Questions lecture 4: Regulatory variation & Precision medicine

1. Understanding the relationship between a geno- and a phenotype is still a black box. Explain why, and how recent genomic analyses have advanced our understanding of in what way most variants seem to be implicated.
2. Understand the importance of regulatory polymorphisms by discussing the HIV example.
3. What is an eQTL? Describe in simple terms how we detect eQTLS.
4. What the GTEx Initiative revealed in terms of how abundant cis-eQTLs are and why they could be useful?
5. What is a cis- versus a trans-eQTL? Which one of the two tends to be most significant?
6. Describe in more general terms the nature of these trans-eQTLs?
7. What are tfQTLs?
8. Explain how the mapping of eQTLs and tfQTLs can aid in uncovering the full molecular chain of causality underlying a decreased risk of myocardial infarction (note: the purpose is not to memorize the names of TFs or genes but rather understand the flow of molecular information). This would be a nice example of an integrative question.
9. Provide 3 reasons why determining each person's genetic make-up may be important. Provide an example for each.
10. a) What important insight did recent cancer genome profiling analyses provide us? Explain the underlying concept (hint: the MRCA principle); b) chromotrypsis in a way opposes this insight→explain why by defining what chromotrypsis is and why it is dramatically different from canonical tumorigenesis.
11. Explain the most commonly used gene therapy using bubble boy as an example.
12. Provide at least three possible problems with such kind of gene therapy.
13. Briefly sketch the natural principle of CRISPR, then explain how it has been co-opted as a very promising genome editing tool. Finally, provide several actual applications of the technology.
14. Describe the two anticipated CRISPR-based therapy strategies.