Genomic Medicine II

Bethesda, MD

December 5-6

Eric Green

- Genomic Medicine working group
- Need to be smarter with our resources
- NHGRI wants to stimulate
- Can be “conveners”

TAM and Geoff Ginsburg
Summary of GM I

- How are we going to do this?
- What is actually going on in the field?
- What role should NIH/NHGRI play to support and accelerate progress
- Identify areas of active translational implementation determine commonalities and uniqueness
- Define demonstration projects
- What are the barriers
- What are solutions to those barriers?
- What can NHGRI do

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

Possible Outcomes of Chicago meeting

- Enchance appreciation and understanding of oningoin efforts
- Writing groups
  - Perspectives Papers
  - Best practice guidelines
- Planning groups for workships conferences
- Loose confederation

GMI

- >20 GM centers
- Supported wide mechanisms
- Similar efforts that could be aligned
- Stimulate investigator-initiated efforts
- Establish Genomic Medicine Working groups with rotating membership

- Evidence development for effectivness
- Tools
- Policy
- Eduction training

Marc Williams
summary of ClinAction meeting

Bill Evans
St. Jude—Institutional Leaders

- Started in 1984
  - To assign ALL treatment
  - Interited germline variants that influence treatment TPMT
- Academic system rewards discovery more than translation
- Added to the strategic plan for the institution
  - Enables institutional thinking and rewards
- Strongly integrated into EHR. TPMT deficiency appears on problem list
- How and when to move from lab to clinic
- Barriers
  - Sick care rather than prevention
  - Genetic exceptionalism
  - Lack of decision support
  - Preemptive testing
- Fewer barriers at St. Jude
- DMET chip up front
- Does under a protocol with migration as a goal
  - Withold some information
  - Incidental findings
- Longterm goal is to use proactive pharmacogenomics testing as the STANDARD OF CARE for all St. Jude patients
- With just 2 genes 15% of unselected patients had poor metabolizer issues
- St Jude family Adivsory council
- 500 whole genomes sequenced (generating 2 whole genomes per day)

Joanne Wade
Geisinger Perspective

- Patient driven mission
- Vision
  - Quality
  - Innovation
  - Market leadership
  - Geisinger Family
- Research enterprise part of the clinical enterprise
- Have an edw equivalent
- Have Center for Health Research
- External scientific advisors
- Discuss research with the Board at every meeting.
- THRee board members involved in regular meeting around personalized health care
- General support among physicians for “changing the we they did medicine”
- Approval
  - Full communication campaign
  - Formalize a 10 year business plan
  - Define metrics for quality, value and outcome
  - Risk mitigation
- Patient focus
  - Research was not “icing” but was integral

Charis Eng

- Lynch syndrome screening
- Pheochromocytoma
  - Looking at 10 genes if there are mutations
  - Genetic counselors

Murray Brilliant
Oral Microbiome

Geoff Ginsberg

- Family history implemetation in Primary Care
- Collects 3 generation family history
- Both patient and physician get reports
- Allows patient entry

Howard McLeod

- Pharmacogenomics a proof of principle for genomic medicine: it about the endpoints
- Listed 8 or so existing tests that are used today
- New audience. Now clinic administrator, payers, patients
- New endpoints
  - selection from amongs equal therapies,
  - return on investments for medical home,
  - quality measures,
  - patient satisfaction
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Mark Ratain

- 1200 patients projects
- Something a expert says would likely have an effect
- Phase I study of a new system
- Thinks of these results as consults (not labs)
- Collaborative opportunity—phase II

Alan Shuldiner

- PAPI-2

Howard Jacob

- The Milwaukee Approach
  - Nominated by two physians
    - Actionable
    - End a diagnostic oddessy
  - Case Review

  - All resonable clinical testing has been performed
  - Likely monogenic etiology
  - Rare
  - Able for WGS to assist/enhance medical decision-making
  - Conclude a WGS assessment
  - Consent
    - Data return discussed
    - Multiple counseling sessions
    - Total 6-8 hrs
  - What does actionable mean?
  - Alignment vs de novo assembly
  - Limited availability of genomic sequence
  - Little clinical data

Gail Jarvik

- Exome variant server es.gs.washington.edu/EVS

Scott Weiss

- CLIA certified lab does testing for over 200 genes
- WGS, outsourcing to Ilumina and Complete Genomics

Eric Topol

- Welderly over 80 genomics of health aging (1000 complete genomics sequencing)
- Point of care genotyping
  - Hepatitis C – genotyping to predict interferon response
  - Variable response to metformin
- Michigan paired sequencing of tumor and germline, exome and RNAseq

David Craig
TGEN

- Core premise--oncology
  - Integrative molecular profiling through arrays
  - Outcome measure of time to progress
  - 50 patients in last year
  - Collected in CLIA, then samples split
  - Multiple high utility events are frequently found in metastatic disease
  - Use of WGS in the context of disease management
  - Outcomes and Data sharing

Maren Scheuner

- Change healthcare provider behavior
- Family history education to improve genetic risk assessment

Bill Gahl

- NIH Clinical center
  - Direct collaboration
  - Bench to bedside grant $135k per year for 2 years

Les Bieseker

- Using exoms to solve rare mendelian disease
- 600 exomes in cardiovascular disease (ClinSeq)
- Iterative phenotyping
- Possible collaboration

Cancer

- Lynch Syndrome Screening
  - Improve recommendations for screening
  - Create a resoure to evaluate successful implementation of screening
  - Aggregate/integrate germline sequencing
- Neuroendocrine Cancer Screening
  - Implement routine screening for thyroid cancer
  - Create a resource to evaluate successful implementation
  - Link to family history and TCGA
- Important crumbs left behind
  - Moderate risk variants
  - Very rare phenotypes
  - Germline and somatic variation for tumor progression
- RW: how to gather data together

Periodontal Microbiome

- Pilot 1: Pharmacogenetics for Dentistry
  - Warfarin dosing prior to dental proceedures
- Pilot 2 T2D and periodontal disease and microbiome
  - T2D and dental access data
- Role of dentist in genomic medicine

Geoff Ginsberg
Family History

- Validaton of family history information
- Integration of family data
- Assemble a group
- Develop adaptive patient questionnaires
- Building models with all the data
  - Integrate risk data
- Need to create an advisory group on family history

Pharmacogenomics Breakout

- Pgx is ready for prime time
- Is array based genotyping better than sequencing?
- Demo project: Compare next gen sequencing head to head over directed platforms or “low tech” chip based approaches
  - Outcomes to measure
    - Technical aspects of variant calling
    - Related drug response/AE
- What is the role of rare variants, apply NGS to rare AEs for both discovery

Sequencing Breakout

- Change the practice of medicine so it can be routinely ordered to improve healthcare
- Standards for phenotypes and genome annotation
- Layer different categories of data, SNPs, standard phenotypes mined from EHR layered on sequence
- Grand vision: sequence 100,000 patients with detailed electronic medical records
- Analytical best practices
- Wetlab bakeoff
- Improved reference set for clinical analytics
- Establish mimimum standards for genomic and clinical phenotyping data
- Work with NIST to make sure the standards are related to the Grand Vision

Miscellanea

- CliniAction/Genomic Medicine collaboration
- Projects
  - implementation

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 Step

- 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