DNA & Genomics

Molecules to know

<u>Nucleotide</u>

- Structure
 - 1. Pentose sugar
 - Deoxyribose
 - Ribose
 - 2. Phosphate group
 - 3. Nitrogenous base
 - Purines
 - Adenine
 - Guanine
 - Pyrimidines
 - Thymine (in DNA)
 - Uracil (in RNA)
 - Cytosine
- To note:
 - Deoxyribonucleotide (DNA) -> For replication
 - Ribonucleotide (RNA) -> For transcription
 - Nucleotide -> In general
 - Deoxyribonucleoside triphosphate -> Only if talking about formation of phosphodiester bond

Nucleic Acids

- Polymerase catalyses the formation of a phosphodiester bond between adjacent nucleotides forming a sugar-phosphate backbone
- 5' end ends with free phosphate group
- 3' end ends with free hydroxyl group

<u>DNA</u>

- Double-stranded
- Made up of deoxyribonucleotides → Nitrogenous bases could be A, T, G or C
- Right handed double helix structure
- 1 complete turn of double helix has 10 base pairs and spans 3.4nm
- 2 DNA strands are antiparallel
- Complementary base pairing
 - Adenine forms 2 hydrogen bonds with Thymine
 - Cytosine forms 3 hydrogen bonds with Guanine
 - Hydrogen bonds formed between complementary bases help to stabilise the structure
 - Pairing between a purine and a pyrimidine ensures the DNA molecule has a

constant width of 2.0nm

• Allows for semi-conservative replication where each DNA strand can serve as a template, ensuring the precise replication of the DNA strands

**Role of DNA

- Store and pass on information from one generation to the next
 - Replicated <u>accurately</u> ⇒ Daughter cells are genetically identical to parent cells
 - Weak hydrogen bonding allows parental DNA strands to separate and act as templates for new strand synthesis
 - Complementary base pairing where adenine forms 2 hydrogen bonds with thymine and cytosine forms 3 hydrogen bonds with guanine ensures that newly synthesised strand is complementary to parental DNA strand
 - Stable molecule ⇒ Prevents loss of coded information when passed on to next generation
 - Numerous hydrogen bonds hold 2 strands of DNA together
 - Adjacent nucleotides joined by strong covalent phosphodiester bonds
 - 3. <u>Backup</u> of code
 - Double stranded
 - One strand can serve as template for repair if mutation occurs
 - 4. Readily utilised and accessed
 - Weak hydrogen bonding allows template strand to separate from non-template strand allowing transcription to take place
 - Complementary base pairing allows faithful transfer of info from DNA to RNA during transcription which will be translated to protein subsequently

<u>RNA</u>

- Generally single stranded \Rightarrow No 1:1 ratio
- Made up of ribonucleotides → Nitrogenous bases could be A, U, G or C
- Types
 - 1. mRNA
 - Structure
 - Single stranded polynucleotide formed from transcription of a specific region of DNA → Synthesised by complementary base pairing with DNA serving as a template where adenine base pairs with thymine and guanine bonds with cytosine
 - Coding Region: Starts with start codon (AUG) and ends with stop codon (UAA/UAG/UGA) to determine first and last amino acids to be added to a polypeptide chain
 - Recognition sites that allow it to bind to small ribosomal subunit to initiate translation
 - Function

- Acts as a carrier of genetic code
- Messenger to bring information out of gene in nucleus via nuclear pores to cytoplasm where translation takes place in ribosomes
- Template for translation
 - Anticodons on specific tRNA carrying specific amino acid complementary base pair with codons on mRNA
- Contains codons each coding for an amino acid
 - Specific sequence of codons in mRNA determine sequence of amino acids in <u>single polypeptide chain</u>
- 2. tRNA
 - Structure
 - Folds back upon itself and held in shape by <u>hydrogen bonding</u> between <u>complementary base pairs</u> at certain regions to form a <u>3D</u> <u>L-shaped structure</u> with <u>3 loops</u>
 - One of the loops contain <u>3 specific unpaired triplet bases</u> which form an <u>anticodon</u> that binds to a specific <u>mRNA codon</u> via <u>complementary base-pairing</u>
 - Another of the loops contain 3' CCA stem where the <u>specific amino</u> <u>acid</u> corresponding to the <u>specific anticodon</u> is attached to
 - Aminoacyl-tRNA synthetase catalyses the formation of a bond between specific amino acid and the 3' CCA stem of the specific tRNA with the specific anti-codon during tRNA activation
 - Function
 - Facilitates <u>translation</u> by bringing in <u>specific amino acids</u>, in a sequence corresponding to the <u>sequence of codons</u> in the mRNA strand, to the growing polypeptide
 - 3' CCA stem able to bind to <u>specific amino acid</u> which matches the specific anticodon
 - <u>Specific anticodon</u> on tRNA molecule complementary base pairs with specific <u>mRNA codon</u>

3. rRNA

- Structure
 - Single-stranded chain wound into complex structure
 - Synthesised in nucleus within nucleolus
- Function
 - Associates with ribosomal proteins to form large and small subunits of ribosomes
 - Makes up interface between large and small subunits of the ribosome such that mRNA can bind via <u>complementary base</u> <u>pairing with rRNA in mRNA binding site</u> in small ribosomal subunit
 - Makes up <u>P site and A site</u> of large ribosomal subunit which enables the <u>binding of aminoacyl-tRNAs</u> to the P site and A site by complementary base pairing
 - Makes up peptidyl transferase in the large ribosomal subunit which catalyses the formation of the peptide bond between the amino acid and the growing polypeptide strand

<u>Gene</u>

- Specific sequence of nucleotides in a DNA molecule which codes for a specific sequence of amino acids in one polypeptide chain
- Gene → Sequence of amino acids → Unique 3D conformation of protein → Function
 → Phenotype
- Components
 - Promoters → Recognistion site for binding of RNA polymerase and general transcription factors to initiate transcription
 - Determine which strand is template strand for transcription
 - Termination sequence → Causes synthesis of RNA to stop
 - Transcription unit
 - Sequence of DNA that is transcribed into RNA
 - Template strand = Non-coding strand → Used in transcription
 - Non-template strand = Coding strand

Central Dogma

- 1. Replication
 - Key molecule: DNA polymerase
 - Location: Nucleus
 - Product: DNA
- 2. Transcription
 - Key molecule: RNA polymerase
 - Location: Nucleus
 - Product: mRNA/tRNA/rRNA
- 3. Translation
 - Key molecule: Ribosomes
 - Location: Rough ER and cytoplasm
 - Product: Polypeptide

The Genetic Code

- 1. Triplet Code
 - Each triplet of nucleotides in mRNA called a codon codes for one amino acid
- 2. Universal
 - Same triplet of nucleotides codes for the same amino acid in <u>all organisms</u>
- 3. Degenerate
 - A given amino acid may be <u>coded for by more than one codon</u>
- 4. Non-overlapping
 - Read as successive groups of 3 nucleotides
- 5. Continuous
 - No nucleotides are skipped between the codons
- 6. Stop and Start sequences

- Start codon, AUG, codes for methionine and signals initiation site of translation of mRNA into a sequence of amino acids
- Stop codons, UAG/UAA/UGA, that do not code for any amino acid and act as stop signals for the termination of polypeptide chain synthesis during translation

Prokaryotes vs Eukaryotes

Point of Comparison	Prokaryotes	Eukaryotes
Protein Factor	Sigma Factor General Transcription Factors	
RNA polymerase and Protein Factor complex	Holoenzyme	Transcription initiation complex
Binding of RNA polymerase	Can bind directly to DNA	Can only bind if there is a general transcription factor
Location	Occurs in the cytoplasm	Occurs in the nucleus before being exported to the cytoplasm for translation
Termination signal	Terminator sequence folds back to form a hairpin loop which acts as the termination signal	Polyadenylation signal (AAUUAAA)
Post-transcriptional modification	No post-transcriptional modification	pre-mRNA must undergo processing to produce mature RNA
5' 7-methylguanosine cap	No 5' 7-methylguanosine cap added	5' 7-methylguanosine cap added to 5' end of pre- mRNA
RNA splicing to remove introns	mRNA of prokaryotes does not contain introns thus, no splicing is required	mRNA of eukaryotes contains both introns and exons thus, splicing is required to excise the introns and join the exons together to form mature

		RNA
3' poly-A tail	No 3' poly-A tail added	3' poly-A tail added to 3' end of pre-mRNA
Degradation	Can be degraded by RNase	5' 7-methylguanosine cap and 3' poly A tail protects mRNA from degradation
Time of events	Transcription and translation occurs simultaneously	Translation can only occur after post-transcriptional modification is completed

DNA Replication vs Transcription vs Translation

Point of Comparison	Replication	Transcription	Translation
Location	Nucleus, Mitochondria, Chloroplast	Nucleus	Cytoplasm
Begins at	Origin of replication	Promoter	Start Codon (AUG)
Ends at	Where 2 adjacent replication bubbles meet/Telomeres	Termination sequence	Stop Codon (UAA/UAG/UGA)
Template	Both strands of DNA	Template strand of DNA	mRNA
Regions used	Entire DNA molecule replicated	Only transcription unit tr anscribed	Entire mRNA molecule translated except for methylguanosine cap and poly-A tail
Monomers	Deoxyribonucleotid es Thymine used	Ribonucleotides Uracil used	Amino Acids
	2 double stranded DNA molecules	1 single stranded	

Products	synthesised each containing one parent strand and one newly synthesised strand	mRNA, tRNA, rRNA molecule synthesised	1 Polypeptide chain synthesised
Product destination	Nucleus	Cytoplasm	Cytoplasm, Cell Membrane, Outside Cell
Complementary base pairing	Adenine and Thymine Cytosine and Guanine	Adenine and Uracil Thymine and Adenine Cytosine and Guanine Guanine and Cytosine	Between Codons and Anticodons
Enzymes involved	DNA polymerase, Helicase, Primase, DNA ligase, Topoisomerase	RNA polymerase	Aminoacyl-tRNA synthetase Peptidyl transferase
Bonds within molecule formed	Phosphodiester bond Hydrogen bond	Phosphodiester bond	Peptide bond
Ribosome involvement	No	No	Yes
Template strand read in	3' to 5'	3' to 5'	5' to 3'
Molecule synthesised in	5' to 3'	5' to 3'	From amino end to the carboxyl end
Proof reading	Yes	No	No
Others	- Single-strand binding proteins - Presence of leading strand and lagging strand	- Spliceosome, Poly-A polymerase, Endonuclease in eukaryotes	

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