From gene to protein

Premedical biology
Central dogma

of Biology, Molecular Biology, Genetics

replication

transcription

reverse transcription

translation

DNA

RNA

Protein
RNA

- chemically similar to DNA, except it contains **ribose** instead of deoxyribose and **uracil** instead of **thymin**
- almost always consist of a **single strand**
- less stable
RNA

- some molecules are able to **self-replicate**
- mistakes in replication bring a variability = **family** of closely related RNA sequences
- some molecules are able to **self-catalyse**

example:

**Ribosyms** (ribosome, spliceosome)

**Coenzymes** - some are **ribonucleotids**, rRNA, mRNA
Table 17.1 Types of RNA in a Eukaryotic Cell

<table>
<thead>
<tr>
<th>Type of RNA</th>
<th>Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Messenger RNA (mRNA)</td>
<td>Carries information specifying amino acid sequences of proteins from DNA to ribosomes.</td>
</tr>
<tr>
<td>Transfer RNA (tRNA)</td>
<td>Plays catalytic (ribozyme) roles and structural roles in ribosomes.</td>
</tr>
<tr>
<td>Ribosomal RNA (rRNA)</td>
<td>Plays structural and catalytic (ribozyme) roles in ribosomes.</td>
</tr>
<tr>
<td>Primary transcript</td>
<td>Serves as a precursor to mRNA, rRNA, or tRNA and may be processed by splicing or cleavage. In eukaryotes, pre-mRNA commonly contains introns, noncoding segments that are spliced out as the primary transcript is processed. Some intron RNA acts as a ribozyme, catalyzing its own splicing.</td>
</tr>
<tr>
<td>Small nuclear RNA (snRNA)</td>
<td>Plays structural and catalytic roles in spliceosomes, the complexes of protein and RNA that splice pre-mRNA in the eukaryotic nucleus.</td>
</tr>
<tr>
<td>SRP RNA</td>
<td>Is a component of the signal-recognition particle (SRP), the protein-RNA complex that recognizes the signal peptides of polypeptides targeted to the ER.</td>
</tr>
</tbody>
</table>
Transcription and translation

In Bacterial cells

transcription and translation is **coupled**. mRNA is immediately translated without processing.

In Eukaryotic cell

The nucleus provides a separate compartment for transcription. The pre-mRNA is processed in various ways before leaving nucleus as mRNA. Translation of eukaryotes occurs in **cytoplasm**.
Transcription - eukaryotic

- Synthesis of RNA under direction of DNA
- Information is simply copied from one to another according to complementarity of bases
- enzyme RNA polymerase (RNAP)

- beginning = promoter with initial code
- Initiation, elongation, termination phases with specific transcription factors (TF)
Promotor

Typical promoter region for a protein-encoding eukaryotic gene. The promoter is sequence, where RNAP binds the DNA.
RNA processing – in nucleus

- The template strand is used as a template for RNA synthesis.
- The product is pre-mRNA primary transcript (eukaryotic cells).
- 7methyl guanosin cap is added immediately to 5’ end for protection from degradation by hydrolytic enzymes and serves as „attach“ sign (mark) for ribosomes.
- poly(A) tail - polyadenylation of 3‘ end, which inhibit degradation of the RNA.
primary transcript = pre-mRNA

RNA processing
RNA processing - nucleus

- **exons** = encoding parts
- **introns** = non-encoding parts, which are cutted out
- cut and paste job = **splicing**
- during the **RNA processing** is created messenger RNA – mRNA
- **snRNPs** = spliceosome cut and regulate
Translation

eukaryotic in cytoplasm

Initiation, elongation, termination phase with specific factors

Translation requires ribosomes, GTP translation factors

Origin of peptide bond – new amino acid and carboxyl end

the former amino acid
Ribosomes

- **subunits: proteins and ribosomal RNA** (made in nucleolus (eu))
- facilitate specific coupling of anticodons in tRNA with codons in mRNA
- Amino acid is added to the growing end of a polypeptide chain in ribosome.
tRNA

mRNA sequences represent codons.

Interpreter is transfer RNA, which transfers amino acids to ribosome.

Nucleotide triplet called anticodon (in tRNA) links a particular mRNA codon.
Aminoacyl tRNA-synthetase

20 enzymes, which joins a specific amino acids to a tRNA at the expense of hydrolysis of ATP. They create covalent attachment of amino acids to its tRNA.
The triplet code

Triplet code means three nucleotides in particular order.
Genetic code
nucleotide triplets specify amino acids

We have 4 nucleotides together, which specify according to base-pairing rules 20 amino acids in the form of **triplets**.
Genetic code is almost universal. The system is shared by the simplest bacteria to the most complex plants and animals. The genetic code must have evolved very early in the history of life.

**AUG** for methionin and it is Initial codon. **AUG** for formyl-methionin in prokaryotes. Initial codon is common for all proteins of all organisms.
Termination codons:

UAG, UGA, UAA

(stop signals). These codons mean stop of translation, no amino acid is incorporated into peptide chain.

Genetic code is degenerated

61 of 64 triplets code for 20 amino acids. There is redundancy, and it is not random.

Codons for the same amino acids differ in third base of triplet.
Number of tRNAs is 45, some tRNAs have anticodons, that can recognize two or more different codons.

Important is correct reading frame.

Mutation as deletion or duplication (more or less than three triplets) change reading frame = frame shift mutations.
Comparing protein synthesis in prokaryotes and eukaryotes

It is very similar, but with certain differences.

There are **different polymerases**. Euk. transcription depends on transcription factors. **Ribosomes are different.**

Transcription and translation simultaneously run at the same gene and protein (at the same time and place) in Prokaryotes.

Nuclear envelope **segregates transcription and translation** in Eukaryotes.

Processing stages provide ways to regulate and coordinate proteosynthesis and gene expression in eukaryotic cells.
Polyribosomes – in prokaryotes

Polyribosome (or polysome) is a cluster of ribosomes, bound to one mRNA molecule and read one strand of mRNA simultaneously.

ORFs
From polypeptide to functional protein

One gene encodes one polypeptide, tRNA, rRNA

Genes determine the primary structure, the primary structure determines the conformation.

Coiling and folding are spontaneous actions given by chemical properties or aminoacids. Helpful are small specific proteins called chaperones.

Posttranslational modifications: certain amino acid are modified by attachment of sugars, lipids, phosphate groups.

Two or more polypeptides may join to become the subunits of a protein.
Synthesis of proteins with defined posttranslational modifications using the genetic noncanonical amino acid incorporation approach.
Protein structures

*Primary structure:* amino acid sequences

*Secondary structure:* local structures stabilized by hydrogen bonds. The most common examples are the *alpha helix, beta sheet and turns.*

*Tertiary structure:* the overall shape of a single protein molecule; most commonly the formation of a hydrophobic core, but also through salt bridges, hydrogen bonds, disulfide bonds. The tertiary structure is what controls the basic function of the protein.

- also synonymous with the term *fold*

*Quaternary structure:* the structure formed by several protein molecules (polypeptide chains), usually called *protein subunits* in this context, which function as a single protein complex.
Levels of Protein Structure

(a) Primary structure
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure
Thank you for your attention