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
    • Outcomes 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.