**Molecular Basis of Inheritance Notes 2019**

**Concept: DNA is the Genetic Material**

Genes are on Chromosomes

T.H. Morgan working with Drosophila (fruit flies) found genes are on chromosomes but is it the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ or the DNA of the chromosomes that are the genes?

-through 1940 proteins were thought to be genetic material… Why?

The “Transforming Factor”

Frederick Griffith used Streptococcus pneumonia bacteria

-was working to find cure for pneumonia

-Used harmless live bacteria mixed with heat-killed infectious bacteria causes disease in mice

substance passed from dead bacteria to live bacteria = “\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Factor”

DNA is the “Transforming Factor”

Avery, McCarty & MacLeod purified both DNA & proteins from Streptococcus pneumonia bacteria

-which will transform non-pathogenic bacteria?

-injected protein into bacteria had no effect

-injected \_\_\_\_\_\_\_\_\_\_\_\_ into bacteria and found transformed harmless bacteria into virulent bacteria

Confirmation of DNA

Hershey & Chase used a classic “blender” experiment. They worked with \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

viruses that infect bacteria which grew phage viruses in 2 media, radioactively labeled with either

35S in their proteins and 32P in their DNA. They infected bacteria with labeled phages

Radioactive phage & bacteria in blender

35S phage -radioactive proteins stayed in supernatant

-therefore protein did \_\_\_\_\_\_\_\_\_\_\_\_ enter bacteria

32P phage

-radioactive DNA stayed in pellet therefore DNA did enter bacteria

-Confirmed DNA is “transforming factor”

Chargaff

DNA composition: “Chargaff’s rules” varies from species to species. All 4 bases not in equal quantity

bases present in characteristic ratio. In humans:

 A = 30.9%

 T = 29.4%

 G = 19.9%

 C = 19.8%

Structure of DNA

Watson & Crick developed double helix model of DNA

-other scientists working on question:

-Rosalind Franklin

-Maurice Wilkins

-Linus Pauling

**Concept: Many Proteins work together in DNA replication and repair**

Copying DNA

Replication of DNA: Base pairing allows each strand to serve as a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ for a new strand

Semi-conservative Replication

 - Meselson & Stahl

-label “parent” nucleotides in DNA strands with heavy nitrogen = 15N

-label new nucleotides with lighter isotope = 14N

 Make predictions…

15N strands replicated in 14N medium

1st round of replication?

2nd round?

The “Central Dogma”

DNA🡪RNA🡪Protein

Directionality of DNA

You need to number the carbons cuz it matters!

The DNA Backbone

Putting the DNA backbone together

refer to the 3’ and 5’ ends of the DNA

-the last trailing carbon

Anti-parallel strands

Nucleotides in DNA backbone are bonded from phosphate to sugar between 3’ & 5’ carbons

-DNA molecule has “direction”

-complementary strand runs in opposite direction

Base pairing in DNA

Purines: adenine (A) and guanine (G)

Pyrimidines: thymine (T) and cytosine (C)

Pairing: A : T which has 2 bonds; C : G has 3 bonds

Copying DNA: Replication of DNA

-base pairing allows each strand to serve as a template for a new strand new strand is 1/2 parent template & 1/2 new DNA

 - Large team of enzymes coordinates replication

Replication: 1st Step

Unwind DNA by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ enzyme

-unwinds part of DNA helix

-stabilized by single-stranded binding proteins

Replication: 2nd Step

Build daughter DNA strand that add new complementary bases using DNA polymerase III

Energy of Replication:

Where does energy for bonding usually come from? ATP!!!!! And others!!!!

The nucleotides arrive as nucleo\_\_\_\_\_\_\_\_\_\_\_\_\_

DNA bases with P–P–P

 P-P-P = energy for bonding

-DNA bases arrive with their own energy source for bonding

-bonded by enzyme: DNA polymerase III

Replication:

Adding bases

-can only add nucleotides to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_end of a growing DNA strand

need a “starter” nucleotide to bond to

-strand only grows 5’-3’

Leading and Lagging Strands:

Limits of DNA polymerase III

can only build onto 3’ end of an existing DNA strand

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand

-Okazaki fragments pieced together

-joined by ligase; “spot welder” enzyme

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand: continuous synthesis

Replication Fork/Bubble:

Starting DNA: RNA Primers:

-The limits of DNA polymerase III is that it can only build onto 3’ end of an existing DNA strand

-RNA primer is built by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. It serves as starter sequence for DNA polymerase III

Replacing RNA Primers with DNA:

DNA polymerase I: removes sections of RNA primer and replaces with DNA nucleotides

But DNA polymerase I still can only build onto 3’ end of an existing DNA strand

Chromosome Erosion:

\_\_\_\_\_\_\_\_\_\_\_\_ DNA polymerases can only add to 3’ end of an existing DNA strand

-Loss of bases at 5’ ends in every replication

-chromosomes get shorter with each replication which limit to number of cell divisions?

Telomeres:

-Repeating, non-coding sequences at the end of chromosomes = protective cap

-limit to ~50 cell divisions

-Telomerase

-enzyme extends telomeres

-can add DNA bases at 5’ end

-different level of activity in different cells

-high in stem cells & cancers -- Why?

DNA Polymerases:

-DNA polymerase III

-1000 bases/second!

-main DNA \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

DNA polymerase I

-20 bases/second

-editing, repair & primer \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Editing and proofreading DNA:

-1000 bases/second = lots of typos!

DNA polymerase I will proofreads & corrects typos

-repairs mismatched bases

-removes \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ bases

-repairs damage throughout life

-reduces error rate from 1 in 10,000 to 1 in 100 million bases

It takes E. coli <1 hour to copy 5 million base pairs in its single chromosome

-divide to form 2 identical daughter cells

Human cell copies its 6 billion bases & divide into daughter cells in only few hours

-remarkably accurate

-only ~1 error per 100 million bases

-~30 errors per \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Concept: A Chromosome Consists of a DNA Molecule Packed Together with Proteins**

Chromosomes:

-A bacterial chromosome is \_\_\_\_\_\_\_\_\_\_\_ double-stranded, circular DNA molecule associated with a small amount of protein.

-Eukaryotic chromosomes are linear DNA molecules associated with large amounts of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

In eukaryotic cells, DNA and proteins are packed together as chromatin.

-As DNA becomes more highly packaged, it becomes less accessible to transcription enzymes, which reduces gene expression.

-In interphase cells, most chromatin is in the highly extended form (\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_) and is available for transcription.

-When the euchromatin condenses to chromosomes during mitotic division, the more condensed chromatin (\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_) is no longer available for transcription.

-Heterochromatin is largely inaccessible to transcription enzymes and thus generally not transcribed.

-Barr bodies are another example of heterochromatin.