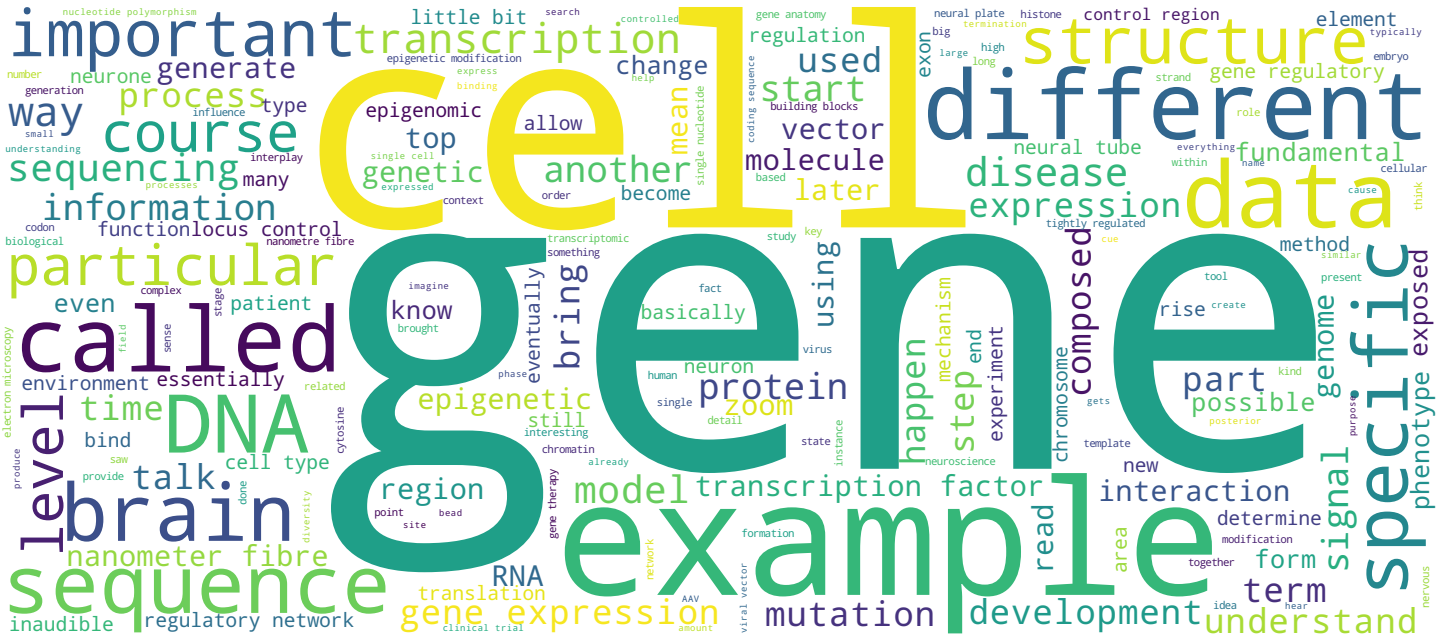

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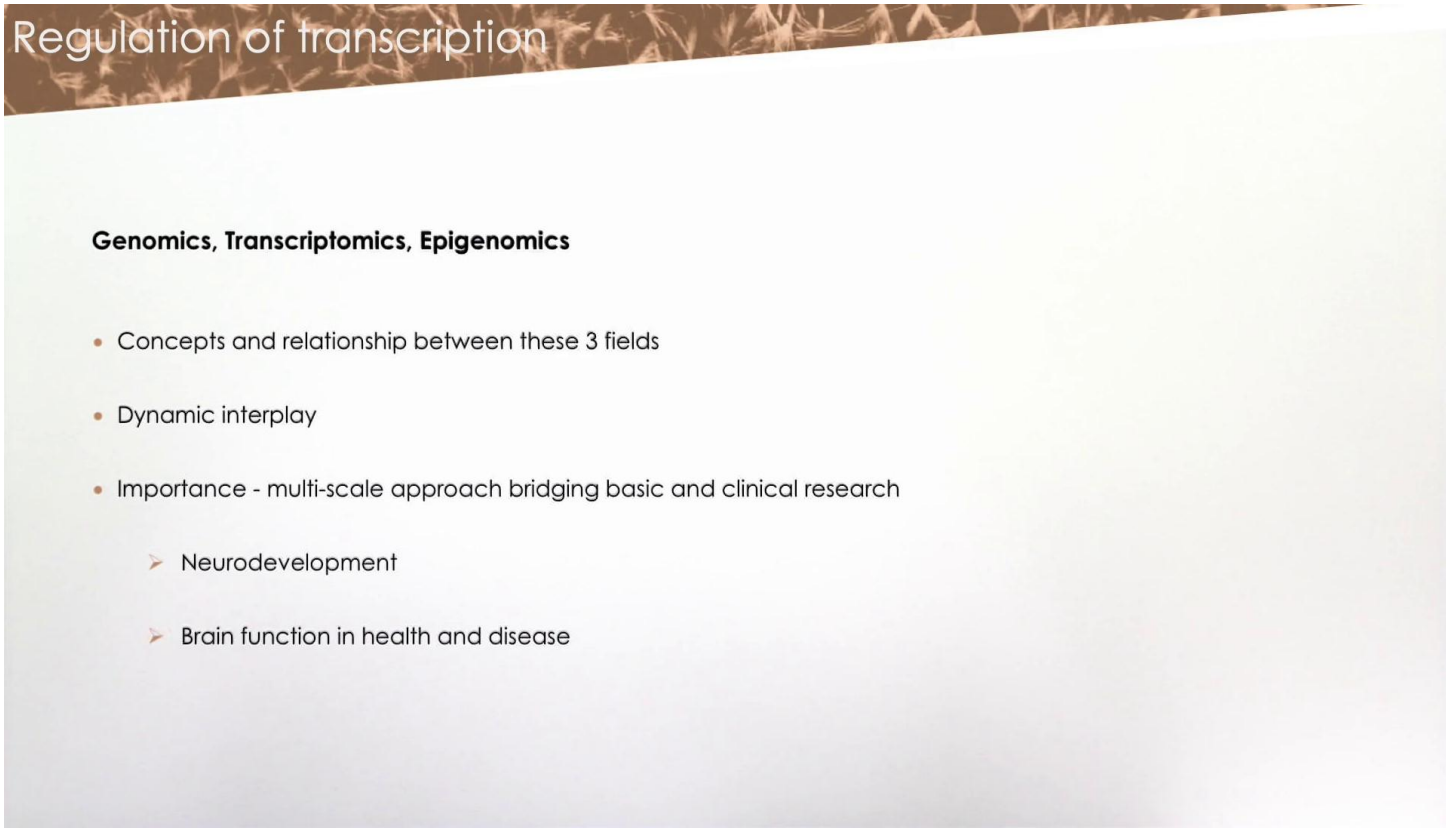
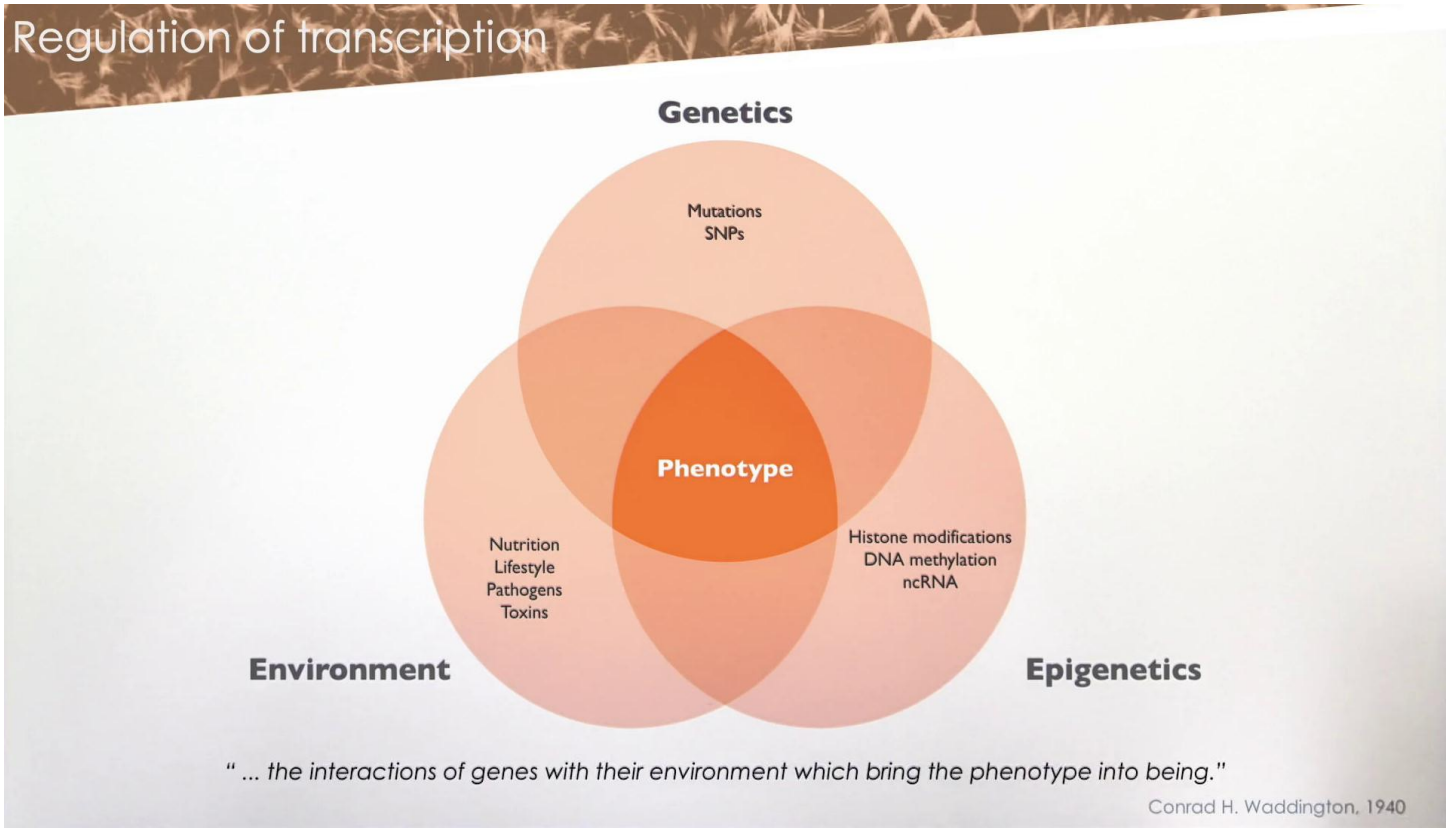


When we talk about 21st-century neurogenetics, it is important to understand that we cannot talk about genetics alone. We really have to talk about the interplay between genomics, transcriptomics, and epigenomics. This is because with the exception of a few monogenetic diseases such as sickle cell anaemia or Huntington's disease, a brain disorder, it is rather rare that we have one gene that causes one phenotype and one disease. It is rather that we have the interaction of genes that give rise to a certain phenotype on the transcriptome level, and that this is all regulated by epigenomics. It is important to understand that there is an intricate relationship between these three fields. There's a dynamic interplay, and altogether, this brings up a multiscale approach that bridges basic and clinical research. This fact that genomics gives rise to transcriptomics, which is regulated by epigenomics, is particularly important for neurodevelopment and also for brain function in health and disease.

Notes

Summary

0m 09s

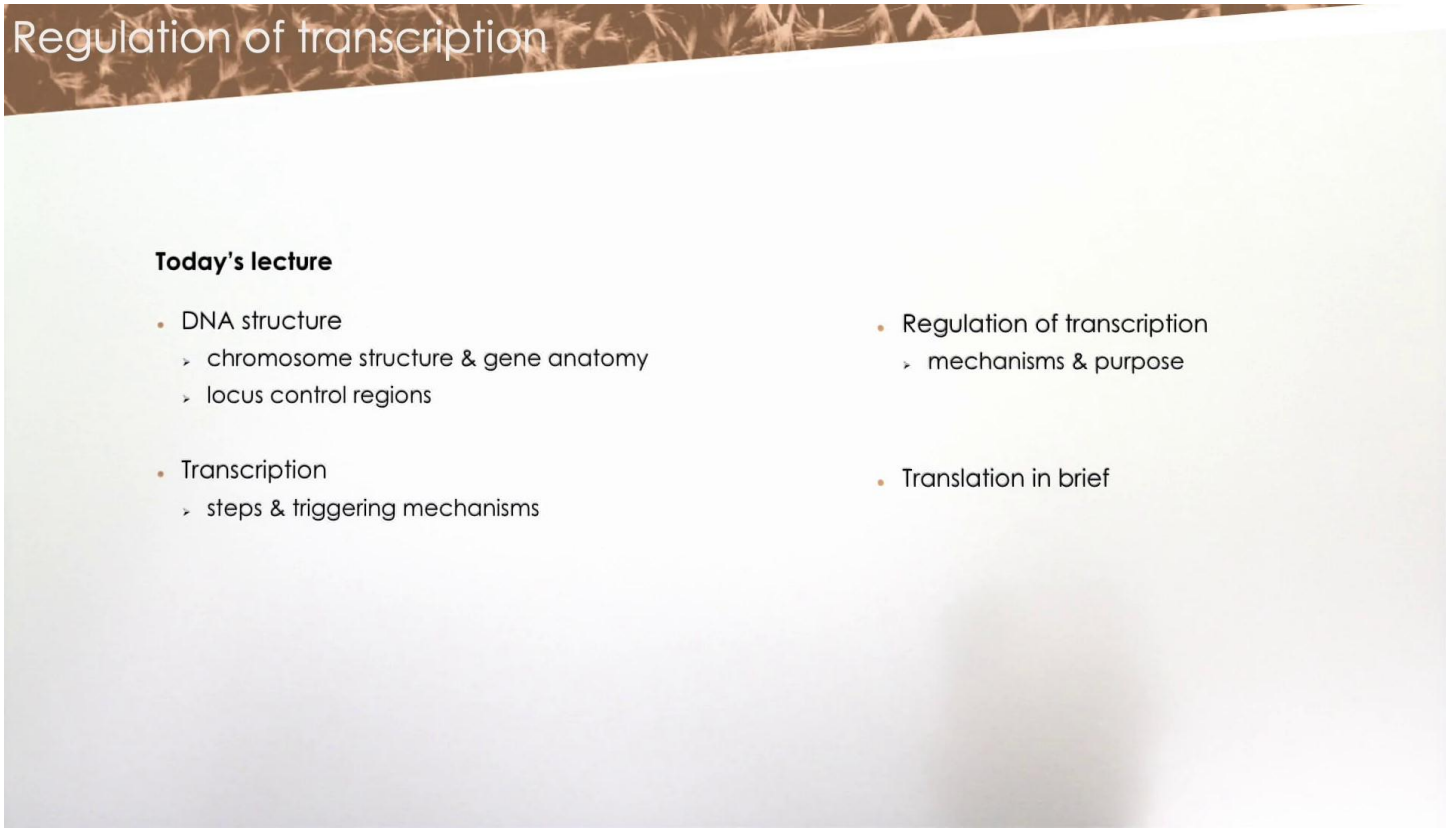


Then what is really neurogenetics? Neurogenetics is really the interplay between three different pillars. On the top, we have genetics, which can be brought about by point mutations or single-nucleotide polymorphisms or SNPs. On the bottom left, we have the environment, which is everything we do, essentially, and every environment that the cell is exposed to. This can be our nutrition, our lifestyle, pathogens we're exposed to, and also toxins we're exposed to. Finally, the third pillar are the epigenetic modifications in terms of post-translational histone modifications, in terms of DNA methylation, and in terms of non-coding RNAs. And it is really the epigenetics that bring the phenotype into being. So the epigenetics is really the interaction of genes with their environment, which bring the phenotype into being, as was proposed already in 1940 by the developmental biologist Conrad Waddington.

Notes

Summary

1m 20s

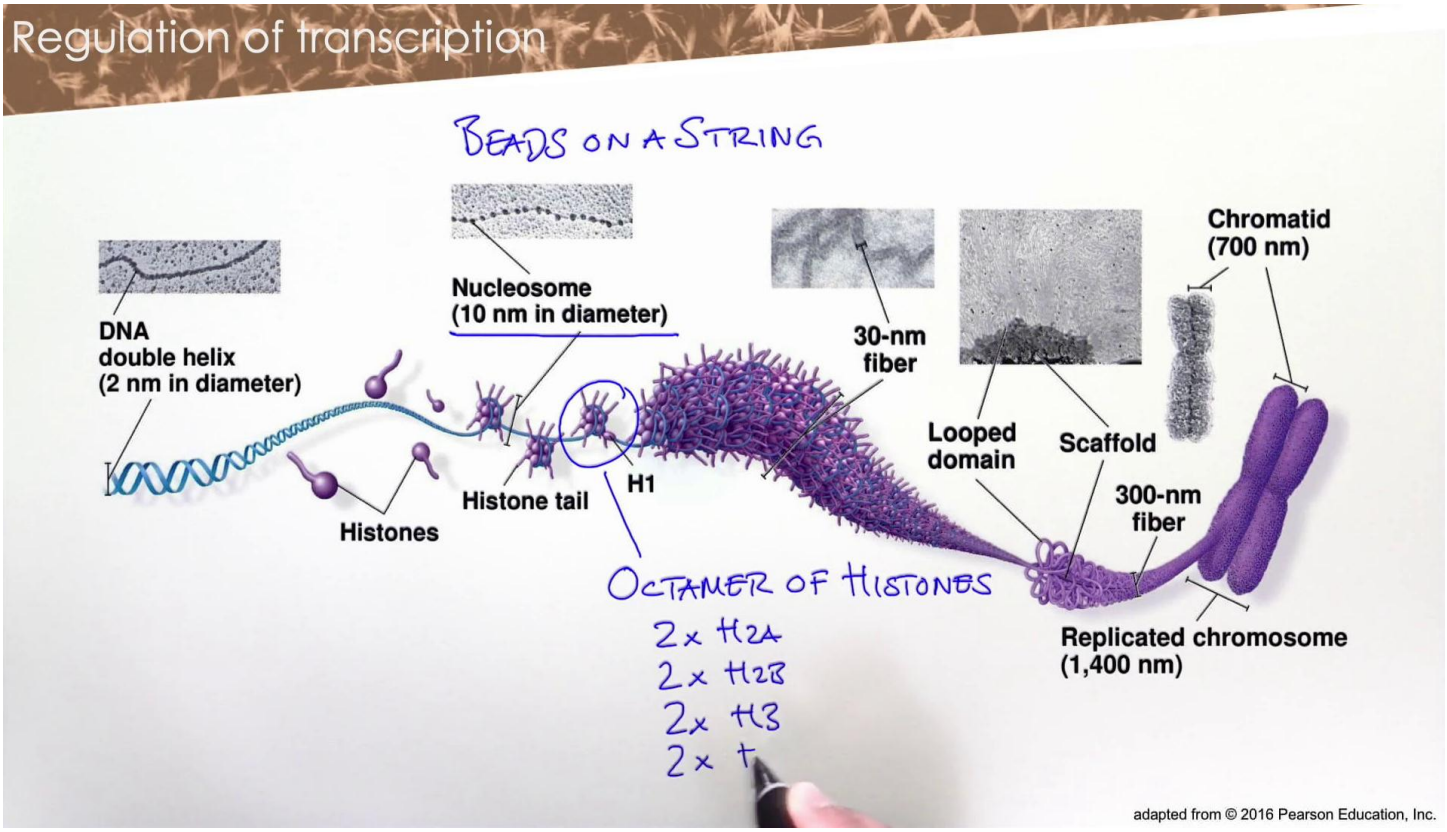


What we're going to cover today is really the structure of the DNA for one. When we talk about the DNA, we also mean the chromosome. We also mean gene anatomy. We will hear about the concept that is called the locus control region. Furthermore, we're going to see steps and triggering mechanisms of transcription. We're going also to see how transcription can be tightly regulated, its mechanisms and its purpose. Finally, we're going to end with a brief introduction of what is translation, which is the final step that brings a gene from its genetic form into a protein form, and which is then the effector state.

Notes

Summary

2m 27s

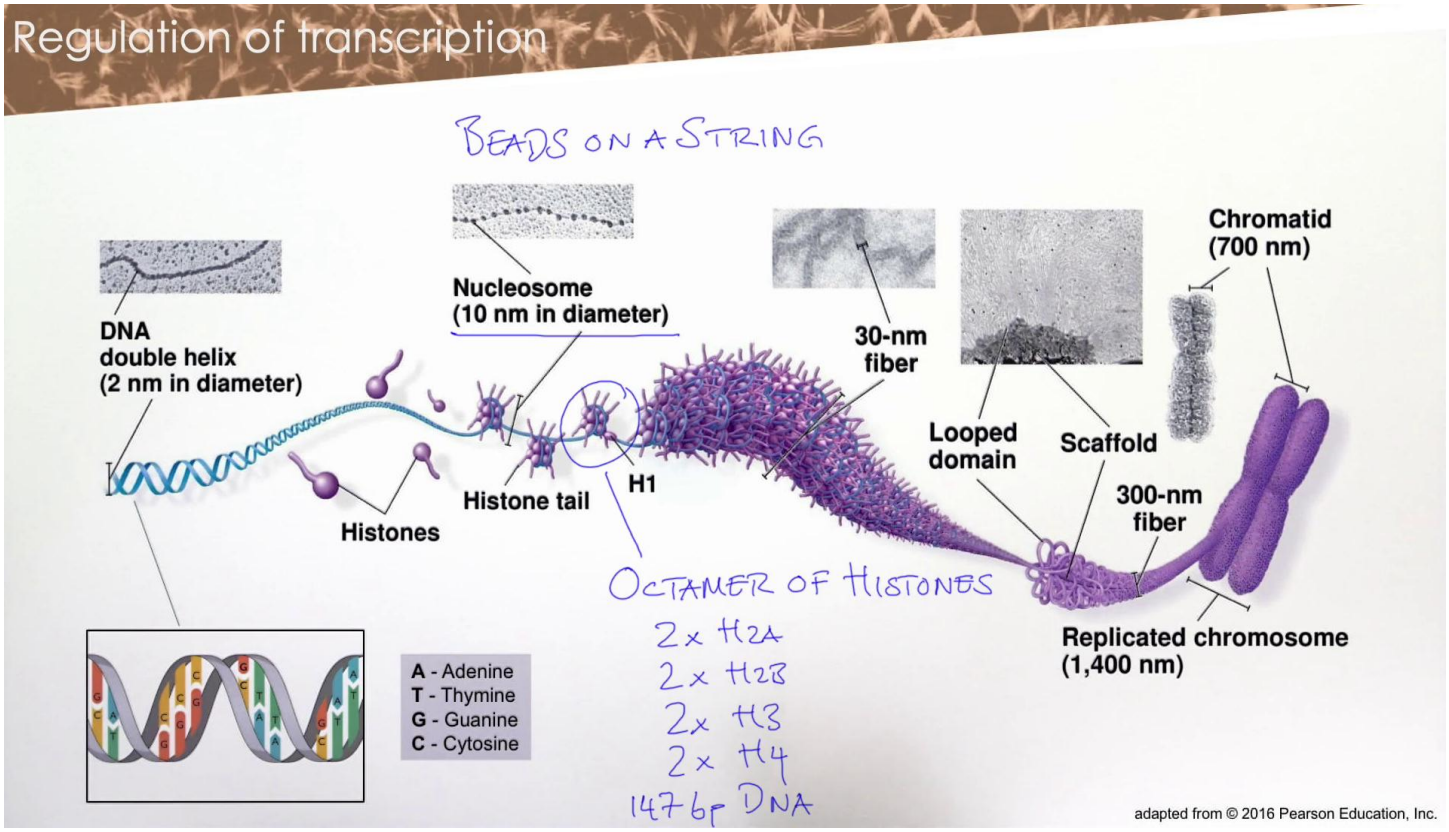


What are the building blocks of a gene? The building blocks of a gene are really the chromosome. On the right side here, we can see that in its replicated form, we can see a very characteristic structure that is 1.4 micrometres in diameter, which is composed of two sister chromatids. But if we zoom into this structure a little bit further, we can see that it is actually a compilation of different tightly regulated structures. For instance, we have the 300-nanometre fibre here that is composed by a scaffold and looped domains. And if we are to zoom into this 300-nanometre fibre even further, we can see by electron microscopy up here that there's a very characteristic 30-nanometer fibre. When we zoom into this 30-nanometer fibre, we can see another fibre which is essentially compiled upon each other to form this 30-nanometer fibre. And this is the 10-nanometer fibre here that is called beads on a string. What composes this beads on a string structure is a structure that is called the nucleosome, which is essentially an octamer of histones. And we have two times each of the following proteins, H2A, H2B, H3, and H4.

Notes

Summary

3m 11s



Together they form this nucleosome structure, which we can see here in electron microscopy, around which the DNA, and more precisely, 137 base pairs of DNA are wrapped around. Then on the far left side, we have, of course, the naked DNA that is composed of a double helix and our four bases, which are adenine, thymine, guanine, and cytosine that are paired with one another by Watson-Crick base pairing.

Notes

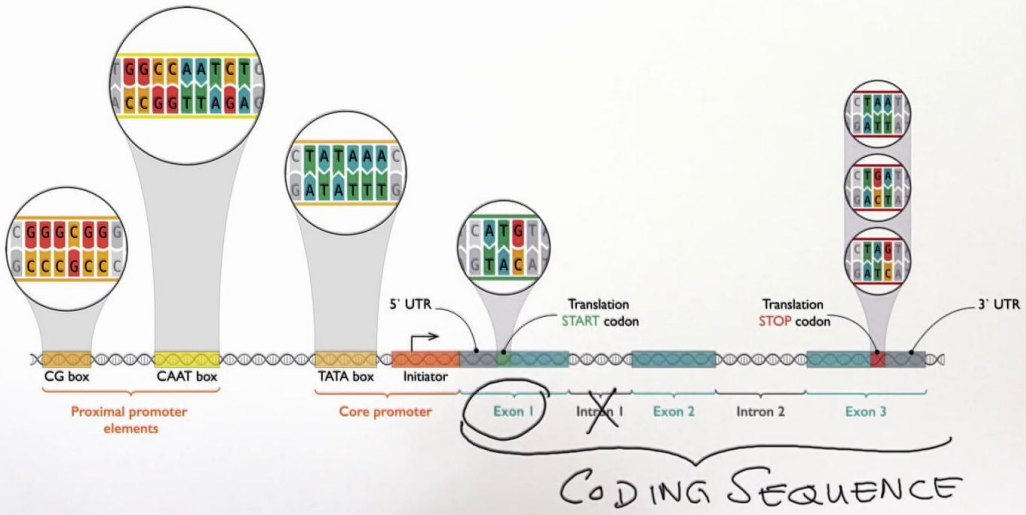
Summary

4m 44s

Regulation of transcription

Gene anatomy

- Coding sequence (CDS)
  - Introns
  - Exons
- Regulatory sequences
  - Enhancers
  - Silencers
  - Promoters
  - Locus control regions



If we leave the chromosomal scale and zoom in into a gene's anatomy, then we can appreciate that there are certain characteristic elements that are specific for each gene. For instance, we have what is called a coding sequence that is composed of exons which are going to remain in the final product of the gene, as we will see later, and of introns which are essentially going to be cut or spliced out, as we will see later. Then, of course, we have a certain number of regulatory sequences, such as enhancers that promote the transcription of a gene, such as silencers that shut off the transcription of a gene. Then we have elements that are called promoters, which are important for transcription factors to bind and find the gene that they have to transcribe. And all of this is controlled by a region that is called a locus control region.

Notes

Summary

5m 13s