SUMMING-UP

1 Gene regulation in prokaryotes

- In all cells, certain proteins are produced at a relatively constant rate; others are produced only when necessary. In the second case, **control of gene expression** is regulated in a very precise way.
- In prokaryotes the control of gene regulation occurs above all during the *transcription phase*: an inactive gene is not transcribed and (temporarily) is unable to produce the protein it encodes; an active gene, however, is transcribed and translated immediately.
- The model that explains the regulation of transcription in prokaryotes is called **operon**.
- The operon is comprised of a number of inter-related **structural genes**: the **promoter**, which is the sequence of DNA to which RNA polymerase attaches at the time of transcription; and the **operator**, a sequence of DNA that can bind a regulatory protein called the **repressor**.
- The action mechanisms of the repressor take two forms:
  a) in some operons, the repressor permanently blocks the operator and is removed only when a specific molecule called the **inducer** arrives from the outside,
  b) the repressor acts only in the presence of an external molecule, the **corepressor**, which enables it to bind to the operator. The corepressor then **activates** the repressor.

2 Initial regulation of transcription

- In multicellular eukaryotic organisms, gene regulation is the basis of **cell differentiation**: while sharing the same gene, an individual's somatic cells actually express the gene in different ways depending on the function they perform.
- In eukaryotic organisms certain gene regulation mechanisms can intervene before a gene is transcribed into the corresponding mRNA. These mechanisms are based on a *change in the structure of chromatin* carried out by **protein remodelling**. According to recent studies, about fifty enzymes may be responsible for the remodelling of chromatin.
- In an analogous way, the transcription of entire chromosomes can be prevented, for example by one of the two female X chromosomes.

3 Regulation during transcription

- The mechanisms for the regulation of gene expression in eukaryotes are more numerous and complex than for bacteria. Unlike prokaryotic cells, in fact, eukaryotic cells are able to increase or decrease transcription.
- **Differential transcription** of genes is one of the ways in which eukaryotic organisms vary the amount of protein produced according to need. The **transcription rate** of genes is modulated by the existence of specific DNA sequences and specific proteins.
- Genes that have coordinate functions in eukaryotes can be regulated together, although being situated at some distance on a chromosome, due to the existence of common **regulatory sequences**.
- Finally, if it is necessary to increase the production of one protein over another, the cells can use **gene amplification**. This process involves the creation of multiple copies of the same gene that are all transcribed. By increasing the rate of transcription, the cell also increases the rate of protein synthesis.

4 Regulation following transcription

- Genes that code for proteins and the sequences necessary for the control of gene expression represent, as a whole, only a quarter of the entire human genome.
- The non-coding nucleotide sequences are present both between one gene and another, and also within some genes. These interruptions in the gene are called **introns** and separate sequences of the gene, called **exons**, which code for each part of the polypeptide chain. The genes that exhibit both introns and exons are called **interrupted genes** (or **split genes**). About half of human genes are **interrupted genes**.
- The production of mRNA from an interrupted gene requires, in addition to transcription, an additional step: **RNA splicing**. This process consists of the cutting and removal of introns from pre-mRNA and the joining together of the exon sequences.
- A similar mechanism underpins a process of gene expression regulation that occurs after transcription: **alternative splicing**. In this case, from a single pre-mRNA, depending on the exons that are deleted, different proteins are obtained.

SUMMING-UP

5 Adjustment during and after translation

- Regulation of protein production can also occur *after the mRNA has been transcribed* and reworked (or elaborated). In mammals, only about 1/20 of the total mass of transcribed mRNA leaves the nucleus; specific enzymes degrade the remainder.
- In eukaryotic cells there are many mechanisms that regulate gene expression that takes place after the mRNA has migrated from the nucleus to the cytoplasm, at the time of the translation of a protein (**translational controls**), or even after they have been synthesised (**post-translational controls**).
- Post-translational control mechanisms mainly concern the residence time of the protein inside the cell. The action of the protein becomes limited by its degradation or through chemical modifications to its structure that affect its functionality.