HST.950/6.872 Problem Set 1

Due 9/27/2005

1. Sickle cell anemia is an autosomal recessive disorder caused by a defect in the HBB gene, which codes for hemoglobin. In the Unites States, it affects around 72,000 people, most of whose ancestors come from the Sub-Saharan region. The disease occurs in about 1 in every 500 African-American births. What is the proportion of African Americans carrying the mutant allele?

2. In a genomic study, we have recruited 10 individuals and genotyped two consecutive loci. The alleles of the resulting 20 chromosomes are listed in the following table. Chromosomes with ID 1 and 2 are from individual 1, chromosomes with ID 3 and 4 are from individual 2, and so on. Compute the degree of linkage disequilibrium between the two loci.

ID	SNP1	SNP2
1	A	G
2	A	G
3	A	G
4	T	T
5	A	G
6	T	G
7	A	G
8	A	G
9	T	T
10	T	T
11	A	G
12	T	G
13	A	G
14	A	T
15	A	G
16	T	T
17	A	G
18	A	G
19	T	G
20	T	T

3. Design your genetic study.

You have just received a call for applications from a foundation offering up to $14,000 to support genotyping efforts. You want to write a proposal where you plan to investigate the genetic bases of a disease of your choice. You call the local genotyping facility and the Laboratory Director tells you that they charge $0.40 to genotype one locus in one subject. Find a disease you are interested in and:

0. Explain the rationale of your choice: why knowing the genetic basis of this desease should be desirable, what impact this knowledge would have on the cure, prevention or management of this disease, and which are the factors that make the existence of a genetic basis for this disease likely to exist and to be found.

1. Identify a set of at least 4 candidate genes you want to genotype and, for each gene, justify its selection (hint, you may want to start from the OMIM database at NCBI).

2. For each gene, identify a set of SNPs or other varations you want to genotype. Justify your strategy and your selection (you may be interested in http://snpper.chip.org and http://www.hapmap.org).

3. Select a study design for your patient population and justify its choice.

4. Describe the type of analysis you want to undertake once you have obtained the data and justify it.

5. Describe what outcome should your study achieve to be considered a success and why.