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HST.161 Molecular Biology and Genetics in Modern Medicine  
Fall 2007

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## Questions for reading assignment 2

It includes three papers:

1. Watkins H, Thierfelder L, Anan R, Jarcho J, Matsumori A, McKenna W, Seidman JG, Seidman CE.

Independent origin of identical beta cardiac myosin heavy-chain mutations in hypertrophic cardiomyopathy.

Am J Hum Genet. 1993 Dec;53(6):1180-5

2. Koenig M, Beggs AH, Moyer M, Scherpf S, Heindrich K, Bettecken T, Meng G, Müller CR, Lindlöf M, Kaariainen H, et al. The molecular basis for Duchenne versus Becker muscular dystrophy: correlation of severity with type of deletion.

Am J Hum Genet. 1989 Oct;45(4):498-506.

3. Liebhaber SA, Griese EU, Weiss I, Cash FE, Ayyub H, Higgs DR, Horst J.

Inactivation of human alpha-globin gene expression by a de novo deletion located upstream of the alpha-globin gene cluster.

Proc Natl Acad Sci U S A. 1990 Dec;87(23):9431-5.

## Questions:

1. In Watkins et. al., explain why the data in Table 1 for the haplotypes associated with the Arg453Cys mutation in the MHC gene in each family support the view that the mutations in Families E, AE and B occurred independently and were not due to a mutation in a common ancestor of the three families.

2. What two factors do the authors suggest lead to the observation of recurrent mutations at the sites within the MHC gene observed in this study?

3. In Koenig et. al. Figure 1, explain how the bands on the Southern blot which are present and absent for each patient define the exons which are deleted for that patient

4. In Liebhaber et. al., Figure 4 which restriction enzyme digests give useful information for determining the sites of the breakpoints for the deletion causing alpha thalassemia in proposita IJ and explain how these results lead to the conclusions on the position of the deletion in the copy of the alpha globin region patient IJ inherited from her father

5. The analysis carried out by Koenig et. al for DMD can now be carried out by PCR. However, the analysis of a patient of with an alpha thalassemia deletion similar to patient IJ would still be challenging to carry out by PCR. Explain why the ability to apply PCR to these two analyses would be different.