National Human Genome Research Institute

National Institutes of Health

U.S. Department of Health and Human Services

NHGRI's Genomic Medicine Portfolio

U.S. Department of Health and Human Services
National Institutes of Health
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Teri Manolio, M.D., Ph.D.
CSER and Beyond Program Review Meeting
September 28, 2015

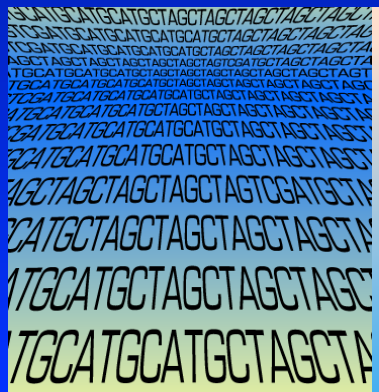
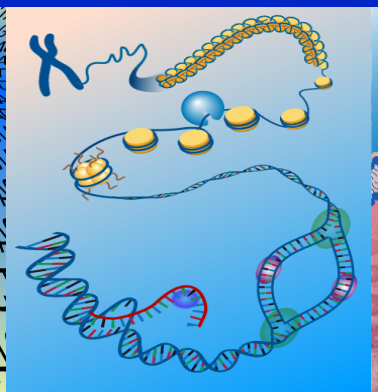
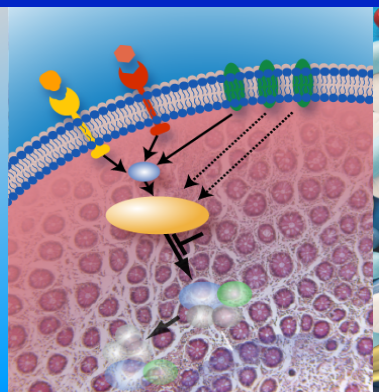
NACHGR Genomic Medicine Working Group Members

Carol Bult	Jackson Lab
Rex Chisholm	Northwestern
Geoff Ginsburg	Duke
Howard Jacob	HudsonAlpha
Howard McLeod	Moffitt Cancer Ctr
Mary Relling	St. Jude
Dan Roden	Vanderbilt
Marc Williams	Geisinger
Eric Green	
Teri Manolio	
Laura Rodriguez	

Genomic Medicine Working Group - Charge

Assist in advising NHGRI on research needed to evaluate and implement genomic medicine

- Review current progress, identify research gaps and approaches for filling them
- Identify and publicize key advances
- Plan genomic medicine meetings on timely themes
- Facilitate collaborations, coordination
- Explore models for long-term infrastructure and sustainability of resulting efforts

Genomic Medicine Colloquium, June 2011

GM VII: Genomic CDS, Oct 2014

GM IV: Physician Education, Jan 2013

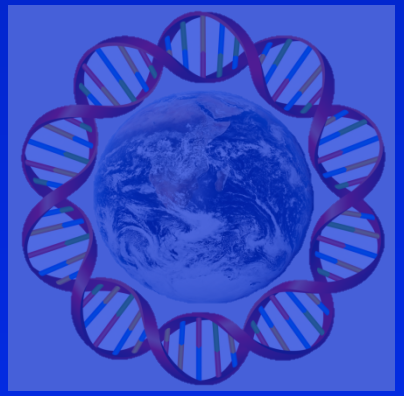
GM VIII: NHGRI's Genomic Medicine Programs, June 2015

Policy Framework

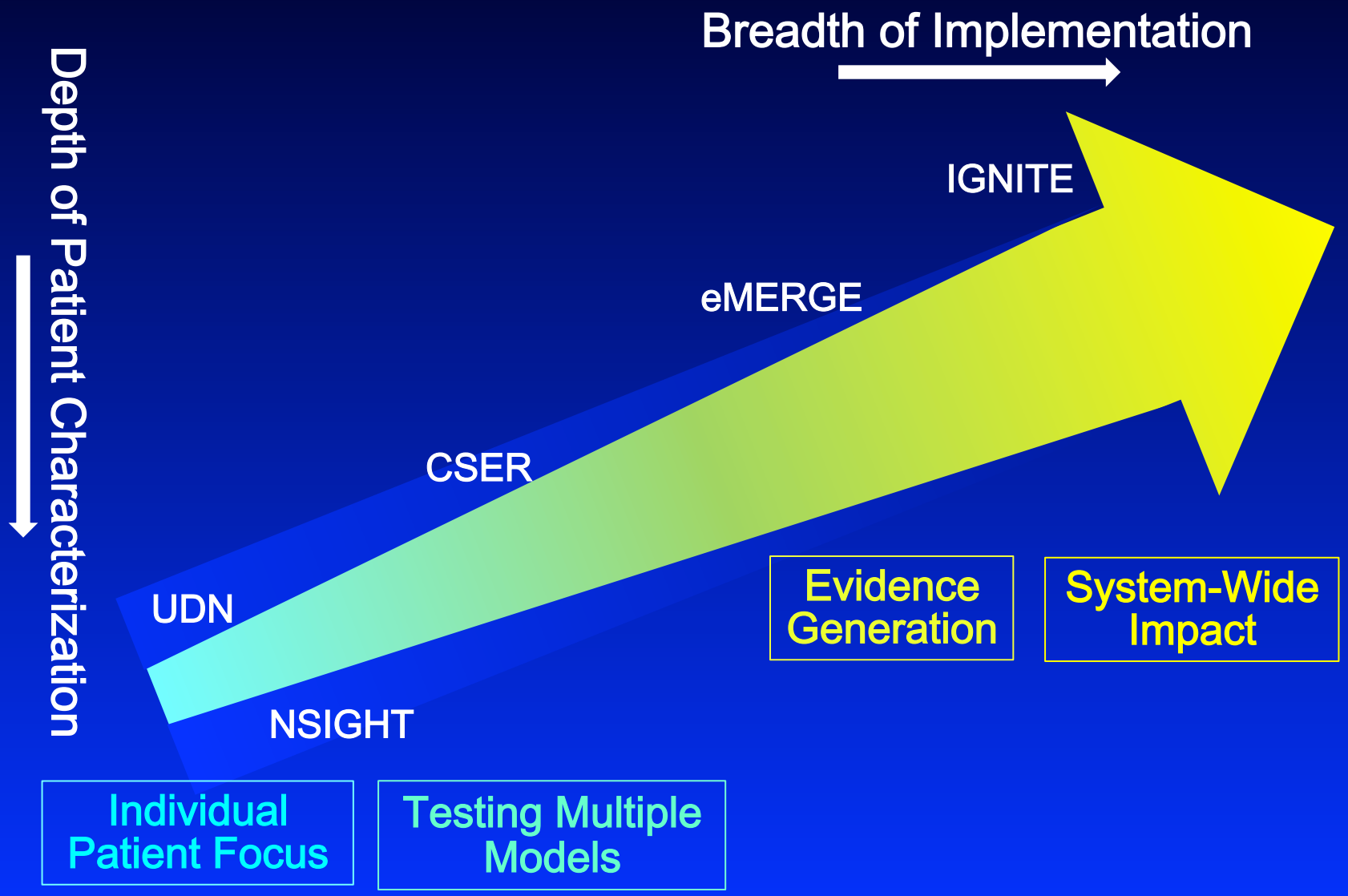
The College of American Pathologists
Debra G.B. Leonard, MD, PhD, FCAP

GM III: Stakeholders, May 2012

GM VI: Global Leaders, Jan 2014



Spectrum of Genomic Medicine Implementation: Intensity vs. Breadth



NHGRI's Genomic Medicine Research Program

Program	Goal	Σ $M	Years
UDN	Diagnose rare and new diseases by expanding NIH's Undiagnosed Diseases Program	67.9	FY13-17
NSIGHT	Explore possible uses of genomic sequence information in the newborn period	10.0	FY13-16
CSER	Explore infrastructure, methods, and issues for integrating genomic sequence into clinical care	65.0	FY12-16
RoR	Investigate whether/when/how to return individual research results to ppts in genomic research studies	5.7	FY11-13
eMERGE III	Use biorepositories with EMRs to assess penetrance of 100 clinically relevant genes 25,000 individuals, develop e-phenotypes, CDS	56.0	FY15-18
IGNITE	Develop and disseminate methods for incorporating patients' genomic findings into their clinical care	32.3	FY13-16
ClinGen	Develop and disseminate consensus information on variants relevant for clinical care	25.0	FY13-16

Genomic Medicine VIII: NHGRI's Genomic Medicine Programs, June 8-9, 2015

- Objectives
  - Review NHGRI's genomic medicine portfolio, identify gaps, opportunities for collaborations
  - Identify related programs of other NIH ICs or other funders and opportunities for collaborations
  - Identify research needs in genomic medicine for NHGRI and partner agencies to pursue
  - Enhance approaches to capturing and disseminating best practices
  - Examine potential methods for assessing impact of programs

NHGRI's Genomic Medicine Portfolio

Focus Programs	Related Programs	
UDN	AFMS	IOM Roundtable
NSIGHT	CMG	ISCC
CSER	CPIC	LSAC
eMERGE	ENCODE	MVP
IGNITE	GA4GH	NCI-ALCHEMIST
ClinGen	GAPH	NCI-MATCH
	GGR	PAGE
	GS-IT	PCORNet
	GTEx	PGRN
	H3Africa	Phenx
	HMORN	PMI

Program Summaries

Program Name and Website: Clinical Genome Resource, www.clinicalgenome.org

PIs and Funded Sites:

U41 H	
U01 H	
U01 H	
ClinV	

Mission

Objecti

-
-
-

Program Name and Website: Newborn Sequencing In Genomic medicine and public HealTh (NSIGHT), http://www.genome.gov/27558493

PIs and Funded Sites:

Principal Investigator	Institution	Title
Robert Green and Beggs		d Screening for born Illness
Stephen Kingsmo		ations of 2-day ly Ill Newborns
Steven Brenner, Koenig, Puiyan K Jennifer Puck		Blood Spot DNA Newborn
Cynthia Powell a Jonathan Berg		a Newborn niversal

Objectives:

1. Acquisitio available of data
2. Perform newborn dentifiable via
3. Conduct research related to the ethical, legal and social implications (ELSI) of the possible implementation of genomic sequencing of newborns

- Title, website, funded sites
- Objectives
- Funding period and FY14 total
- Current working groups
- Resources and tools produced
- Key publications
- Major obstacles or needs
- Approaches to meet needs

Google “Genomic Medicine VIII”

National Human Genome Research Institute
Advancing human health through genomics research

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Home › Research Funding › Research Funding Divisions › Division of Genomic Medicine › Genomic Medicine Activities › Genomic Medicine VIII (GM8)

Genomic Medicine Meeting VIII: *NHGRI's Genomic Medicine Portfolio* (GM8)

On June 8-9, 2015, the National Human Genome Research Institute (NHGRI) will sponsor its eighth Genomic Medicine meeting - ***Genomic Medicine Meeting VIII: NHGRI's Genomic Medicine Portfolio*** - at the Hilton Washington D.C./Rockville Hotel & Executive Meeting Center in Rockville, Md.

The meeting will convene leadership from NHGRI's genomic medicine programs and

Program Summaries - Focus and Related PDF

es

- Identify related programs of other NIH ICs or other funders and opportunities for collaborations with NHGRI programs.
- Identify research needs in genomic medicine for NHGRI and partner agencies to pursue.
- Enhance approaches to capturing and disseminating best practices for genomic medicine.
- Examine potential methods for assessing impact of programs.

YouTube Video Playlist

View meeting videos and slides from: June 8 June 9

Meeting Agenda | Objectives Matrix | Common Barriers Matrix | Program Summaries - Focus and Related

Executive Summary | Full Meeting Summary new | Compiled GM8 Documents new

E-Booklet | Tweets from the Meeting: #GenomicMed8

Common Objectives of NHGRI's Genomic Medicine Programs

- Improve genomic diagnostic methods
- Integrate genomic data into patient care
- Incorporate actionable variants into EMR, CDS
- Educate clinicians and patients on genomics in clinic
- Assess outcomes of using genomics in clinical care
- Translate implementation outside specialized centers
- Define and share processes of implementation
- Assess actionability of genes/variants for clinical use
- Identify, address barriers to genomic medicine implementation
- Promote interaction and collaboration, reduce duplication

Specific Goals of Genomic Medicine Programs

	UDN	NSIGHT	CSER	eMERGE	IGNITE	ClinGen
Facilitate research in undiagnosed/Mendelian diseases	++	+	+			
Study ELSI in genomic seq		+	+	+		
Interpret sequencing data in variety of contexts		++	+	+		
Investigate use of genomic data in newborn care		++				
Develop electronic phenotypes				+		
Identify variants related to complex traits	+		+	+		
Characterize Pgx variants, use in care				+	+	
Assess penetrance of potentially actionable variants			+	+		
Standardize clinical annotation and interpretation			+			++
Create genomics-enabled learning healthcare systems			+	+	+	

Barriers Facing Multiple Programs

- Lack of evidence base
- Need for common data elements
- Frequency, impact of variants in ancestrally diverse populations
- Rapid evolution of evidence on variants
- Limited usefulness and interoperability of CDS
- Regulations impeding return of results
- Need for cloud computing
- Reimbursement policies and regulations
- Need for bedside back to bench research

GM VIII Recommendations Related to Payers

- Measure outcomes of value to patients, clinicians, payers…; involve them in design prior to launching studies (2.7)
- Facilitate coverage with evidence development studies through payers (4.3)
- Identify payers' needs for evidence across diverse payers, integrate with HCSRN and AHIP (4.5)

GM VIII – Specific Studies or Approaches

- Add FHx tool to large-scale sequencing effort to produce > 20K individuals with both, determine when FHx adds to sequence information (3.5)
- Consider “cooperative sequencing groups” like COGs allowing rapid entry into studies (4.2)
- Conduct clinical trials of added value of WGS to more limited testing, include follow-up costs (5.0)
- Expand, support, and expect common measures and other program-wide efforts (5.3)
- Identify specific health disparities research questions related to genomics (5.3)
- Develop dedicated programs for non-EA populations to fill key gaps (6.1)

GM VIII – Clinical Care

- Accelerate rapid genotype-phenotype explorations at speed that would benefit patients (4.1)
- Study impact and consequences of changes in variant annotation and duty to inform (6.1)
- Assess and improve effectiveness and understandability of genetic test reports by diverse medical practitioners (6.3, 7.2, 7.4)
- Examine impact of adding genome consult service on clinicians' understanding and appropriate use of genomic findings (6.4)
- Compare and unify sequencing clinical reports from major clinical sequencing labs, consider bake-off of data comparability (6.5)

GM VIII – Expand Reach, Interactions

Clinical Labs

- Encourage consensus nomenclature, variant definitions, unique allelic identifiers for CDS (4.7)
- Build tools for facilitating ClinVar submissions (5.4)

Patients

- Explore/exploit potential of crowd-sourcing for assessing phenotypic manifestations and actionability among carriers of rare variants (5.5)
- Ensure patient access to their genomic data at levels they specify and desire (7.5)

Basic scientists

- Engage basic scientists more actively in program planning (5.9)

Please…

- Consider GM VIII recommendations in your deliberations
- Email them to you now?
- Consider appropriate role for clinical sequencing in NHGRI's genomic medicine programs
- Recognize NHGRI emphasis on genome-wide, disease-ome-wide efforts
- Identify disease-specific efforts that may be paradigm setting and open to partners

Many Thanks…

Joy Boyer
Lisa Brooks
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Eric Green
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Jeff Struewing
Simona Volpi
Ken WIley
Anastasia Wise
Carol Bult
Rex Chisholm
Geoff Ginsburg
Howard Jacob
Howard McLeod
Mary Relling
Dan Roden
Marc Williams
GM Mtg Participts
All of You!

Immediate Plans for Follow-Up

- Engage basic scientists in GM IX meeting on bedside back to bench

- Phenotypes c/w model organisms
- Variant nomenclature
- Function → annotation

Immediate Plans for Follow-Up

- Engage basic scientists in GM IX meeting on bedside back to bench
- Pursue infrastructure needs internally
  - Knowledgebase of genomic medicine studies
  - Patient-oriented ontology
  - Implementation commons
  - Common data elements
  - Increased patient engagement
- Comparative effectiveness research
  - WGS vs. targeted panel sequencing
  - WGS w/ vs. w/o adequate FHx