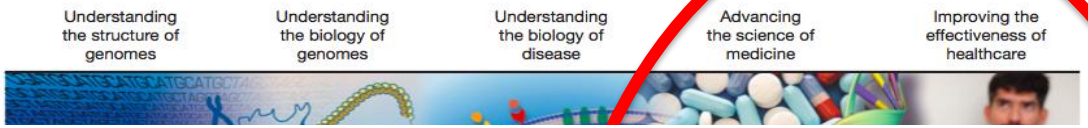
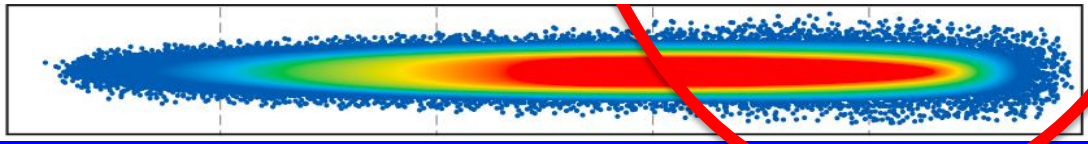
Motivation and Inspiration



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?



Green ED, Guyer MS. *Nature* 2011; 470:204-13.

Genomic Medicine Institutes Colloquium June 29, 2011, Chicago

- MCW
- Mt Sinai
- Marshfield Cliniic
- Northwestern
- Loyola
- Cleveland Clinic
- UCSD
- Morehouse
- Duke
- Maryland
- Intermountain Healthcare
- UAB
- Geisinger
- Baylor
- OSU
- Mayo Clinic
- Partners Healthcare
- U Chicago
- Penn
- St Judes
- Vanderbilt
- Johns Hopkins
- Washington
- NHGRI
- NCI
- NIMH
- NINDS
- NHLBI

- ~ 40 Attendees

Tasks

- Identify areas of active translational and implementation research across the various groups and determine potential commonalities and uniqueness
- Define demonstration projects in genomic translation ready for investigation now or in the near future and what is needed to actualize them
- Stimulate development of a consortium for conducting genomic translational research

Name of Genomic Medicine (GM) Group	Clinical Genetics Institute
Institution	Intermountain Healthcare
Lead GM Investigator	Marc S. Williams, MD
Brief Description of Center, Mission	The Center includes the director, who is a medical geneticist, an informaticist and a health care analyst/modeler. We have close collaborative relationships with the oncology genetic counselor and the Homer Warner Center for Informatics Research. Our Mission is to advocate for excellence in the quality and value of healthcare throughout our service area by evaluating and implementing current developments in genetics/genomics within Intermountain Healthcare.
Primary Funding Sources	Budget for institute is a line item expense for the organization. Offsets through grants and contracts are welcome but not necessary to maintain operations.
Description of Major Project	Tumor-based screening for Lynch syndrome.
Clinical decision intended to be influenced	Identify patients with Lynch syndrome to apply syndrome-specific care measures and identify at risk family members for testing and enhanced surveillance (if positive)
Expected change in outcome	Prevention and/or earlier detection of Lynch-syndrome associated cancers resulting in decreased attributable morbidity and mortality.
Data collected	Screening status; Immunohistochemistry results; *BRAF* and *MLH1* promoter methylation status for tumors with negative MLH1 staining; reports to pathology, oncology, oncology genetics; patients with confirmatory testing; family expansion and familial mutation testing.
Sample size (current and anticipated) and characteristics (age, gender)	~300 annual cases of Colorectal cancer system-wide
Consent components, reporting of results	No consent for screening. Full informed consent for confirmatory molecular testing.
Availability of biospecimens	Residual tumor is maintained per clinical requirements.
Use of decision support tools, integration into medical record	Used systematic process improvement to create system that results in all tissues being screened without need for reminders. Dashboard tracks all screening results and reports to pathology and oncology genetics.
Primary obstacles encountered; solutions	System acceptance—Presentation of evidence and formal decision analysis. Process problems—Development of standardized order sets and process modification. Individual institutional opt out—working with other care providers to bring institution on board. Follow-up on screen positive patients not being referred to oncology genetics—moving from physician contact to direct contact by oncology genetics (with permission of clinicians). Completion of confirmatory testing—analyzing reasons for refusal (mostly due to lack of coverage for testing). Family expansion—exploring ways to improve information to at risk family members.
Health outcomes of interest	Medical outcomes—Reduction of morbidity and mortality from Lynch syndrome-associated cancers by prevention and/or earlier detection. Process outcomes—Increase identification of at risk patients and family members; increased compliance with Lynch syndrome-specific surveillance recommendations.
Implementation stage	Implemented across 70% of Intermountain system with implementation pending in other 30%.
Next step if project successful	Extension to endometrial cancer. Adequate information now exists to show that immunohistochemical screening for mismatch repair proteins can be done on endometrial cancer tissue. Screening program is slightly different in that *BRAF* testing is not needed for endometrial tumors with abnormal MLH1 staining. This requires modification of order sets. Implementation will be initiated with these modifications later this year.

Investigator	Institution	Major Projects
David Bick/David Dimmock	MC Wisconsin	Using whole genome sequencing to establish diagnosis in patients with currently undiagnosed genetic disorders
Erwin Bottinger	Mount Sinai	• CYP2C19 testing for antiplatelet rx post percutaneous coronary intervention • Personalized decision support for CVD risk management incorporating genetic risk info
Rex Chisholm	Northwestern	Using pharmacogenomics evidence (from GWA genotyping) to guide prescriptions in primary care and assess risk for other conditions such as HFE/hemochromatosis
Charis Eng	Cleveland Clinic	Tumor-based screening for Lynch syndrome, endometrial cancer
Kelly Frazer	UCSD	• Screening for actionable mutations in malignant gliomas and glioblastomas for biomarker based RCTs • Targeted rx (such as RET inhibitor) of metastatic solid tumors based on tumor mutation status
Gary Gibbons	Morehouse	• Exome sequencing of 1200 early onset severe African American hypertension cases and 1200 controls
Geoff Ginsburg	Duke	• Computer-based family hx collection and CDS tool with 1-yr follow-up for perceptions, attitudes, behaviors related to thrombosis and breast, ovarian, and colon cancer • SLCO1B1*5 genotyping and statin adherence • Effect of genetic risk info on anxiety and adherence in T2DM

Investigator	Institution	Major Projects
Bruce Korf	Alabama	Planning stages for projects in risk assessment, pharmacogenetic analysis, identification of families for further research
James Lupski/ Richard Gibbs	Baylor	Whole exome and whole genome sequencing in Mendelian disorders to improve diagnosis
David Ledbetter	Geisinger	• Selection for gastric bypass surgery vs other wt loss means based on genetic variants predictive of long-term benefit from surgery • IL28B variants and response to hepatitis C treatment • KRAS and BRAF mutational analysis in thyroid cancer patients
Clay Marsh	Ohio State	• Personalized genomic med study of CHF and HTN pts randomized to genetic counseling vs usual care • CYP2C19 testing in interventional cardiovascular procedures for clopidogrel
Michael Murray	Harvard	Whole genome sequencing with integration in EMR and CDS; pilot of 3 patients to start
Daniel Rader	U Penn	Genotyping for assessment of MI risk in Preventive Cardiology program
Mary Relling	St. Jude's	Pre-emptive PGx genotyping in children
Dan Roden	Vanderbilt	Pre-emptive PGx genotyping for clopidogrel, warfarin, or high-dose simvastatin
Alan Shuldiner	U Maryland	Develop and apply evidence-based gene/drug guidelines that allow clinicians to translate genetic test results into actionable medication prescribing decisions
R. Weinshilboum	Mayo	• PGx driven selection/dosing of antidepressants • CYP2C19 genotyping for antiplatelet rx post PCI
Marc Williams	Inter-Mountain	Tumor-based screening for Lynch syndrome

Another Set of Questions

- What are the barriers at your institution to clinical adoption of genomics in medicine?
- What are the solutions you have been able to achieve and how?
- What role can NHGRI play to facilitate translation and adoption of genomics into medicine
  - what infrastructure should NHGRI support?
  - what research programs should NHGRI pursue?

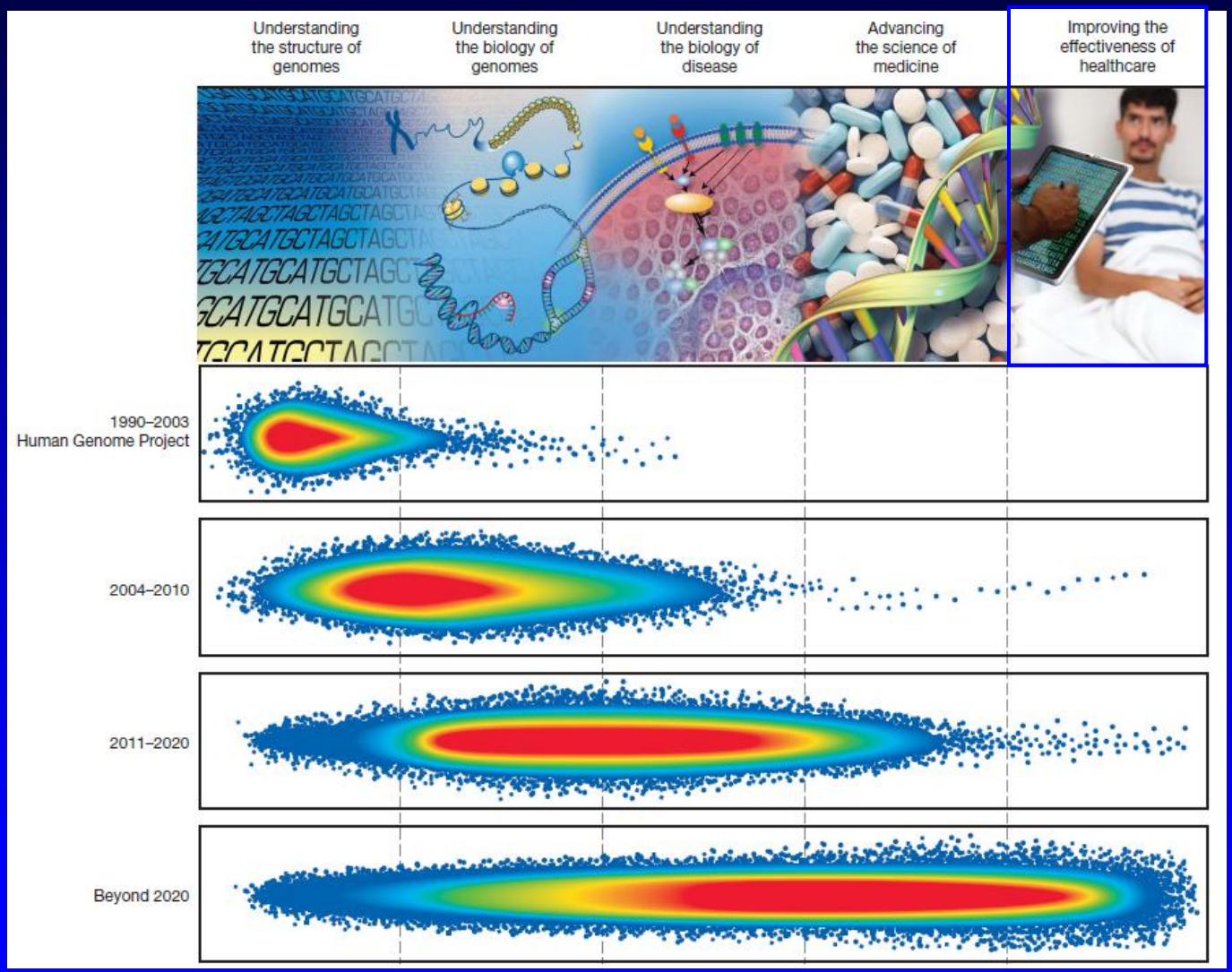
Barriers -1

- Lack of evidence for benefit/value
- Institution and physician acceptance
- Education of patients, physicians, public
- Availability of testing, licensure, CLIA certification
- EMR integration of genomic results, custom reporting tools and decision support software
- Optimizing turnaround time

Barriers - 2

- Need for genetic counseling
- Consent
- Improving information for at-risk family members
- Sample availability and biobanking
- Recruitment for genetic studies
- Logistics of follow-up, loss to follow-up
- Research funding and reimbursement
- How do we know a genetic signal applies to our population?

Keeping Our Eye on the Ball…



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Possible Outcomes of Chicago Meeting

- Enhanced appreciation and understanding of ongoing genomic medicine efforts NIH-wide
- Writing groups
  - Perspectives papers
  - Best practices
- Planning groups for workshops or conferences
- Loose confederation or consortium for collaborative studies

Leveraging Existing Efforts

- Over 20 genomic medicine centers at varying stages of implementation
- Supported through multiple NIH and institutional mechanisms
- Numerous similar and overlapping efforts that would benefit from collaboration
- Numerous shared needs
- Would benefit from periodic interactions and degree of coordination, consensus building
- Critical to facilitate but not impede

Proposed Goals of Genomic Medicine Effort

- Identify research directions and priorities
- Promote collaboration among existing groups
- Stimulate investigator-initiated efforts and issue funding solicitations as needed
- Learn more about genomic medicine centers at NHGRI/NIH staff level by visiting
- Establish Genomic Medicine Working Group as subcommittee of Council
  - Rotating membership
  - At least one Council member
  - Report back to Council regularly

Genomic Medicine Working Group Possible Tasks

- Identify topics for subsequent meetings of genomic medicine groups, plan those meetings
- Identify topics for separate working groups or workshops
- Monitor production of white papers, assist and/or prod as needed
- Review progress in given area for readiness for exploration in subsequent working groups

Genomic Medicine Working Group Possible Tasks (cont)

- Review progress overall in genomic medicine implementation and identify gaps, opportunities
- Identify related efforts and integrate as appropriate
  - ClinVar and actionable variants
  - eMERGE and clinical decision support, pilot implementation studies
  - Clinical Sequencing Exploratory program
  - Trans-NIH dissemination network
  - Clinical Translational Science Awards

Current/Planned Working Groups and Workshops

- Databases and actionable variants

  Dec 1-2, 2011

- Collaborative demonstration projects

  Dec 5-6, 2011 (this meeting!)

- Standardization, quality control of clinical genomic testing and reporting

  May 3-4, 2012

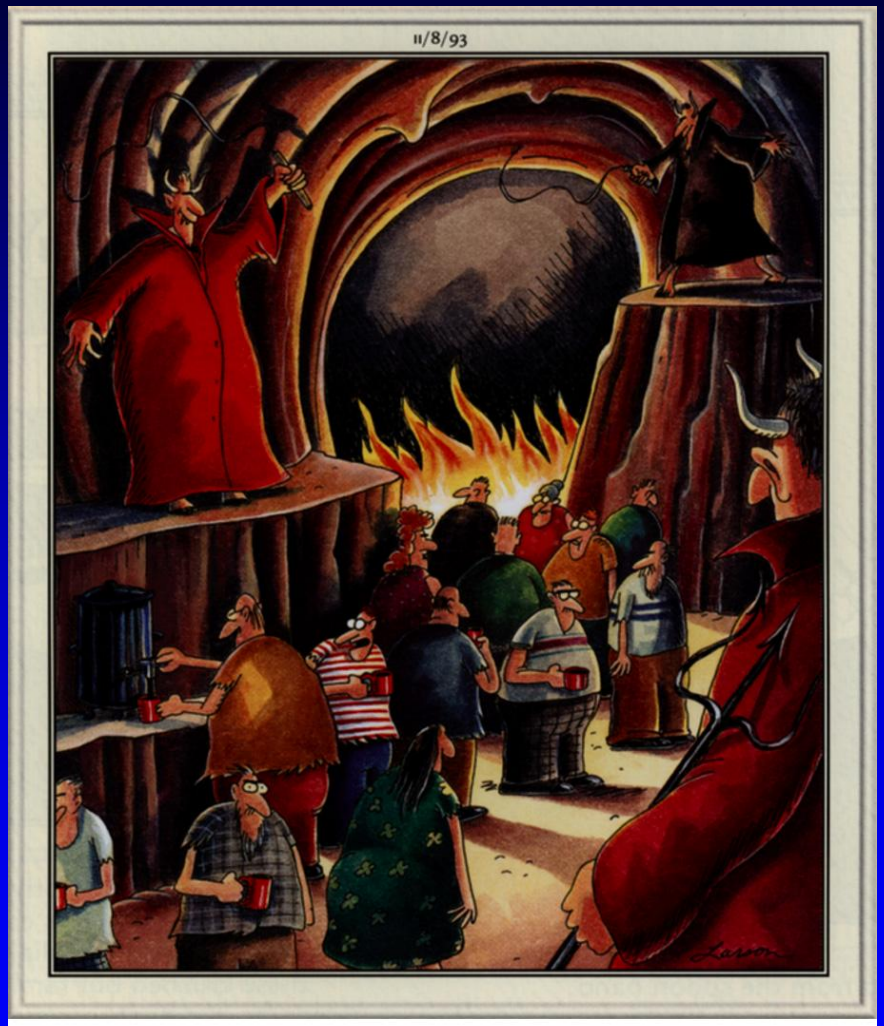
- Evidence development (discovery, validation) for actionable variants

  Sep 2012?

Potential Working Groups and Workshops: Infrastructure and Research Needs

- Evidence development for effectiveness of genomic medicine
- Tool development for genomic medicine (CDS, clinical algorithms)
- Policy needs (consent, CLIA, reimbursement)
- Education, training, user support

Avoiding Meeting Hell



"Oh, man! The coffee's *cold!* They thought of *everything!*

Larson, G. *The Complete Far Side*. 2003.

Proposed Genomic Medicine II (Fall 2011)

- Broaden involvement of relevant groups
- Identify low-cost pilot projects to build on similar efforts across sites
- Convene working groups and workshop planning to address obst/opport from GM I
- Identify additional groups to participate
- Determine appropriate next steps for group as whole (meetings, white papers?)