Breakout Group Report: Pharmacogenomics

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On behalf of the Working Group

Charge to Working Group

Identify one or more collaborative demonstration projects that would advance implementation of pharmacogenomics into clinical practice.

Items of consensus:

- Perhaps more than any field of Genomic/Personalized Medicine, pharmacogenomics has advanced to the point where we are ready to implement Pgx into clinical practice.
  - We know about specific ‘actionable’ variants and mechanisms by which they act
- Pharmacogenomics is less shrouded with ethical, legal and social issues than some other areas of PM.
- Broad preemptive Pgx diagnostics is preferable over single variant ‘reactive’ Pgx testing.
- There is need for a coordinated effort to develop best practices for implementation and to develop a framework to advance new discoveries
  - Technologies for variant detection
  - Defining which variants are ‘actionable’
  - Sharing genotype-phenotype definitions, suggested actions, education materials, local best practices, etc.
  - Centralized annotation of rare/new genotypes of unknown significance
- Leverage ongoing PGRN efforts to begin to address above
  - CPIC
  - TPP
  - VIPgx sequencing platform (with eMERGE)

Questions to address (1):

NextGen Sequencing is highly valuable for discovery research, but …

- For implementation of Pgx, do sequencing platforms add value over directed genotyping platforms?
  - Some Pgx genes are sequenced poorly on ‘off the shelf’ whole genome sequencing platforms.
  - We know the relevant ‘actionable’ variants, so why sequence?

- Proposed collaborative project
  - Compare ‘head to head’ whole genome sequencing, directed sequencing (VIPgx sequence platform), and ‘low tech’ chip-based (or other) genotyping platforms
    - Ourcomes to measure:
      - Technical aspects of variant calling
      - Relating drug response/AE phenotypes to genotypes

Questions to address (2):

What is the role of rare variants in Pgx implementation?

- Proposed collaborative project
  - Apply Nextgen sequencing technologies to rare serious adverse events (SAEs) for
    - Discovery
    - Family-based Pgx implementation
  - Develop repository of well-annotated rare variants in Pgx genes, evidence for functional, clinical consequences, etc.