

Although some studies suggest that the consequence of different isoelectric profile mostly concerns the neoantigenicity risk, it seems that this phenomenon rather impacts the half-life of the molecule, which will be more or less rapidly eliminated by the receiving patient body. Indeed, the sugar chains, notably depending on their sialic acid capping, protect the protein from capture and degradation by hepatic cells.

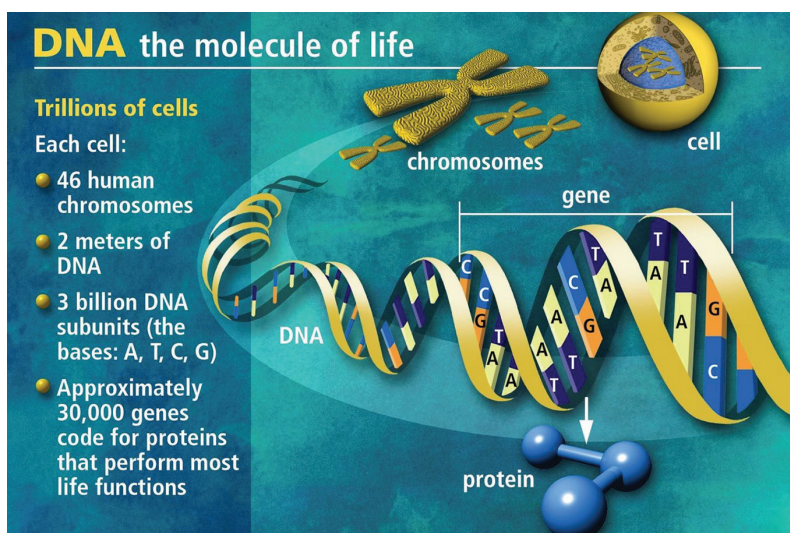
Thus, a recombinant protein will have to have an adapted glycosylation, as well as a correct sialic acid level (in the NANA form), to not to be eliminated too quickly and keep a sufficient pharmacological activity and reduce any potential to generate in patients a defense reaction with the formation of antibodies to the protein of interest.

Whereas the molecules with PTM may have one species forming most of the protein component, the other glycans and components may be just as important in determining the final activity of the product. For example, erythropoietin (EP) specification states that it should have specific distribution ranges for its eight isoforms to be similar to the reference standard.

## 9.6 Protein Expression Variability

A clear understanding of how the recombinant DNA technique works is necessary for the understanding of factors that may contribute to protein structure variability, besides the inherent properties as described previously. The genes are DNA portions carrying a message that ultimately leads to the production of proteins. They are present in genomes of all living creatures and are sequences of nucleotides (A, T, G and C). Each of these genes' sequence is specific for a protein (Figure 9.13).

Cells transcribe the genes (DNA) into mRNA, which in turn are translated into proteins. These steps are represented in the sequence shown in Figure 9.14.



**FIGURE 9.13** Structure of DNA. (From [http://freepages.genealogy.rootsweb.ancestry.com/~ncscotts/GG/DNA\\_Gallery.htm](http://freepages.genealogy.rootsweb.ancestry.com/~ncscotts/GG/DNA_Gallery.htm).)