Biosynthesis of Nucleotide Co-Enzymes.

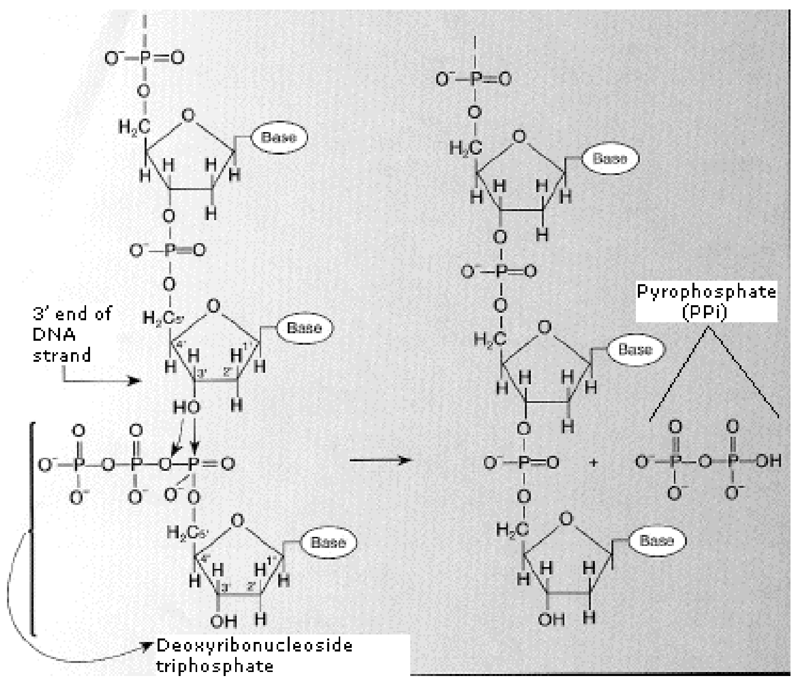
FAD,the pyridine nucleotides(NAD) and Co-enzyme A are derivatives of Adenylic acid.

ASSIGNMENT: Write out the biosynthetic pathway of NAD^{+} and Co-enzyme A.

DNA Replication

Transfer of genetic information from generation to generation requires the faithful reproduction of the parental DNA. DNA reproduction produces two identical copies of the original DNA in a process termed DNA replication.

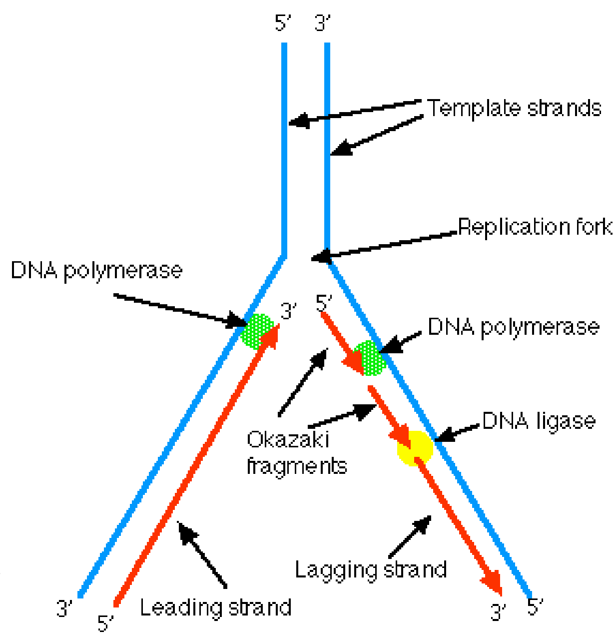
The Biochemical Reactions



- DNA replication begins with the "unzipping" of the parent molecule as the hydrogen bonds between the base pairs are broken.
- Once exposed, the sequence of bases on each of the separated strands serves as a template to guide the insertion of a complementary set of bases on the strand being synthesized.

- The new strands are assembled from **deoxynucleoside triphosphates**.
- Each incoming nucleotide is covalently linked to the "free" 3' carbon atom on the pentose (figure) as
- the second and third phosphates are removed together as a molecule of **pyrophosphate** (**PPi**).
- The nucleotides are assembled in the order that complements the order of bases on the strand serving as the template.
- Thus each C on the template guides the insertion of a G on the new strand, each G a C, and so on.
- When the process is complete, two DNA molecules have been formed identical to each other and to the parent molecule.

The Enzymes



- A portion of the double helix is unwound by a **helicase**.
- A molecule of a **DNA polymerase** binds to one strand of the DNA and begins moving along it in the 3' to 5' direction, using it as a template for assembling a **leading strand** of nucleotides and reforming a double helix. In eukaryotes, this molecule is called DNA polymerase delta (δ).
- Because DNA synthesis can only occur 5' to 3', a molecule of a second type of DNA polymerase (epsilon, ε, in eukaryotes) binds to the other template strand as the double helix opens. This molecule must synthesize discontinuous segments of polynucleotides (called Okazaki fragments). Another enzyme, **DNA ligase I** then stitches these together into the **lagging strand**.

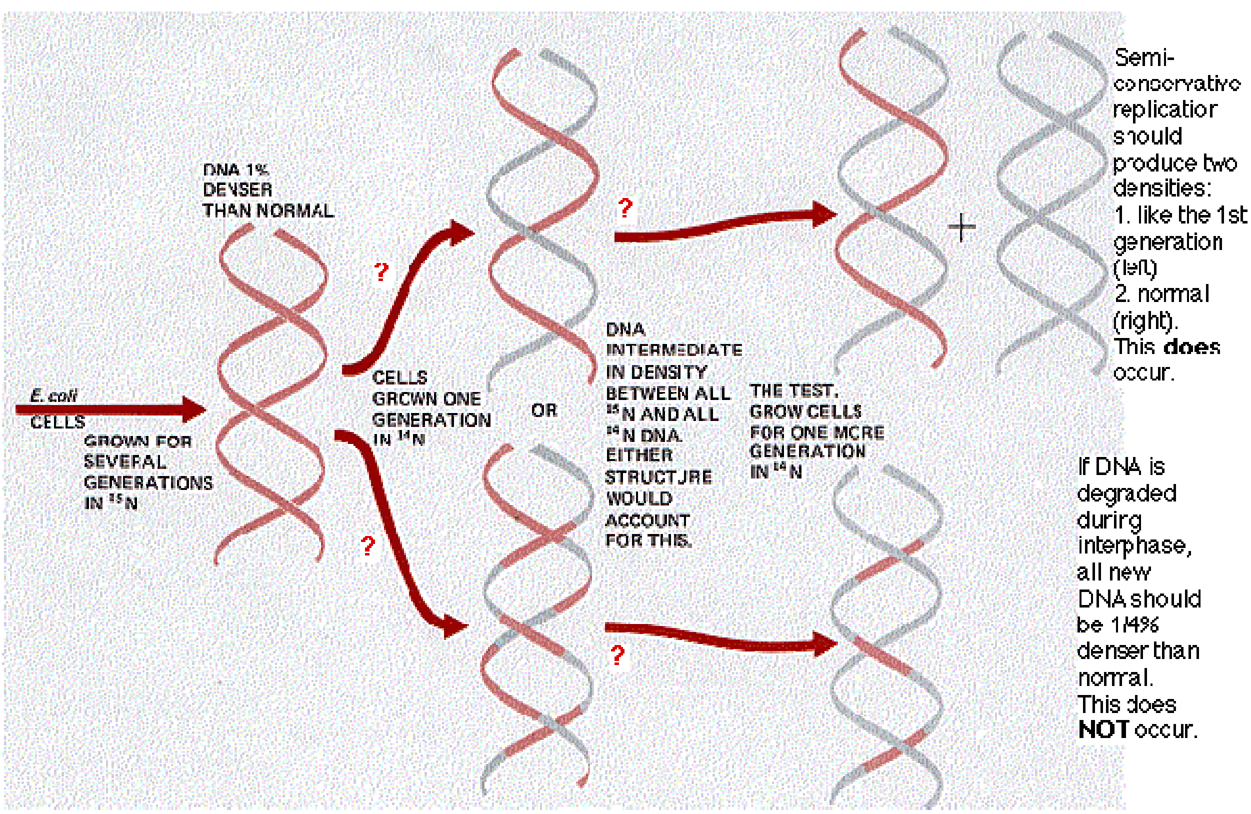
DNA Replication is Semiconservative

When the replication process is complete, two DNA molecules — identical to each other and identical to the original — have been produced. Each strand of the original molecule has

- remained intact as it served as the template for the synthesis of
- a complementary strand.

This mode of replication is described as semi-conservative: one-half of each new molecule of DNA is old; one-half new.

Watson and Crick had suggested that this was the way the DNA would turn out to be replicated. Proof of the model came from the



experiments of Meselson and Stahl.

Transcription and Translation

The majority of genes are expressed as the proteins they encode. The process occurs in two steps:

- **Transcription = DNA → RNA**
- **Translation = RNA → protein**

Taken together, they make up the "central dogma" of biology: DNA → RNA → protein.

Gene Transcription: DNA □ RNA

DNA serves as the template for the synthesis of RNA much as it does for its own replication.

The Steps

- Some 50 different protein **transcription factors** bind to **promoter** sites, usually on the 5□ side of the gene to be transcribed.
- An enzyme, an **RNA polymerase**, binds to the complex of transcription factors.
- Working together, they open the DNA double helix.
- The RNA polymerase proceeds to "read" one strand moving in its 3□ → 5□ direction.
- In eukaryotes, this requires — at least for protein-encoding genes — that the nucleosomes in front of the advancing RNA polymerase (RNAP II) be removed. A complex of proteins is responsible for this. The same complex replaces the nucleosomes after the DNA has been transcribed and RNAP II has moved on.
- As the RNA polymerase travels along the DNA strand, it assembles **ribo**nucleotides (supplied as triphosphates, e.g., ATP) into a strand of RNA.

- Each ribonucleotide is inserted into the growing RNA strand following the rules of base pairing. Thus for each C encountered on the DNA strand, a G is inserted in the RNA; for each G, a C; and for each T, an A. However, each A on the DNA guides the insertion of the pyrimidine uracil (**U**, from uridine triphosphate, UTP). There is no T in RNA.

> Quality control. Occasionally RNA polymerase will select and insert an incorrect, mismatched, ribonucleotide. When this occurs in bacteria (and perhaps in all organisms), the enzyme backs up, removes the incorrect nucleotide (and the one preceding it) and tries again. (Described by Zenkin *et al*., in the 28 July 2006 issue of **Science**.)

- Synthesis of the RNA proceeds in the 5′ → 3′ direction.
- As each nucleoside triphosphate is brought in to add to the 3′ end of the growing strand, the two terminal phosphates are removed.
- When transcription is complete, the transcript is released from the polymerase and, shortly thereafter, the polymerase is released from the DNA.

Note that at any place in a DNA molecule, either strand may be serving as the template; that is, some genes "run" one way, some the other (and in a few remarkable cases, the same segment of double helix contains genetic information on both strands!). In all cases, however, RNA polymerase transcribes the DNA strand in its 3′ → 5′ direction.