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HST.161 Molecular Biology and Genetics in Modern Medicine
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Reading assignment #4—Trinucleotide Repeat Disorders

First, the 2007 review in *Annual Reviews of Neuroscience* by Harry Orr and Huda Zoghbi is posted as a required reading. This review was chosen because it covers all of the trinucleotide repeat disorders comprehensively. I believe it is a very clear and up to date discussion of the trinucleotide repeat disorders. It complements the material covered in lecture and I think you will find it quite useful.

In addition, to the Orr-Zoghbi review, you will get the opportunity to explore a specific aspect of the trinucleotide disorders in greater depth. There were many questions in class and there are quite a range of topics in which I think you may be interested. After a bit of further thought, I will try to make the written assignment much more concrete.

I will require you to read one review paper and one primary literature paper. The list below will give you a sense of how these reviews and papers are related to topics brought up in class or of possible interest to you.

The written assignment will be as follows:

1. From the review paper, identify a specific hypothesis about an aspect of one or more trinucleotide repeat disorder.

Examples of such hypotheses are given below although you are not limited to these examples and I would prefer that you choose something you have found particularly of interest.

a. The mechanism by which expanded trinucleotide repeat expansions in myotonic dystrophy type 1 is through the sequestration of the splicing factor muscleblind.

b. Antagonism of mGluR function is a possible pathway to therapeutic intervention in Fragile X syndrome.

c. The action of the mismatch repair protein Msh2 is necessary for repeat expansion during transmission from one generation to the next in Huntington's disease.

After stating the hypothesis you have chosen, give a concise rationale for this hypothesis based on what you have read in the review paper.

2. Choose one primary paper that includes data germane to the hypothesis stated in part 1. Identify one Figure or Table in the paper which includes data which specifically addresses the hypothesis and explain how the data in this Figure or Table either supports or refutes the hypothesis.

Papers to choose from:

I will post a series of review papers and primary papers which relate to them. You may if you wish choose a primary paper which I have not supplied to you but is referred to in the review paper you have chosen.