Questions lecture 2: Genomic variation

1) A) Define common, versus rare and very rare variants.
B) Are major blood type variants common and why are there so many distinct alleles?

2) What is short read alignment and why does it represent an important computational challenge?

3) Which genome of which human population (Caucasian, Asian, Yoruban) tends to harbor the most variation, and why?

4) How many SNPs are circulating in the "human genome", how many in each human genome? Are most rare or common, clarify your answer.

5) What are LD bins? Explain why the HapMap Project deemed these bins useful for inferring missing genetic information, thereby discussing the implicit trade-off in settling for a threshold of 0.8 or greater linkage.

6) What is population stratification? Why is this important when linking allele frequencies to disease prevalence, i.e. in GWAS studies?

7) a) What is the major conclusion from the 1000 genome project in terms of how variants impact coding and non-coding function? b) Are we still evolving? Provide an illustrative example that supports your answer

8) a) Is the principle of a "meta-genome" still valid and what is mosaicism? Clarify your answer and be able to discuss distinct mutation scenarios. What are the consequences of this finding and what is mosaicism?

9) How is the exome typically captured and sequenced?

10) Explain at least three disease gene identification strategies using exome sequencing.

11) Please explain the difference between the common versus the rare variant contribution to complex disease hypotheses.

12) Know how to calculate the odds ratio.

13) Why is the term "genome-wide" association studies a misnomer? (see also question 5)

14) What's a Manhattan plot?

15) (Patients with = disease) $\neq$ (Patients with = underlying biological disorder). Please explain this statement. How does this relate to personalized medicine?

16) A. What is meant with the missing heritability and where could we find it?
B. What is meant by "nature via nurture" or "it takes two to tango"?