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

Teri Manolio, M.D., Ph.D.
Division of Genomic Medicine, NHGRI
August 4, 2016

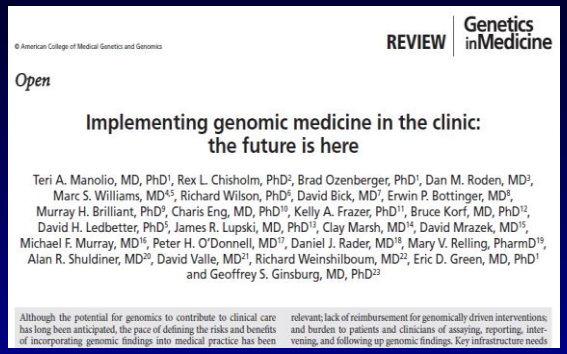
NACHGR Genomic Medicine Working Group Members

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 Relling	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



GM II: Forming Collaborations, Dec 2011

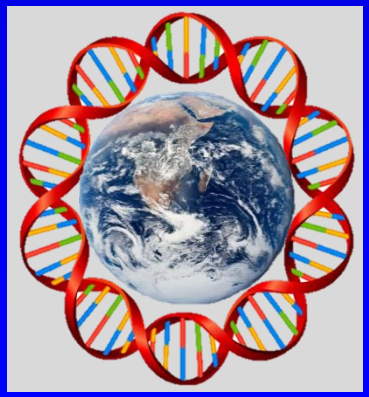
GM VII: Genomic CDS, Oct 2014

GM IX: Bedside Back to Bench, April 2016

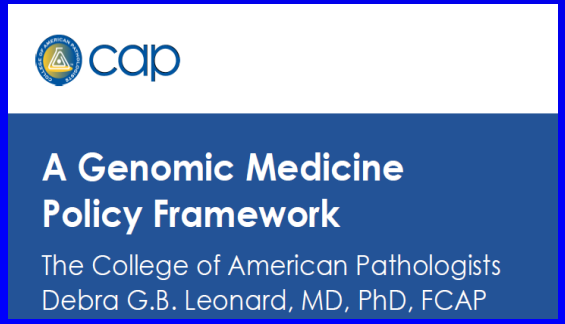
GM III: [illegible] 2

Google "NHGRI Genomic Medicine"

GM VI: Global Leaders, Jan 2014



GM V: Federal Strategies, May 2013



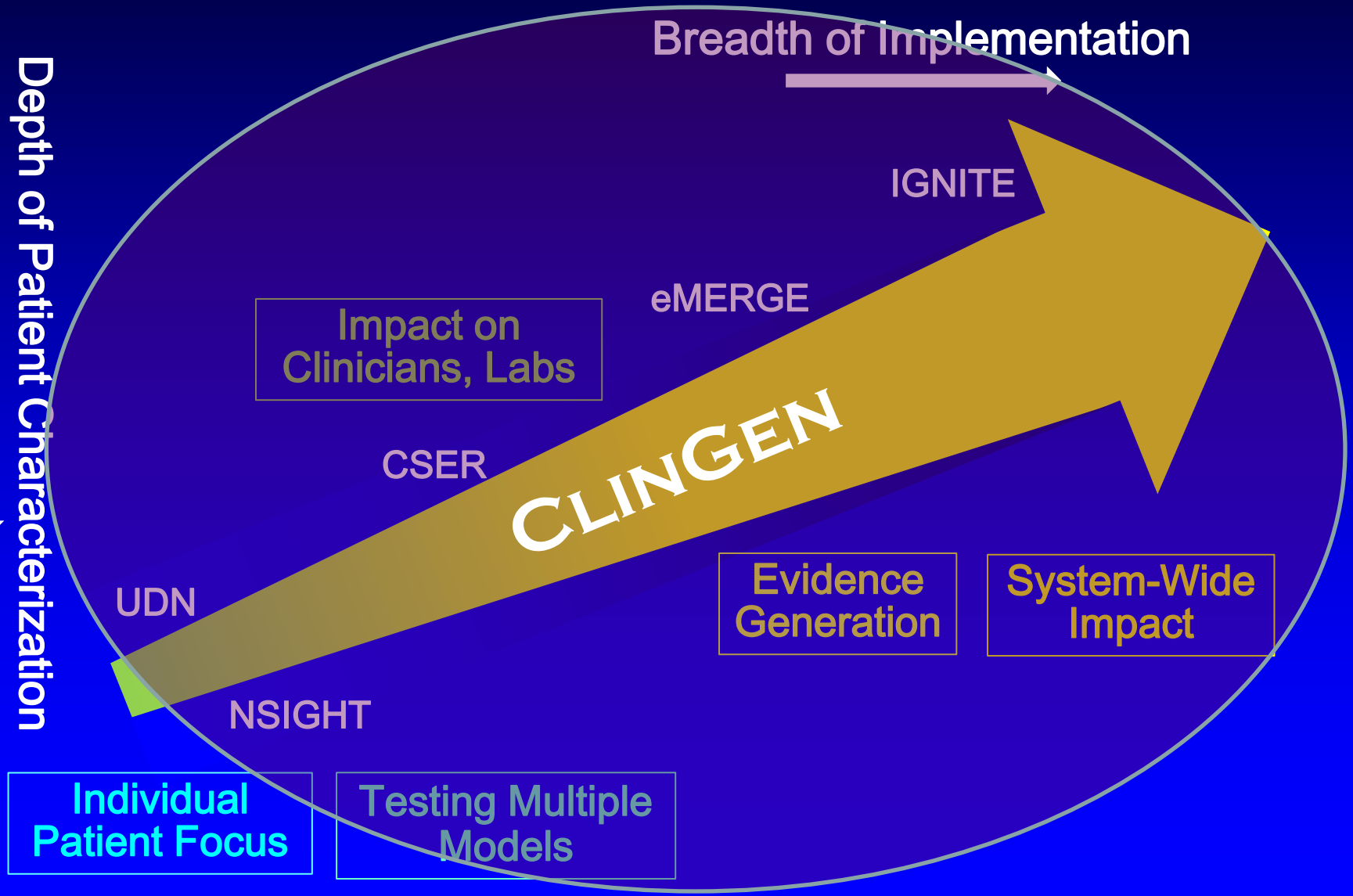
GM IV: Physician Education, Jan 2013

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

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

Spectrum of Genomic Medicine Implementation: Intensity vs. Breadth



Undiagnosed Diseases Network: Training

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

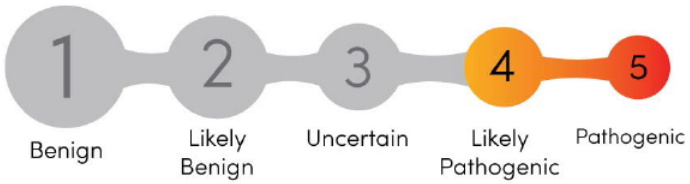
Practitioner Education Working Group

cser
Clinical Sequencing Exploratory Research

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 diseases 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.

Genetic Counseling Working Group

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

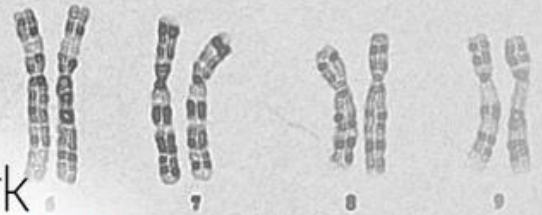
Amendola et al. *Per. Med. (2015) 12(3):283--95.*

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

LOGIN TO EMERGE

emerge network
ELECTRONIC MEDICAL RECORDS AND GENOMICS



451	47	55,028
Number of network publications	Number of phenotypes developed	Number of participants in the Network Cohort

MyResults.org

Search ...

FOR HEALTH PROFESSIONALS

- Azathioprine
- Clopidogrel
- Warfarin
- CAG Child Survey
- **EDGE (Test)**
  - EDGE: All Genes
    - 10p12.31
  - **EDGE: By Disease**
  - EDGE: By Drug

EDGE Disease Genes List

Text Size: a a a

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*

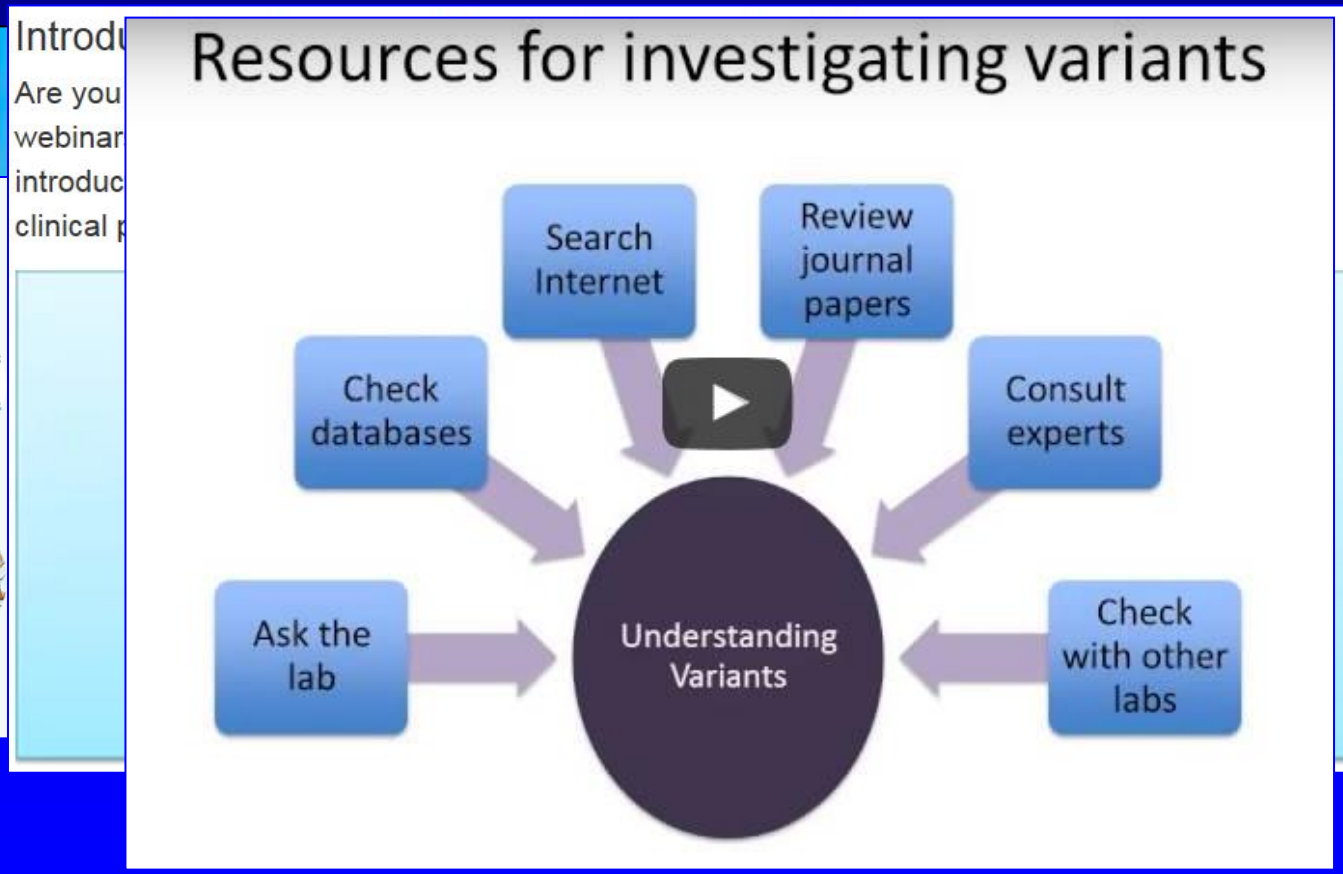
IGNITE SPARK Toolbox

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

https://ignite-genomics.org/spark-toolbox/clinicians/

Education, Engagement, and Counseling Working Group

Fostering clinician engagement with the ClinGen Resource



Many Thanks…

GenomMed Programs Investigators and Participants!

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Ken Wiley
Anastasia Wise
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Rex Chisholm
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Howard Jacob
Howard McLeod
Mary Relling
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Marc Williams