OECG

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Tags	

Upstream region

- Consists of promoter/enhancer/silencer

Describe the effects of methylation

- Methylation of residues at CPG Islands, particularly within transcription factor binding sites can physically hinder binding of transcription factors to DNA, blocking activators from accessing the promoter, preventing initiation of transcription and hence prevent gene from being expressed
- Recruit DNA binding proteins which in turn recruit other proteins such as histone deacetylase to the area, causing the chromatin to be compact further, preventing transcription

Why is changes in CpG islands not regarded as mutational changes?

- Do not alter DNA sequence

Outline the roles of non-coding DNA

Non-coding DNA: it codes for non-functional proteins

Telomeres:

- They are non-coding tandem repeat sequences found at both ends of linear chromosomes

- Telomeres determine the senescence(Aging) of cell as DNA polymerase unable to replace the RNA primer sequence at the ends of chromosomes due to absence of free 3OH group, causing the ends of chromosomes to shorten after each round of replication
- Since telomeres are non-coding, this ensures vital genetic information are not lost in each round
- Cells reaching critically short telomere length in one or more if its chromosomes will trigger a stop to its cell proliferation followed by apoptosis, preventing unlimited proliferation of cells
- Telomeres consists of non-coding DNA which protect important genes near the ends of linear chromosomes by providing a disposable buffer for the shortening of DNA after each round of replication due to the end replication problem before it starts losing genetic information
- The t-loop structure protects and stabilises the ends of chromosome, preventing the 3′ overhang from fusing with the ends of other chromosomes and also prevents the ends of chromosomes from being degraded by exonucleases
- The 3′ overhang of telomeres allows their own extension by providing an attachment point for correct positioning of enzyme telomerase

Centromeres:

- Non-coding DNA consisting of tandem repeat sequences found at one location anywhere along the length of chromosome
- Allow sister chromatids to adhere to each other
- They allow kinectochore to attach where microtubules can then attach to kinectochore so that sister chromatid and homologous chromosomes can be separated to opposite poles

Promoter:

- serves as a recognition site Which initiates a series of binding of multiple general transcription factors at the promoter which aid the RNA polymerase to bind to the promoter in the correct orientation, forming the transcription initiation complex to initiate transcription

- It also has critical elements such as TATA box that determines the precise location of transcription start site and CAAT and GC boxes to improve efficiency of promoter by recruiting general transcription factors and RNA polymerase to promoter

Enhancer :

- is a recognition binding site for activator protein which is specific type of transcription factor. Activator proteins then binds to co-activators which will then facilitate binding to general transcription factors and RNA polymerase on promoter, to promote assembly of transcription initiation complex hence increasing the frequency of transcription
- Activators May also recruit histone Acetyltransferase and chromatin remodeling complexes to decondense chromatin so that promoter can be easily accessed by GTF and RNA polymerase, increasing frequency of transcription

Silencer :

- is a recognition binding site for a specific transcription factor, a repressor protein bind to causing the inhibition of transcription by blocking the binding of activator proteins to their respective control elements and by disrupting assembly of the transcription initiation complex
- It may also recruit histone deacetylase and chromatin chromatin remodeling complexes to condense chromatin and RNA polymerase and GTF cannot easily accessed on, decreasing frequency of transcription

Introns:

- Splicing of pre-mRNA involves cutting out introns and joining exons to form a mature mRNA
- Introns are excised and hence non-coding, so mature mRNA comprises of exons which code for sequence of amino acids in a protein
- In alternative splicing of RNA, splices ones are involved in excision of introns and some exons, joining remaining exons to give different combinations of exons

- One gene produces mature mRNA with different combinations of exons, giving different proteins

Explain how DNA methylation and histone acetylation alter gene expression

- DNA methylation involves DNA methyltransferase adding methyl group to cells cytosine in CpG islands in DNA
- Methylated DNA recruits DNA binding protein which in turn recruit histone deacetylases to remove Acetyl groups from the histone proteins causing, restoring positive charge of histone, tighter interactions between histone and DNA causing chromatin to become more condensed restricting accessibility of GTF and RNA polymerase to their respective control promoter, inhibiting transcription
- Histone acetylation invited histone Acetyltransferase adding Acetyl groups from to lysine side chain of histone tails, neutralising its positive charge and the negatively charged DNA backbone, loosening the chromatin structure, allowing general transcription factors and RNA polymerase to access the promoter more readily, promoting transcription

Describe how DNA is packaged

- Negatively charged sugar phosphate backbone of DNA forms electrostatic attractions with positively charged histone proteins, allowing DNA to coil around histone octamers to form 10nm nucleosomes with linker DMA jointing adjacent nucleosomes
- Nucleosomes coil around each other to form a 30nm chromatin fibre which attach to protein scaffold to form 300nm looped domains which further compact into 1400nm metaphase chromosome

Purpose of the sequence within telomerase enzyme

- It is complementary to the 3′ overhang
- Nucleotides of telomerase RNA anneals and forms complementary base pairs with the single-stranded overhang at 3′ end of telomere, aligning the

telomerase reverse transcriptase with respect to DNA

- The RNA sequence within the telomerase acts as template for the new complementary base pairing of new deoxyribonucleotides to form telomeric repeats
- This is so that RNA primer can be added by primase to the extended sequence which in turn allows DNA polymerase to add deoxyribonucleotides to the 3′ OH end of primers via complementary base Pairing (describe what pairs with what)
- Resulting In tandem repeat sequences

Describe activity of reverse transcriptase in the telomerase complex

- telomerase has an active site that is complementary in conformation and charge to a specific telomeric DNA sequence
- Using telomerase RNA as a template, telomerase reverse transcriptase forms a complementary base pairing, catalysing formation of phosphodiester bonds
- Translocation in the 5′ to 3′ direction to produce a series of tandem repeat, elongating DNA at 3′ overhang

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How alternative splicing allows the formation of a number of different functional proteins

- Alternative splicing occurs when introns and one or more exons removed them exons flanking introns are joined together
- producing **different mature mRNAs with different combinations of exons** from the **pre-mRNA**, translation results in different proteins from different mRNAs as templates.
- translation produces polypeptides with **different amino acids sequences,**which **fold differently** to produce proteins with **specific 3D conformations** hence different functions.

How proteasomes remove unwanted proteins

- Proteasomes recognised ubiquitin-tagged protein before cutting the protein into small peptides

How does poly (A) tail regulate gene expression

- prevents mRNA export from nucleus to cytoplasm
- Short poly (A) tail Reduce stability of translation initiation complex/weaken binding of translation initiation factors/ ribosome
- Shorter poly (A) tail reduced mRNA stability/ shorter half life/ causes faster degradation of mRNA by 3′ exonucleases, lesser protein products can be produced

Differences between telomeres and centromeres

	Telomere	Centromere
Location	Located at both ends of a linear chromosomes	Located within a chromosome
Length of tandem repeat	Shorter	Longer
Number of DNA strands	One end of telomeric DNA has a 3′ overhang, other end remains double stranded	Always Double stranded
Association with proteins	Associate with telomere specific proteins such as telomerase to form a cap structure	Associate with kinectochore proteins for separation of chromosomes/ sister chromatids
Function	1. Protect genes near the ends of chromosomes by serving as a buffer 2. Prevent fusion of ends of chromosomes 3. Determine the senescence of cells	1. Hold sister chromatids in a duplicated chromosomes 2. Attaches to the kinectochore microtubules via kinectochore to facilitate Sepration of sister chromatids to opposite poles during anaphase