

Cohort Sequencing Questions

1. Genetic architecture of the most important diseases across the life course
 - a. Role of rare and common variants
 - b. Risk and protective alleles
 - c. Role of families (family studies)
 - d. Effect modification of environmental exposures (G x E) (susceptibility to infection and maternal environment)
 - e. Pleiotropy
 - f. Genetic modifiers of disease severity or complications or clinical outcomes

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2. Novel drug targets

- a. Natures human XO experiment
- b. LOF protective alleles with no known side effects
- c. Novel pathways contributing to disease
- d. Will facilitate a focus on diseases where we have currently have poor treatment options

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3. Pharmacogenetics

- a. Treatment response
- b. Drug dosing
- c. Adverse outcomes

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- 4. Longitudinal change
 - a. Normal change
 - b. Incident disease
 - c. Outcomes research
 - d. Drug response
 - e. Somatic variation over time

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5. Health disparities

- a. Role of genetic factors
- b. Role of gene x environment interaction

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6. Epigenetics and Somatic variation

- a. Role in disease severity
- b. Environmental interactions
- c. Change across the life course
- d. Difference among tissues
- e. Change of somatic mosaicism throughout life

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7. Annotation of the genome
 - a. Role of conserved regions
 - b. Role of hyper-variable regions
 - c. Distant regulatory regions (eQTL)
 - d. Role of transposon and virus insertion
 - e. Assigning function to unknown motifs