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

Cohort Sequencing Questions

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

Cohort Sequencing Questions

3. Pharmacogenetics

   a.   Treatment response

   b.   Drug dosing

   c.   Adverse outcomes

Cohort Sequencing Questions

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

Cohort Sequencing Questions

5. Health disparities
   a. Role of genetic factors
   b. Role of gene x environment interaction

Cohort Sequencing Questions

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

Cohort Sequencing Questions

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