Chemical Biology 03
Fall 2009
Goutte

Problem Set 5: Gene Regulation

1. What is a common feature of Transcriptional Regulatory Proteins?

2. Two genes located on different chromosomes may encode very different proteins, and yet they may be coordinately regulated at the level of transcription. Explain what this statement means, and how this can be accomplished.

3. We discussed HIF1 as an example of a Transcriptional Regulator.

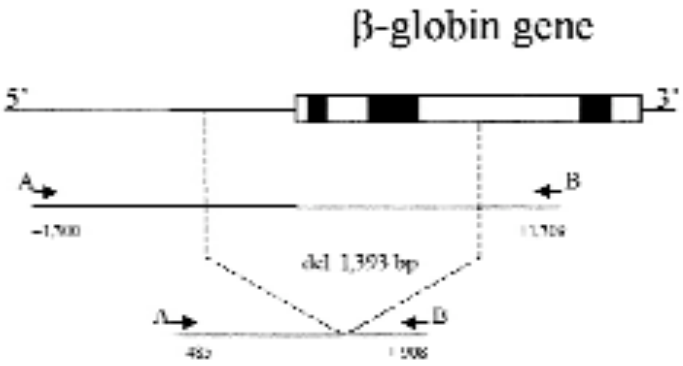
   a. What is the signal that activates/inactivates this Regulator?

   b. How can this regulator control 100 different genes?

   c. What do these 100 genes have in common?

4. Look back at the β globin and α globin gene clusters (lecture 10-23 or 26); why do you think mutations in the α globin gene are more easily tolerated than β globin mutations?

5. At right is a Figure from the Faustino et al '02 paper that we discussed in class. In this paper we heard about an individual who is homozygous for a mutation in the β globin gene called "β^{o}-Black 1,393-bp deletion." At left is shown the normal gene (transcript is indicated as a rectangle and exons are black) and the DNA that is deleted in this mutant chromosome is that which is between the dotted lines. This individual inherited the same mutant version of the gene from his two parents, so it was present in all of his cells.



   a. Consider his mother who carried one regular β globin gene and one mutant β globin gene (she was heterozygous). Because of the regular copy, she did not suffer as much as her poor homozygous son. But what if some of her somatic cells underwent a mutation in her "good" copy of the β globin gene. What would be the consequence to her and her cells if that cell was:
      i. a B lymphocyte?

      ii. A reticulocyte (precursor to RBC)?

      iii. A hematopoetic stem cell?

   b. Look at the diagram of the deleted β globin gene. Below are described two other (hypothetical) types of chromosomal deletion mutants of the β globin gene. For each deletion mutant, discuss how you think the deletion would affect hemoglobin production (assume the individual carrying such a mutation is homozygous for this mutation):

      i. Deletion that starts in the same place as that shown by the dotted line in the figure, but ends just before the transcription start site (transcript is indicated by the rectangle)

      ii. Deletion that stars in the first intron and ends in the same place as that shown by the dotted line in the figure (in intron #2)

6. Describe four ways in which a Transcriptional Regulatory Protein could be inactivated?

7. Cortisol, EPO, and O2 are three very different "signals" that we talked about in class. What do these signals have in common and how do they differ?