Central Dogma

- DNA carries the genetic code and transcribes an RNA copy of the code
- The RNA copy is translated by ribosomes to make protein

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\begin{align*}
\text{DNA} & \quad \xrightarrow{1} \quad \text{RNA} \quad \xrightarrow{2} \quad \text{Protein} \\
\text{Transcription} & \quad \text{Translation}
\end{align*}
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Step 1: RNA SYNTHESIS-TRANSCRIPTION

The process of converting the information contained in a DNA segment into proteins begins with the synthesis of mRNA molecules containing anywhere from several hundred to several thousand nucleotides, depending on the size of the protein to be made.

Each of the 100,000 or so proteins in the human body is synthesized from a different mRNA that has been transcribed from a specific gene on DNA.

Why do we need mRNA if DNA holds all the genetic instructions for the proteins the cell is supposed to produce?

- DNA must be protected...If DNA is damaged in any way, then the coding sequence is changed and a mutation could result which could greatly affect a cell or even the whole organism!

Transcription

- If a protein is required by a cell, that gene is activated (turned on).
- The gene makes an RNA copy of itself in the form of a messenger RNA molecule (mRNA)
- Enzyme RNA polymerase runs along open DNA strand and synthesizes RNA complementary to the DNA
Transcription

• Messenger RNA is synthesized in the cell nucleus by transcription of DNA, a process similar to DNA replication. As in replication, a small section of the DNA double helix unwinds, and the bases on the two strands are exposed. RNA nucleotides (ribonucleotides) line up in the proper order by hydrogen-bonding to their complementary bases on DNA, the nucleotides are joined together by a DNA dependent RNA polymerase enzyme, and a piece of mRNA is produced.

• UNLIKE what happens in DNA replication where both strands are copied, only ONE of the two DNA strands is transcribed into mRNA (remember that RNA is a single-stranded molecule). The DNA strand that is transcribed is called the template strand and is a copy of the DNA informational strand!

Transcription

[Diagram of transcription process]

RNA Polymerase

• Runs along DNA in a 5' to 3' direction (adding bases to the 3' end) and forms mRNA

• Until it hits a STOP signal, falls off and mRNA is released.....DNA reseals...

http://www.ncc.gmu.edu/dna/mRNAanim.htm
How does the RNA pol know where to start reading a Gene?

- The starting point of a gene is marked by a certain base sequence... called a *promoter site*. These sites are recognized by factors (termed "SIGMA") which recognize the promoter sites and "tell" the RNA polymerase where to begin. The RNA polymerase then carries out the process of transcription.

- Similarly, there are other base sequences at the end of a gene that signal a STOP to mRNA synthesis. A factor called "RHO" aids in terminating the process. The interaction of rho with the RNA polymerase causes the enzyme to "fall off" the DNA template strand, thus stopping transcription.

The Genetic Code

If DNA is a long repeating length of...
ACTGAATTGCCCTCATTGCATGGCT

How do you make a useful code???
The Genetic Code

- Based on 3 letter words
- Every 3 nucleotide bases in DNA is a Code...
- In RNA, the 3 complementary bases are a Codon...

The RNA Codon

Remember: RNA travels to cytoplasm to make the protein

- The Codon alphabet consists of 4 nucleotides... AUGC (U replaces T in DNA)
- The words are 3 letter combinations
- How many possible combinations?
  - $4^3 = 64$ possible combinations
- But, what ARE the words being spelled?

The Genetic Code

Every 3 nucleotides on mRNA ‘spell’ for one amino acid

- ACA spells Threonine
- CAC spells Histidine
- GUU spells Valine
- UUA spells Leucine

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**A Redundant Code...**

- The 20 Amino Acids can all be ‘spelled’ with just 20 codons
- But, there are 64 possible codons
- Several triplets account for the same AA...therefore, the code is redundant.
- GUU, GUC, GUA, GUG all ‘spell’ Valine

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**Quiz**

1) What would be the mRNA codon directing a cell to produce a protein beginning with the amino acids, Histidine and Serine?

2) What would be the Corresponding DNA code?

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**How does the Gene end?**

**Stop/Start Codons**

- Also, AUG spells START reading here
- And, UAA spells STOP
- Without a set Start point, the code would be nonsense
The Genetic Code

• The specific sequence of 3 nucleotide bases indicates how a protein is to be constructed
• An mRNA sequence such as: UUU-UUG-GUA-CCC

Means that a protein of Amino Acids… Phenylalanine-Leucine-Valine-Proline is to be made

How to make that Protein? Step 2: Translation

• mRNA is produced in nucleus by RNA pol reading the DNA code
• mRNA travels to cytoplasm where proteins are made… How?
• In a process known as Protein Synthesis or Translation

Translation Requires:

• Message in the form of mRNA...
• A Ribosome…..
• Another type of RNA, called Transfer RNA (tRNA)
• A pool of amino acids in cytoplasm

AA1 AA2 AA3

Free Amino Acids
tRNA...Single stranded RNA which folds into characteristic shape

Job is to carry AA from cytoplasm and drop them into place during protein synthesis

20 different types of tRNA each carry one type of AA...

Translation Process:
Initiation

- Translation is the process of converting the mRNA codon sequences into an amino acid sequence. The initiator codon (AUG) codes for the amino acid N-formylmethionine (f-Met). No transcription occurs without the AUG codon. f-Met is always the first amino acid in a polypeptide chain, although frequently it is removed after translation.
- After the initiation phase the message gets longer during the elongation phase.

Translation: Elongation

- A Ribosome runs along mRNA reading codons, beginning at AUG (Start)
- A tRNA carrying the corresponding AA drops into position and leaves AA off
- New protein emerges from ribosome as a growing peptide chain
**Elongation**

New tRNAs bring their amino acids to the open binding site on the ribosome/mRNA complex, forming a peptide bond between the amino acids. The complex then shifts along the mRNA to the next triplet, opening the A site. The new tRNA enters at the A site. When the codon in the A site is a termination codon, a releasing factor binds to the site, stopping translation and releasing the ribosomal complex and mRNA.

*Text pg 228*
Polysomes...

Often many ribosomes will read the same message and a structure known as a polysome forms. In this way a cell may rapidly make many proteins.

Control of Genes:
The Operon Model

The operon model of prokaryotic gene regulation was proposed by François Jacob and Jacques Monod...
Groups of genes coding for related proteins are arranged in units known as operons. An operon consists of an operator, promoter, regulator, and structural genes.
The regulator gene codes for a repressor protein that binds to the operator, blocking the promoter and thus blocking transcription of the gene.
If the repressor protein is removed, transcription may again occur.

Such regulatory proteins recognize and bind to specific DNA sequences and can either turn-on or turn-off genes.
According to the Central Dogma, all cells transcribe RNA from DNA and translate proteins from mRNA. In Bacteria, control of protein synthesis is at the level of transcription. That is, mRNA is only transcribed when a protein is needed; when a protein is not needed, the mRNA is not made.

Because the enzyme, RNA polymerase, carries out transcription, bacteria have a number of ways to either help RNA polymerase or stop it from doing its job. This is done by using regulatory proteins that bind to DNA near promoter regions. These regulatory proteins switch back and forth between active and inactive conformations (shapes). In the active shape, the regulatory proteins bind to DNA; in the inactive shape, they cannot bind DNA.