Module 1

Genetics

- The study of the variation between and among living things, and how this variation is inherited
- Genome – the total amount of genetic material in a chromosome set
- Gene is a segment of DNA
- Variation may be due to
  - Environmental factors
  - Genetic factors
  - A combination of the two

Environmental Factors

- Fetal alcohol spectrum disorder
  - Environmental factor – alcohol during pregnancy
  - Growth retardation, characteristic facial features, central nervous system anomalies
  - Chronic heavy alcohol use or frequent heavy intermittent alcohol use during pregnancy
  - The gene that metabolizes alcohol is different in individuals so the syndrome could be partially genetic
- A variant in the population

Genetic Factors

- Huntington Disease
  - Repeated sequence of bases
  - On chromosome 4

Combination

- Heat sensitive gene controls coat colour of some animals: white in winter and brown in summer
- Hydrangea: same genotype influence by pH, colour changes

Epigenetics

- Change in gene expression without changing the DNA code
- E.g. Glucocorticoid – a hormone that regulates responses related to stress
- E.g. promoters control gene expression, methylation is an epigenetic event
  - Additions of CH2 to bases in DNA which can prevent gene expression

Structure of DNA

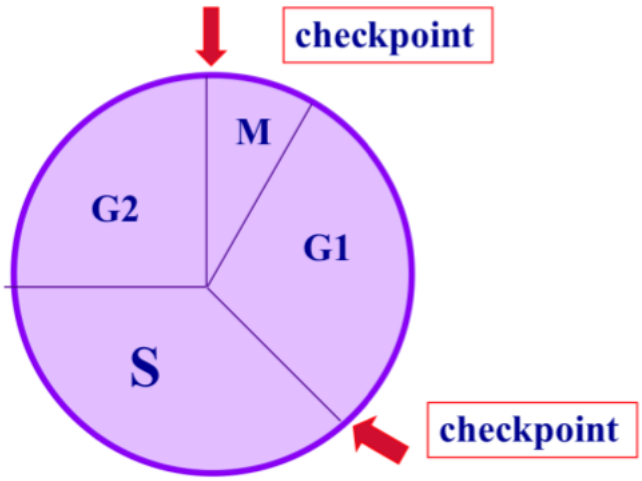
- Double stranded – bond antiparallel
- Outer sugar phosphate strand is very strong, but some enzymes can chop through it
- Base is linked by weak H bonds
- Base / sugar / phosphate – nucleotide
- Polarity depends whether 5’ is up or down
- Purine = A+G, double rings
- Pyrimidine = C+T, single rings
- DNA is wrapped around histones, DNA + protein make nucleosome

Chromosomes

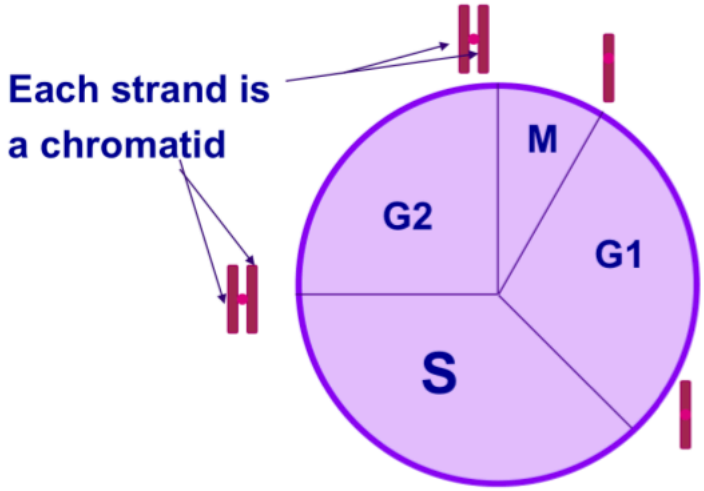
- Polymorphic
- Chromatid = double stranded chromosome

DNA replication

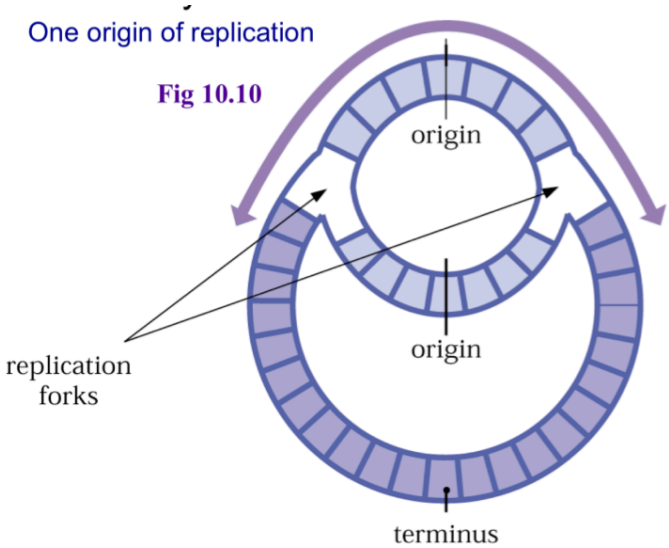
- Occurs at the S stage, DNA content doubles



- Check points are controlled by genes, these are often the ones that mutate in cancer
- Cells divide without control



Prokaryote DNA replication

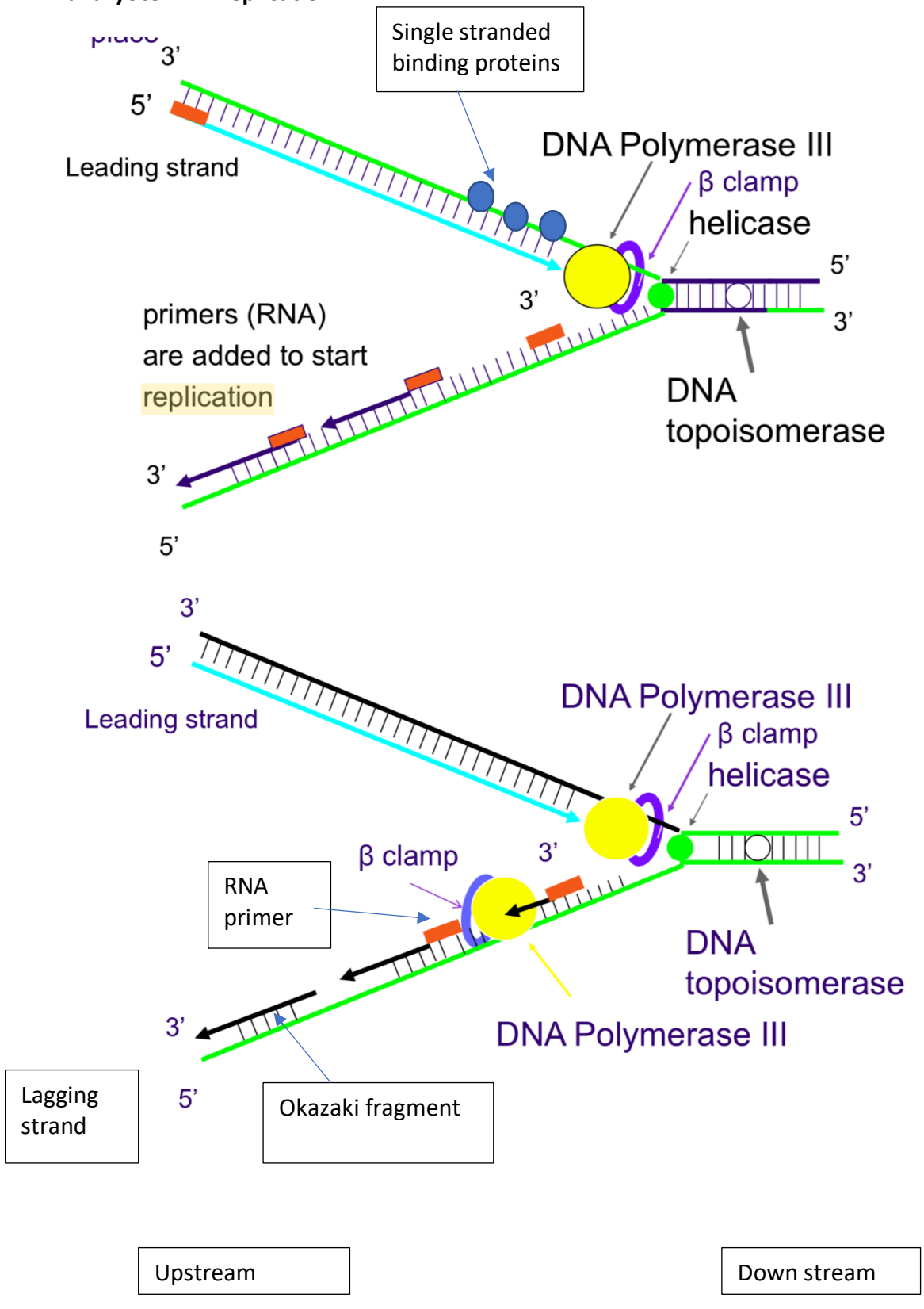


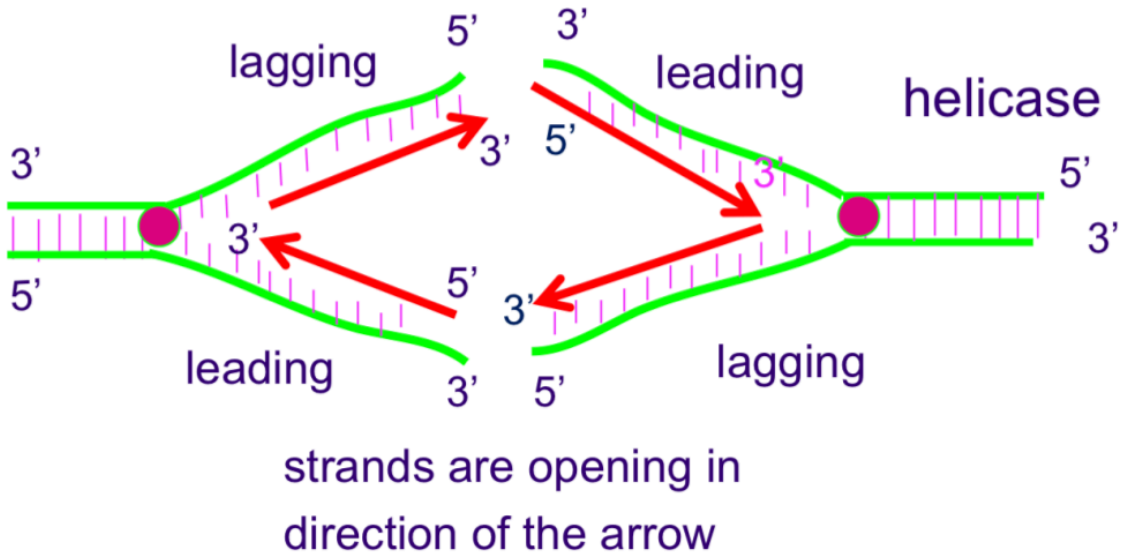
- One origin and synthesis of DNA in both directions
  - Unwinds double helix, initiated by a cut from DNA gyrase
  - Made single stranded in small sections
  - Leading strand grows towards the fork and lagging strand grows away to meet at the terminus and stop
  - Separation achieved by ATP driven enzymes
  - Kept apart by single-strand binding proteins, which bind to single-stranded DNA, prevent from rewinding and ensure there are templates for synthesis of new complementary strands

- dNTPs added to the chain by DNA polymerases
- Attach bases in 5’ to 3’ direction
- Synthesis started by attaching a nucleotide to a free 3’OH group at the end of a pre-existing strand
- Synthesis of lagging strand occurs in short bursts

- In direct contact with the cytosol and is available for replication, transcription and repair

Eukaryote DNA replication





- Many origins of replication on chromosomes
- Formation of two replication forks at each origin which are bidirectional with leading and lagging strands
- Inactive genes tends to replicated late in the S phase

Prokaryotic DNA replication	Eukaryotic DNA replication
- Occurs inside the cytoplasm - Only one origin per molecule of DNA - Origin of replication is about 100-200 or more nucleotides in length - Replication occurs at one point in each chromosome - Only one replication fork is formed - Initiation carried out by protein DNAA and DNAB - DNA gyrase is needed - DNA polymerase III - DNA polymerase I is responsible for repair	- Occurs inside the nucleus - Many origins of replication in each chromosome - Each origin of replication is formed of about 150 nucleotides - Replication occurs at several points simultaneously - Multiple replication forks formed - Initiation carried out by origin recognition complex - DNA gyrase not needed - DNA polymerases (multiples)

DNA repair

DNA proofreading
- DNA polymerase can go backwards 3' to 5' and cut out an error and replace the base
- Protein identifies and DNA polymerise adds the correct nucleotide

Mismatch repair
- Nucleotide mis paired
- Mismatch repair proteins excise the mismatched nucleotide and some adjacent nucleotides
- DNA pol I adds the correct nucleotides
- DNA ligase repairs the remaining nick

Excision repair
- Damaged nucleotide
- Excision repair proteins excise the damaged nucleotide and some adjacent nucleotides
- DNA pol I adds the correct nucleotides by 5' to 3' replication of the short strand
- DNA ligase repairs the remaining nick