments), and found the radioactive proteins in the supernatant and radioactive phosphorus in bacterial cells of the pellet.
- 5) The radioactive cells were returned to the culture medium and they released phages containing radioactive phosphorus.
- 6) In conclusion, DNA of the phage is the material injected into the host cell (leaving behind the

protein coat) and causes the cell to make new viral DNA and proteins.

- in 1947, Chargaff found the amount of the four nitrogenous bases of DNA is different in different species, but existed in a characteristic ratio ($A = T$ and $G = C$); later known as *Chargaff's rules*

Watson and Crick discovered the double helix by building models to conform to X-ray data: *science as a process*

- in April 1953, an American James Watson and Englishman Francis Crick proposed the 3-D, double helix model of DNA; they used evidence from Rosalind Franklin's X-ray diffraction photo of DNA and Chargaff's rules to assemble DNA model

DNA Molecule:

- 1) 2 nm wide
- 2) nitrogenous bases stacked 0.34 nm
- 3) sugar-phosphate back chains outside
- 4) hydrophobic nitrogenous bases inside
- 5) helix makes one full turn every 3.4 nm along its length, so 10 layers of base pairs per turn
- 6) purines always paired with pyrimidines (i.e. $A = T$ and $G = C$)

DNA Replication and Repair

During DNA replication, base pairing enables existing DNA strands to serve as templates for new complementary strands

Semiconservative model- each daughter molecule will have one old strand from the parent molecule and one newly made strand

- in the late 1950's, Meselson and Stahl designed experiments, which supported the semiconservative model predicted by Watson and Crick

A large team of enzymes and other proteins carries out DNA replication

- only about one error per billion nucleotides!

Origins of replication-

Replication fork- Y-shaped region where new strands of DNA are elongating

- proteins initiate DNA replication by recognizing a specific sequence of nucleotides and attach to the DNA, separating the two strands for replication; replication proceeds in both directions until the entire molecule is copied; many origins of replication in eukaryotic chromosomes

DNA polymerases- enzymes responsible for elongation of new DNA during replication; adds complementary base/nucleotides one at a time (about 50 per second in human cells!)

- nucleotides (or nucleoside triphosphates) supplies the energy required for the polymerization of DNA; structurally similar to ATP, but the sugar component is deoxyribose in DNA (as opposed to ribose in ATP); the 2 phosphate groups are hydrolyzed when the monomer joins the growing end of the DNA strand

- DNA strands are antiparallel

- nucleotides are only added to the 3' end (refers to a specific carbon in the deoxyribose sugar attached to the terminal hydroxyl group) of the growing DNA strand, thus elongating in the 5' → 3' direction

Leading strand- the DNA strand formed in the replication fork; elongates continuously

Lagging strand- the DNA strand elongating away from the replication fork; synthesized as a series of segments called *Okazaki fragments* (about 100 to 200 nucleotides long in eukaryotes), which are joined by an enzyme called **DNA ligase**

- DNA polymerases can only add nucleotides to the end of a preexisting polynucleotide chain!

Primer- a short chain of RNA required to initiate elongation (about 10 nucleotides long in eukaryotes); primers later removed and replaced by another type of DNA polymerase with DNA versions; each Okazaki fragment has a primer

Primase- joins the RNA nucleotides to make the primer

Helicase- untwists and separates the two strands of the double helix at the replication fork

Single-strand binding protein- holds the DNA strands apart while they serve as templates for the synthesis of new complementary strands

Enzymes proofread DNA during its replication and repair damage in existing DNA

Mismatched repair- DNA polymerase proofreads the nucleotide against its template, thus fixing errors in base pairing during DNA replication (about 1/10,000 base pairs)

Nuclease- DNA-cutting enzyme excises damaged DNA segments (one of apparently many DNA repair enzymes)

Excision Repair- segments of damaged DNA are excised and filled with properly filled nucleotides via DNA polymerase and ligase

The ends of DNA molecules pose a special problem

Telomeres- special (repetitive) nucleotide sequences at the end of linear, eukaryotic DNA molecules which contain no genes; the repeated units of humans telomeres is TTAGGG (between 100 and 1000 repetitions); protects genes from being eroded by successive rounds of DNA replication

Telomerase- an enzyme responsible for catalyzing the lengthening of telomeres; contains a sequence of RNA which serves as a template for new telomere segments; not present in most cells of multicellular organisms (found in germ cells and interestingly, cancerous somatic cells)