Tissue-specific regulation of transcription

M.Sc. Sem 3

Tissue-specific regulation of transcription

Many enhancer elements in higher eukaryotes activate transcription in a tissue-specific manner—that is, they induce expression of a gene in one or a few cell types. For example, antibody genes are flanked by powerful enhancers that operate only in the B lymphocytes of the immune system. Many enhancers are integral components of complex tissue-specific genetic circuits that underlie complex events in development in higher eukaryotes. Tissue specificity is conferred in one of two ways. An enhancer can act in a tissue- specific manner if the activator that binds to it is present in only some types of cells. Alternatively, a tissue-specific repressor can bind to a silencer element located very near the enhancer element, making the enhancer inaccessible to its transcription factor.

Properties of tissue-specific enhancers

In some genes, regulation can be controlled by simple sets of enhancers. For example, in *Drosophila,* vitellogenins are large egg yolk proteins made in the female adult's ovary and fat body (an organ that is essentially the fly's liver) and transported into the developing oocyte. Two distinct enhancers located within a few hundred base pairs of the promoter regulate the vitellogenin gene, one driving expression in the ovaries and the other in the fat body.

The array of enhancers for a gene can be quite complex, controlling similarly complex patterns of gene expression. The *dpp* (decapentaplegic) gene in *Drosophila,* for example, encodes a protein that mediates signals between cells. It contains numerous enhancers, perhaps numbering in the tens or hundreds, dispersed along a 50-kb interval of DNA. Some of these enhancers are located 5′ (upstream) of the transcription initiation site of *dpp,* others are downstream of the promoter, some are in introns, and still others are 3′ of the polyadenylation site of the gene. Each of these enhancers regulates the expression of *dpp* in a different site in the developing animal. Some of the better characterized *dpp* enhancers are shown in Figure 11-30.

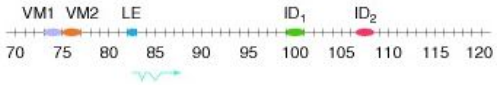

Figure 11-30

A molecular map of a complex gene—the *dpp* gene of *Drosophila*. Units on the map are in kilobases. The basic transcription unit of the gene is shown below the map coordinate line. The abbreviations above the line mark the sites of a few of the many tissue-specific enhancers that regulate this transcript in different stages of development. Tissue-specific expression patterns conferred by these enhancers are shown in Figure 11-32, and the abbreviations are explained there.

The requirement for multiple enhancer elements to regulate tissue-specific expression helps to explain the large size of genes in higher eukaryotes. The tissue-specific regulation of a gene may be quite complex, requiring the action of numerous, distantly located enhancer elements.