



National Human
Genome Research
Institute



National
Institutes of
Health



U.S. Department
of Health and
Human Services

Education across NHGRI's Genomic Medicine Research Portfolio

U.S. Department of Health and Human Services
National Institutes of Health
National Human Genome Research Institute

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NACHGR Genomic Medicine Working Group Members

NHGRI defines genomic medicine as “an emerging medical discipline that involves using genomic information about an individual as part of their clinical care and the health outcomes and policy implications of that clinical use.”

Mary Fleming

St. Jude

Dan Roden

Vanderbilt

Marc Williams

Geisinger

Eric Green

NHGRI

Teri Manolio

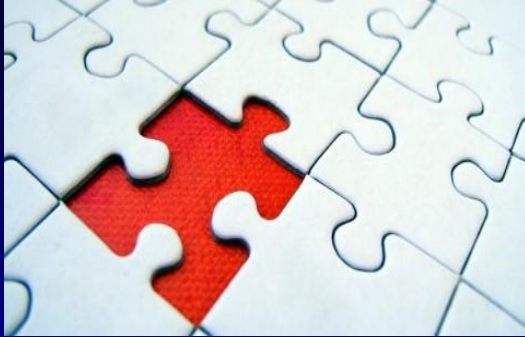
NHGRI

Laura Rodriguez

NHGRI



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



Genomic Medicine Colloquium, June 2011

REVIEW **Genetics in Medicine**

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Open

Implementing genomic medicine in the clinic: the future is here

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Although the potential for genomics to contribute to clinical care has long been anticipated, the pace of defining the risks and benefits of incorporating genomic findings into medical practice has been

relevant; lack of reimbursement for genomically driven interventions; and burden to patients and clinicians of assaying, reporting, interpreting, and following up genomic findings. Key infrastructure needs

GM II: Forming Collaborations, Dec 2011

meTree™

Welcome to MeTree. This program will ask questions about your health and your family's health. Your answers will be used to give you personalized suggestions for your health care. Please answer as best you can.

TOUCH HERE TO START

GM VII: Genomic CDS, Oct 2014



GM IX: Bedside Back to Bench, April 2016



GM III: Health Plans, Dec 2012

Google "NHGRI Genomic Medicine"

Health Plans

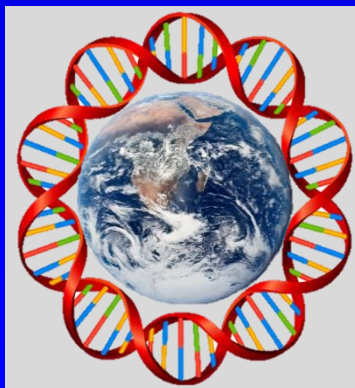
Evidence-based Policies

Medical Policy

Coverage Policy

Payment Policy

GM VI: Global Leaders, Jan 2014



GM V: Federal Strategies, May 2013

cap

A Genomic Medicine Policy Framework

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

GM IV: Physician Education, Jan 2013

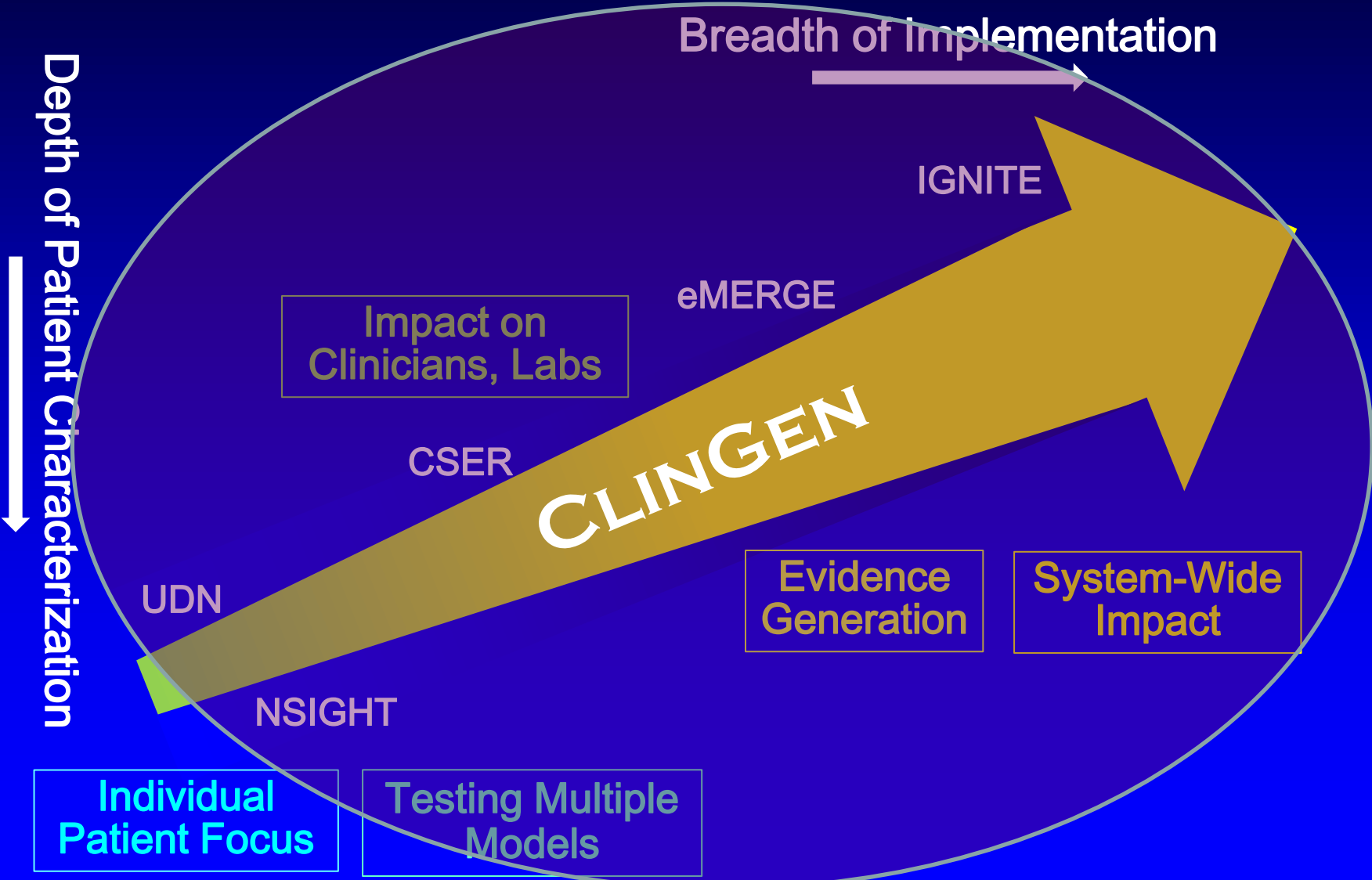


NHGRI's Genomic Medicine Research Program

Program	Goal	Σ\$M	Years
UDN ¹	Diagnose rare and new diseases by expanding NIH's Undiagnosed Diseases Program	121	FY13-17
NSIGHT ²	Explore possible uses of genomic sequence information in the newborn period	25	FY13-17
CSER ³	Explore infrastructure, methods, and issues for integrating genomic sequence into clinical care	83	FY12-16
eMERGE ⁴	Use biorepositories with EMRs for genomics; (III) assess penetrance of 106 clinically relevant genes in 25,000 individuals, develop e-phenotypes, CDS	135	FY07-18
IGNITE ³	Develop and disseminate methods for incorporating patients' genomic findings into their clinical care	32	FY13-16
ClinGen ⁴	Develop and disseminate consensus information on genes and variants relevant to clinical care	28	FY13-16

¹NIH Common Fund; ²Co-Funded by NICHD; ³Co-Funded by NCI; ⁴Co-Funded by OD.

Spectrum of Genomic Medicine Implementation: Intensity vs. Breadth



8 sites with Training Opportunities

- Fellowship programs
- Student trainees
- Volunteers



Train: clinical fellows, residents, undergraduates, masters students, postdoctoral fellows, and faculty

Included in: case conferences, case review, clinical consults, and sequence analysis

Practitioner Education Working Group

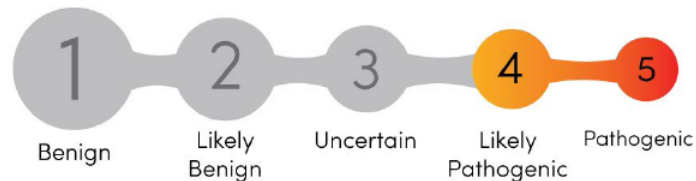
1	Introduction and Overview	3
2	Pathogenic and Likely Pathogenic Results Related to Patient Symptoms	
3	Variant Interpretation	
4	Common Variants	
5	Negative Results	
6	Medical and Research Implications	
7	Pharmacogenetics	
8	Carrier Status	



2: Pathogenic and Likely Pathogenic Results Related to Patient Symptoms

Key Points:

- Pathogenic or likely pathogenic variants in disease genes related to phenotype means that an etiology of the patient's symptoms has been identified.
- Clinically, both pathogenic and likely pathogenic variants are acted upon as if they are likely disease causing.
- De novo loss of function alleles are frequently disease causing.
- De novo missense variants may or may not be pathogenic and require computational analysis and comparison with the patient's phenotype.



Often when a **whole exome** or **whole genome** sequence is done, the primary goal is to answer a diagnostic question in a patient with a specific set of symptoms (**phenotype**). When a genetic

In progress, July 2016.

Courtesy K East, S Plon, D Messersmith, CSER Practitioner Education WG.

Illustrative case studies in the return of exome and genome sequencing results

Amendola et al. *Per. Med.* (2015) 12(3):283-95.



Table 1. Summary of themes, lessons learned and challenges specific to the return of exome and genome sequencing results.

Theme	Lesson(s) learned	Challenges specific to exome and genome sequencing
Managing expectations in pretest and post-test counseling, negative findings do not mean the condition is not genetic	Elicit perceived goals and expectations both during informed consent and after return of results to identify and address misconceptions	Belief that all pathogenic genetic variation can be identified and the clinical significance will be clear
Context matters: follow-up for recommendations from IFs in healthy and ill patient-participants	Both healthy and ill patient-participants who receive IFs may face challenges with adherence to screening/testing recommendations. Ill patient-participants may focus on the diagnostic results and over-interpret a negative result as 'good news'	Limited pretest discussion of the unanticipated condition(s) and implications of results. (Ill) Emphasizing importance of follow-up for medically actionable IFs in the context of more acute concerns. (Healthy) Lack of personal/family history may affect motivation and access to care



451

Number of network publications

47

Number of phenotypes developed

55,028

Number of participants in the Network Cohort



FOR HEALTH PROFESSIONALS

EDGE Disease Genes List

Text Size: **a** **a** **a**

Azathioprine

Clopidogrel

Warfarin

CAG Child Survey

EDGE (Test)

▶ EDGE: All Genes

▶ 10p12.31

▶ **EDGE: By Disease**

▶ EDGE: By Drug

Search EDGE

Search

Phenotype	Locus
3 MCC deficiency	NARS2 and MCCC2 (current link 10p12)
Absent speech	MAP4K4
Acrodysostosis	PRKAR1A
ADHD, Anxiety	ANK3
Adult-onset autosomal recessive ataxia	CLN5
Agenesis of the corpus callosum	H3F3A
Aggressive behaviors	CELSR2COG1/KIF2A
AicardiGoutieres syndrome	ADAR

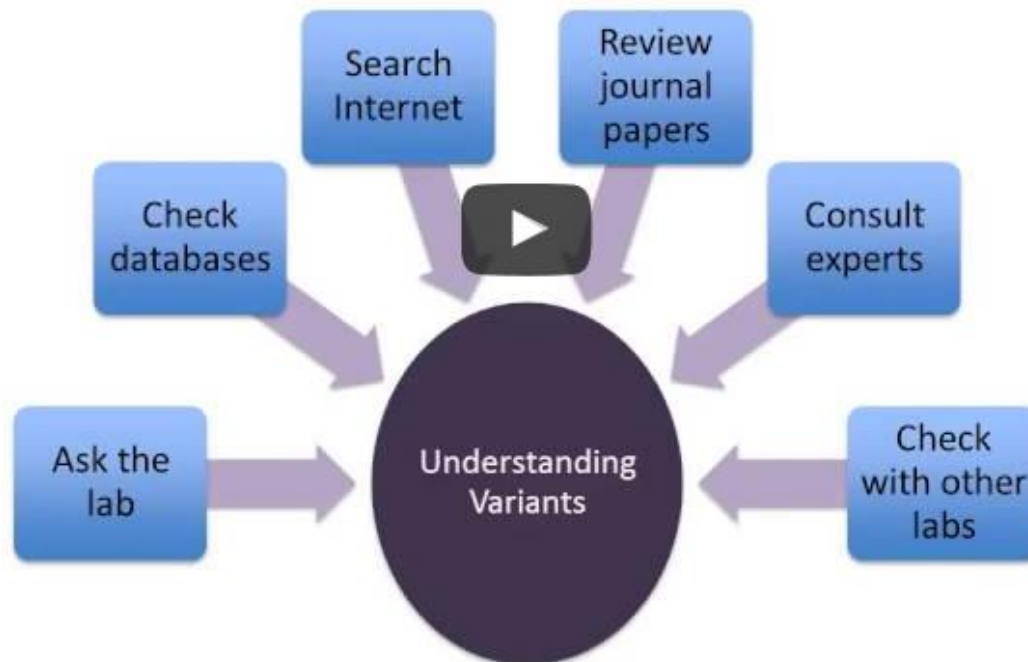
IGNITE SPARK Toolbox

TPMT Diplotype	Phenotype	Metabolism Status	Clinical Priority
*1/*1	Normal Activity	Normal Metabolism	Low
*1/*2	Reduced Activity	Impaired Metabolism	Medium
*1/*3C	Reduced Activity	Impaired Metabolism	Medium
*1/*3B	Reduced Activity	Impaired Metabolism	Medium
*1/*3A	Reduced Activity	Impaired Metabolism	Medium
*2/*2	No Activity	Very Impaired Metabolism	High
*2/*3C	No Activity	Very Impaired Metabolism	High
*2/*3B	No Activity	Very Impaired Metabolism	High
*3C/*3C	No Activity	Very Impaired Metabolism	High
*3B/*3B	No Activity	Very Impaired Metabolism	High
*3A/*3A	No Activity	Very Impaired Metabolism	High
*3A/*3B	No Activity	Very Impaired Metabolism	High
*3A/*3C	No Activity	Very Impaired Metabolism	High
*3A/*2	No Activity	Very Impaired Metabolism	High

Education, Engagement, and Counseling Working Group

Fostering clinician engagement with the ClinGen Resource

Resources for investigating variants



Introduct
Are you
webinar
introduc
clinical p



pairs that meet a
e gene, and are
d process. Learn

cases originally

Many Thanks...

GenomMed Programs Investigators and Participants!

Ebony Bookman

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Lisa Brooks

Erin Currey

Cecilia Dupecher

C. Fletcher-Hoppe

Eric Green

Jyoti Gupta

Lucia Hindorff

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Erin Ramos

Laura Rodriguez

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Robert Wildin

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Rex Chisholm

Geoff Ginsburg

Howard Jacob

Howard McLeod

Mary Relling

Dan Roden

Marc Williams

