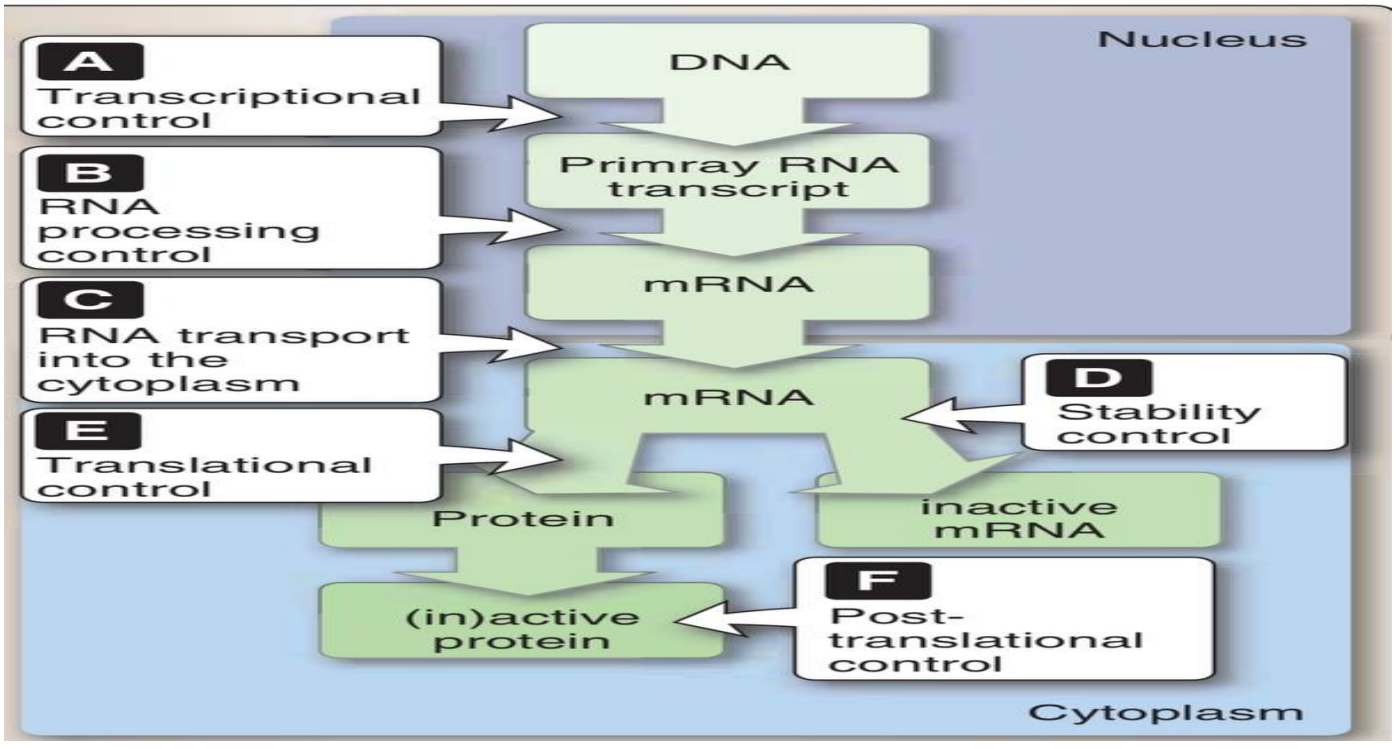
Gene Expression and Regulation

Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product. Products are often proteins and Non-protein coding genes such as ribosomal RNA (rRNA), transfer RNA (tRNA) or, the DNA sequence within each somatic cell contains the information required to synthesize thousands of different proteins and RNA molecules.

Stepwise Regulation of Gene Expression

There are several potential sites for regulation starting with DNA and transcription to posttranslational modification of a newly synthesized protein. While epigenetic changes to the genome involve both chemical and structural modifications to the chromatin and DNA, processing and transport of the newly synthesized mRNA into the cytoplasm are also regulated. In the cytoplasm, the stability of the mRNA can be controlled, as well as its translatability. Most proteins are modified after translation and this can control their activities



Regulation of gene expression can occur at different levels.

A. Transcriptional control

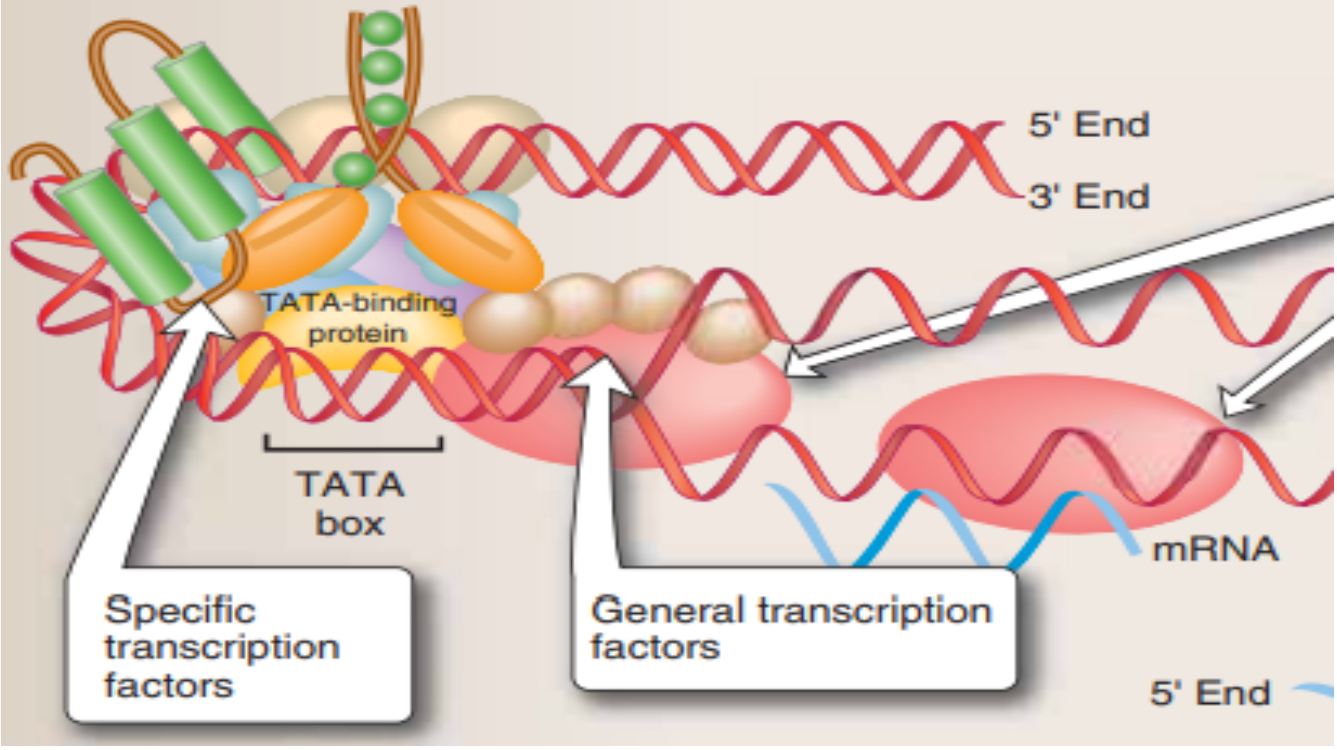
When and how often a gene sequence is copied into RNA is termed transcriptional control and this occurs at two levels:

• Structural-chemical modifications convert compacted chromatin into a less tightly coiled DNA structure, allowing access by transcription factors required for gene expression.

• DNA-binding proteins, known as transcription factors, modulate gene expression to turn transcription on or off. There are two categories of transcription factors, general (or basal) and specific.

1. General (basal) transcription factors: General transcription factors are proteins that assemble on all genes transcribed by RNA polymerase II. These transcription factors are important for activate RNA polymerase II at the start of a protein-coding sequence .

2. Specific transcription factors: Specific transcriptional factors or gene regulatory proteins are present in very few copies in the individual cells and perform their function by binding to a specific DNA nucleotide sequence and allowing the genes that they control to be activated or repressed . These proteins recognize short stretches of double-stranded DNA of defi ned sequence and thereby determine which of the thousands of genes in a cell will be transcribed.



Transcription factors are needed for transcription.

B. RNA processing control

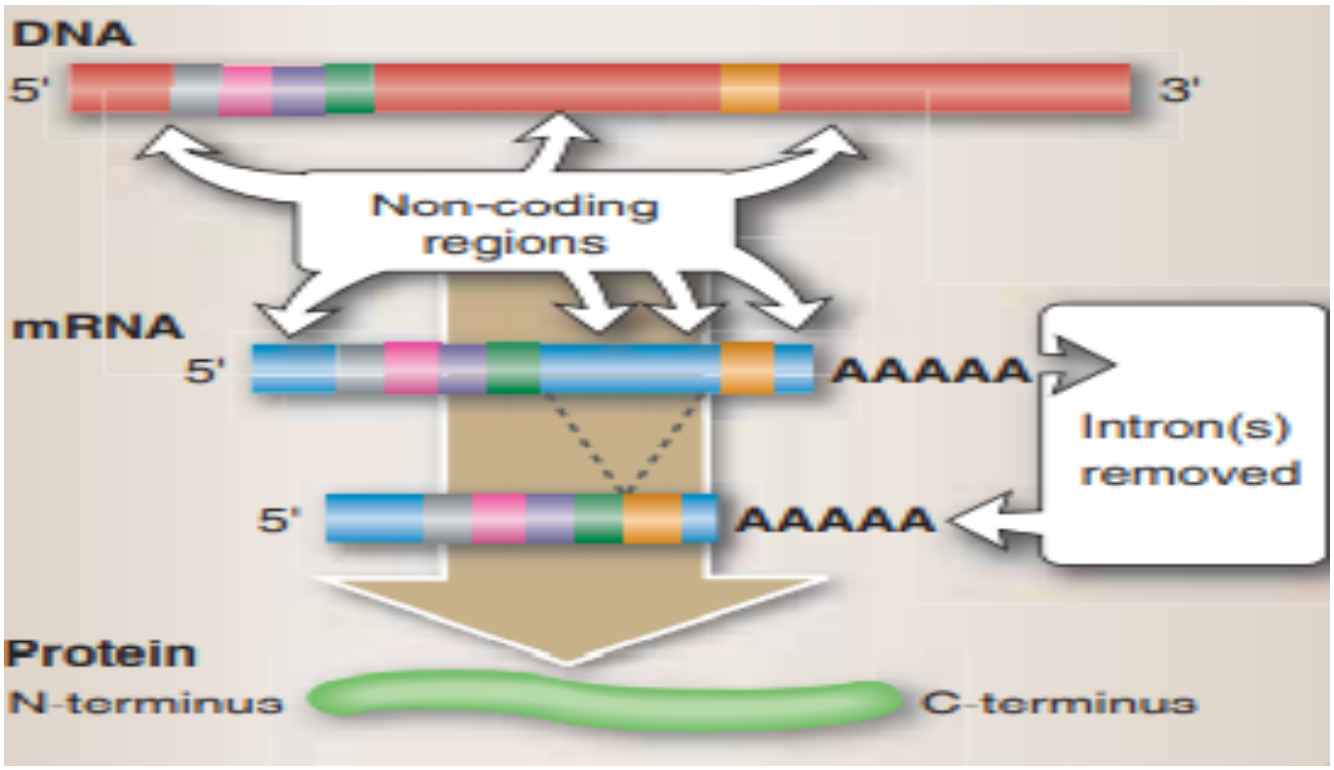
The primary transcript is produced as heterogeneous nuclear RNA containing introns which are eventually spliced out to create the mature mRNA. This process occurs in the nucleus and the subsequent processing is necessary to control the number of mRNA molecules that are eventually translated.

1. mRNA capping: The addition of the 5′ cap structure is critical for an mRNA to be translated in the cytoplasm and is also needed to protect the growing RNA chain from degradation in the nucleus by 5′ exonucleases.

2. Poly(A) tail: The second modification of an mRNA transcript occurs at its 3′ end, the addition of a poly(A) tail (approx. 200 adenine nucleotide residues are added). The

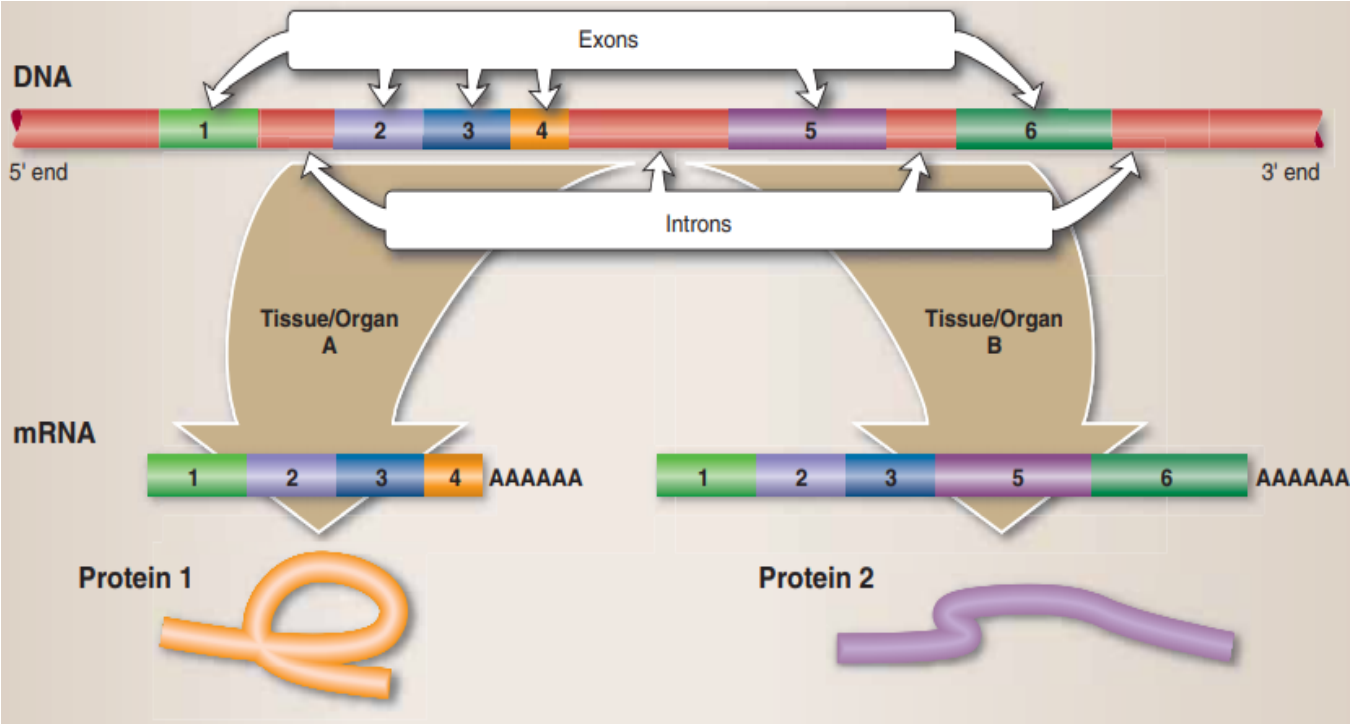
polyadenylation reaction is an important regulatory step because the length of poly(A) tail modulates both mRNA stability and translation efficiency. The poly(A) tail protects the mRNA from premature degradation by 3′exonucleases.

3. Removal of introns: Following the modification of the 5′ and 3′ ends of the primary transcript, the noninformational intron segments are removed and the coding exon sequences joined together by RNA splicing. The specificity of exon joining is conferred by the presence of signal sequences marking the beginning (5′ donor site) and the end (3′ acceptor site) of the intron segment. As these signal sequences are highly conserved, alterations in these sequences can lead to aberrant mRNA molecules.



RNA processing reactions.

4. Alternative splicing: The ability of the genes to form multiple proteins by joining different exon segments in the primary transcript is called alternative splicing. Alternative splicing is made possible by changing the accessibility of the different splice sites to the splicing machinery by RNA binding proteins. These proteins could mask preferred splice sites or change local RNA structure to promote the splicing of alternate sites. In addition, cell specific regulation can determine the type of alternate transcript and eventually the protein product produced. RNA splicing also allows switching between the production of nonfunctional and functional proteins,. The ability to make more than one protein product from a gene may also explain why the human genome has fewer genes than expected .



Alternative splicing of genes to generate multiple proteins.