Summary of NHGRI Genomic Medicine II

Bethesda, MD

December 5-6

Barriers to Genomic Medicine

- Lack of evidence for benefit/value
- Institution and physician acceptance
- Education of patients, physicians
- Consents
- Sample availability and biobanking
- Recruitment for genetic studies

Meeting Goals

- Develop ideas for multicenter collaborative pilot projects in translational genomic medicine
- Learn of new projects ongoing at partner sites
- Identify infrastructure needs and possible solutions to speed the adoption of genomic medicine
- Establish mechanisms for sharing of best practices among genomic medicine centers

Highlights

- Heard from institutional leaders:
  - Make Genomic Medicine part of the institutional strategic plan
  - Need to demonstrate value, especially in the cost arena
  - Genomic research needs to be “part of the cake, not just icing”
- Encourage an institutional leader perspective publication

Working Group: Cancer

- **Lynch Syndrome Screening**
- **Neuroendocrine Cancer Screening**
- **Important crumbs left behind**
  - Moderate risk variants: clinical utility, screening and treatment recommendations
  - Very rare (and probably genetic) phenotypes with no known associated genes
  - Germline and somatic variation for tumor progression and drug resistance
  - Cancers that rarely have somatic alterations (carcinoids, pancreatic endocrine tumors)

Working Group: Periodontal Microbiome

- **Pharmacogenetics for dentistry**
  - Timing of warfarin withdrawal prior to dental procedures
  - Impact of known PGx variants
  - CYP2D6 for pain management
- **T2DM and periodontal disease and/or periodontal microbiome type**
  - Effect of PD on T2D GWAS signals, i.e., can T2D signals be stratified by PD?
  - Effect of oral microbiome on T2D GWAS signals, i.e., can T2D signals be stratified by microbiome?

Working Group: Family History

- Develop an outcomes research agenda
- Implementation science to integrate FH into the clinical workflow: series of small studies that interrogate and evaluate best/cheapest/least time consuming way to collect FH data
- Advisory Group on FH
- Information interface and education of providers
- Explore electronic media tools to help patients create their own family histories and encourage their family members to participate
- Validation of family history information
- Building models with all the data

Working Group: Pharmacogenetics

- **Compare 'head to head' whole genome sequencing, directed sequencing (VIPgx sequence platform), and 'low tech' chip-based (or other) genotyping platforms**
  - Addresses question: "For implementation of Pgx, do sequencing platforms add value over directed genotyping platforms?"
  - Outcomes to measure:
-
- **Apply Nextgen sequencing technologies to rare serious adverse events (SAEs) for discovery, family-based PGx implementation**
  - What is role of rare variants in PGx implementation?
  - Develop repository of well-annotated rare variants in PGx genes, evidence for functional, clinical consequences, etc.

Working Group: Sequencing

- Improved reference set for clinical analyses
- Setting standards for reporting genomic data
- Setting standards for reporting phenotypic data
- Analytical best practices
- Create central repository for clinical comparisons
- Wet lab best practices

Working Group: Clinical/Research Interface

- IRB related issues
- Clinic/Research interface
- Implementation consultants for systems wanting to implement in clinical practice
- Variants for clinical use: Propose working group from this group and ClinAction group to develop criteria
- Develop ‘suite’ of validated methodologies to collect data to answer clinical/research questions
- Qualitative research to understand practitioner ‘experience’ with genomics

Action Items

- Convene CEO of health systems around Genomic Medicine
- Need to advocate and enable a patient role
- Share documentation for clinical use of software for sequence analysis
- Demonstration projects showing cost effectiveness and utility
- The breakout groups should persist to continue toward next meeting

Next Steps

- Have these six working groups continue
- Add others or subgroups (PGx genotyping ready to secede?)
- NHGRI will attempt to help co-arrange
- These chairs to continue?
- Invite them to meet with GMWG periodically
- Present early deliverables at May meeting