



National Human
Genome Research
Institute



National
Institutes of
Health



U.S. Department
of Health and
Human Services

Genomic Medicine Working Group Update

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

Teri Manolio, M.D., Ph.D.
National Advisory Council on Human Genome
Research
September 12, 2016

NACHGR Genomic Medicine Working Group Members

Carol Bult

Rex Chisholm

Geoff Ginsburg

Howard Jacob

Howard McLeod

Mary Relling

Dan Roden

Marc Williams

Eric Green

Teri Manolio

Laura Rodriguez

Jackson Lab

Northwestern

Duke

HudsonAlpha

Moffitt Cancer Ctr

St. Jude

Vanderbilt

Geisinger

NHGRI

NHGRI

NHGRI

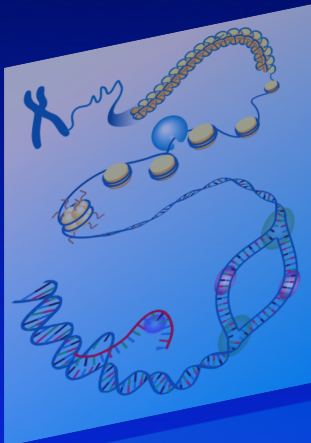


Five Domains of Genomics Research

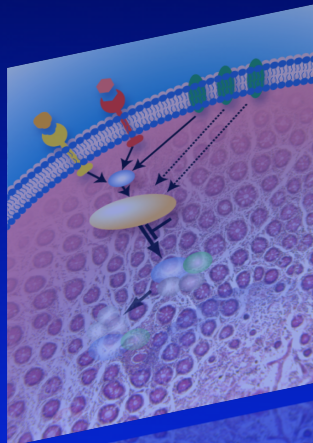
Understanding
the Structure of
Genomes



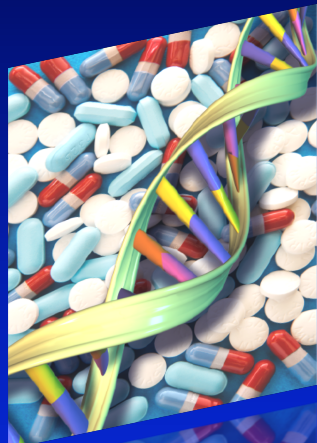
Understanding
the Biology of
Genomes



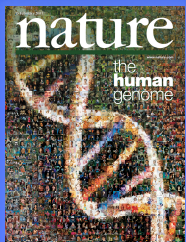
Understanding
the Biology of
Disease



Advancing
the Science of
Medicine



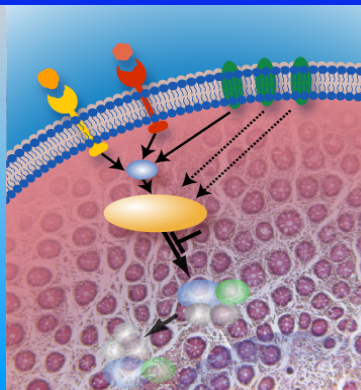
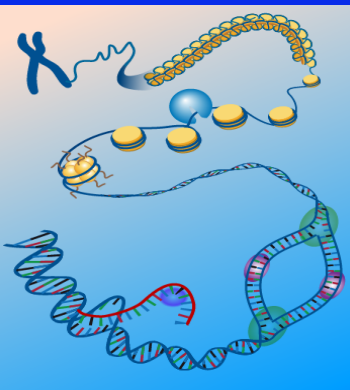
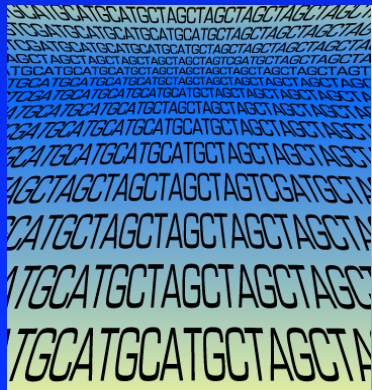
Improving the
Effectiveness
of Healthcare



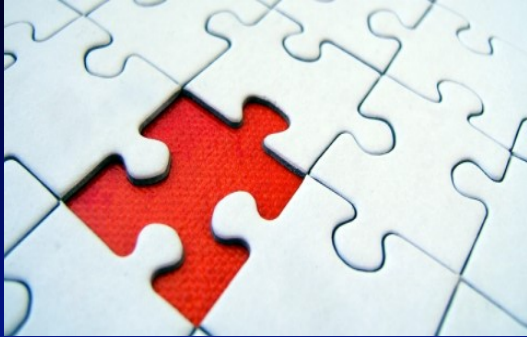
Genomic Medicine Working Group - Charge

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



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

Teri A. Manolio, MD, PhD¹, Rex L. Chisholm, PhD², Brad Ozenberger, PhD¹, Dan M. Roden, MD³, Marc S. Williams, MD^{4,5}, Richard Wilson, PhD⁶, David Bick, MD⁷, Erwin P. Bottinger, MD⁸, Murray H. Brilliant, PhD⁹, Charis Eng, MD, PhD¹⁰, Kelly A. Frazer, PhD¹¹, Bruce Korf, MD, PhD¹², David H. Ledbetter, PhD⁵, James R. Lupski, MD, PhD¹³, Clay Marsh, MD¹⁴, David Mrazek, MD¹⁵, Michael F. Murray, MD¹⁶, Peter H. O'Donnell, MD¹⁷, Daniel J. Rader, MD¹⁸, Mary V. Relling, PharmD¹⁹, Alan R. Shuldiner, MD²⁰, David Valle, MD²¹, Richard Weinsztilbaum, MD²², Eric D. Green, MD, PhD¹ and Geoffrey S. Ginsburg, MD, PhD²³

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

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



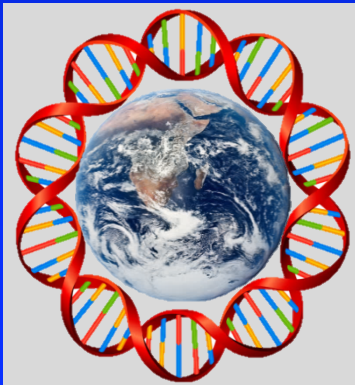
GM III: Health Plans, Dec 2012

Health Plans
Evidence-based Policies

Medical Policy | Coverage Policy | Payment Policy

Google "NHGRI Genomic Medicine"

GM VI: Global Leaders, Jan 2014



GM V: Federal Strategies, May 2013

A Genomic Medicine Policy Framework

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

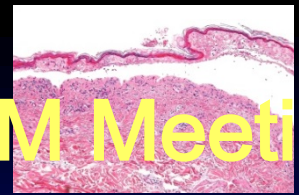
GM IV: Physician Education, Jan 2013





Outgrowths of GM Meetings

PAR-16-275
Serious ADRs



SJS/TEN



G2MC

Harness QI Efforts

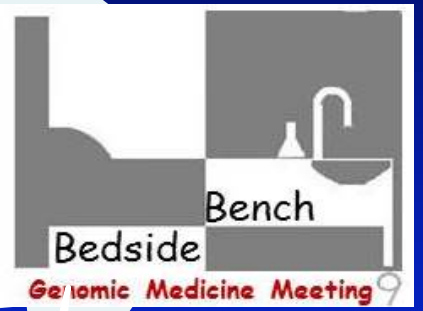


ISCC



Payers

Clin Action



Prioritizing Genes for Functional Study

Knowledge Base of GM Efforts

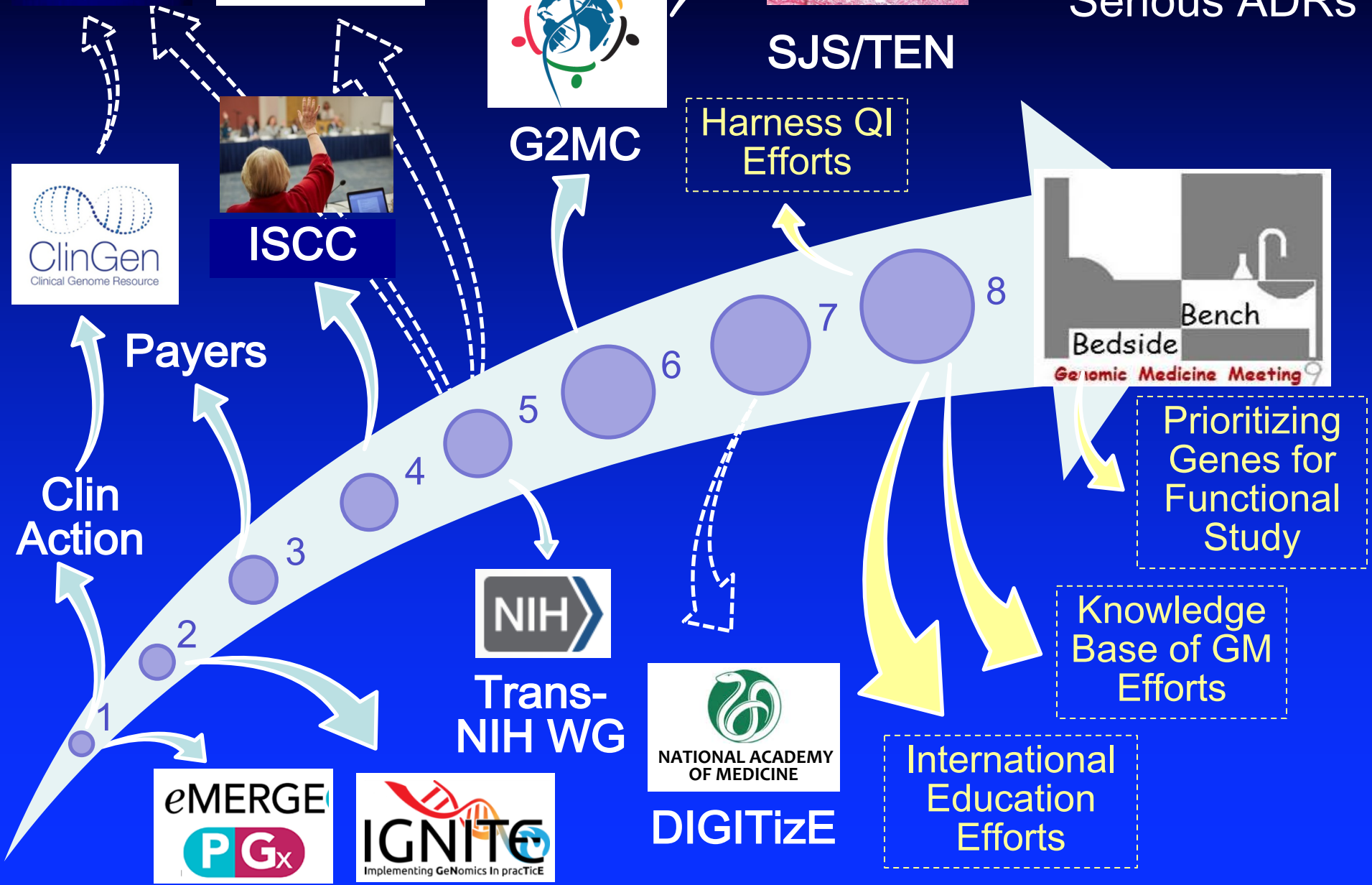
International Education Efforts



Trans-NIH WG



DIGITize



Genomic Medicine X

Research Directions in Pharmacogenomics

May 2-3, 2017, Bethesda MD

- Survey national and international landscape of research programs in PGx implementation
- Examine synergies and promote collaborations
- Identify evidence gaps and studies needed to address them
- Design strategy for large-scale evaluation and implementation of pharmacogenomics in clinical care in the U.S.

Prominent GM VIII Recommendations

- Engage basic scientists more actively in planning of genomic medicine programs

GM IX - Bedside Back to Bench

April 19-20, 2016; Silver Spring, MD



Prominent GM VIII Recommendations

- Engage basic scientists more actively in planning of genomic medicine programs
- Create an implementation commons for sharing tools for implementing genomic medicine

SPARK Toolbox

Supporting Practice through Application, Resources, and Knowledge

Tools by Role

Clinicians



Informing treatment options incorporating genomics into your practice

Researchers



Collecting, assessing and measuring data on genomic implementations

Educators



Teaching clinicians, trainees, and students about incorporating genomics in patient care

Patients



Understanding how genes affect your health and the ideal drugs

Prominent GM VIII Recommendations

- Engage basic scientists more actively in planning of genomic medicine programs
- Create an implementation commons for sharing tools for implementing genomic medicine
- Develop dedicated programs for non-EA populations to fill key gaps

Components of Participating Organizations

National Human Genome Research Institute ([NHGRI](#))

National Cancer Institute ([NCI](#))

National Institute on Minority Health and Health Disparities ([NIMHD](#))

Funding Opportunity Title

**Clinical Sequencing Evidence-Generating Research (CSER2) -
Clinical Sites with Enhanced Diversity (U01)**

Activity Code

[U01](#) Research Project – Cooperative Agreements

Announcement Type

Reissue of [RFA-HG-12-009](#)

Related Notices

- [June 2, 2016](#) - Notice Announcing Pre-application Information Webinar for Clinical Sequencing Evidence-generating Research (CSER2) Requests For Applications (RFAs) and Frequently Asked Questions (FAQ) regarding Clinical Sequencing Funding Opportunities. See Notice [NOT-HG-16-021](#).
-

Funding Opportunity Announcement (FOA) Number

RFA-HG-16-011

Prominent GM VIII Recommendations

- Engage basic scientists more actively in planning of genomic medicine programs
- Create an implementation commons for sharing tools for implementing genomic medicine
- Develop dedicated programs for non-EA populations to fill key gaps
- Maximize sharing of quality improvement (QI) projects by engaging health systems
- Explore joint training opportunities in genomic medicine with other organizations
- Establish and maintain a knowledgebase of ongoing genomic medicine studies

Harness Quality Improvement Projects

- Many organizations are implementing genomic medicine projects as QI programs
- HRSA and NAM: “...systematic and continuous actions that lead to measurable improvement in health care services and the health status of targeted patient groups.”
 - Individualized to meet needs of specific health service delivery system
 - Evidence-based
 - Designed to improve patient safety and outcomes
 - Often complex and multi-disciplinary

Harness Quality Improvement Projects



- Contact GMWG members' QI chiefs
- Organize small meeting to discuss QI opportunities in genomics
- Present genomics seminars at annual meetings

Explore Joint Training Opportunities

- Genomics England dedicating £25M over three years through Health Education England, mandate to expand internationally
- U Miami concurrent Master of Science in Genomic Medicine
- Inter-Society Coordinating Committee for Practitioner Education in Genomics
- Jackson Lab “Precision Medicine for Your Practice” series
- ASHG, ACMG, NHGRI Genomic Healthcare Branch and training programs

International Genomics Education Meeting August 4-5, Bethesda MD



- Genomics England
Ma...ates



- Aus...for
ad...s



- Genetics Education
Canada



- G2...d
Ro...

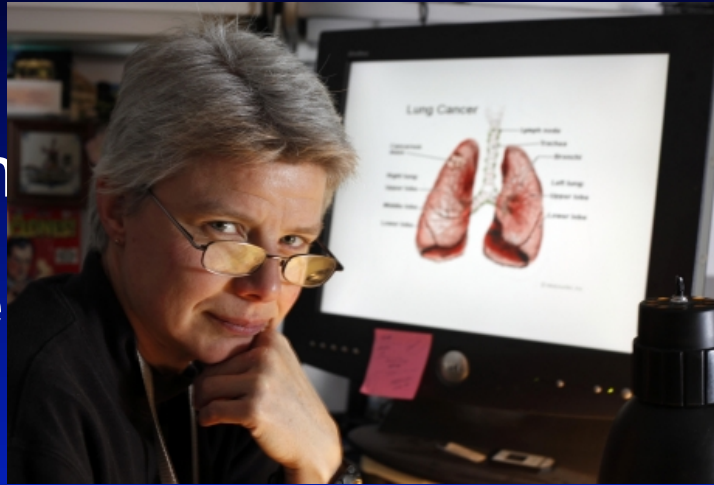


- U...MS
in Genomic Medicine



Knowledgebase of Genomic Medicine Studies

- Compile and implement genomic medicine
- Stimulate and synthesize more effective evidence
- Develop self-nomination site with auto-curation modeled on MGD and ClinVar
- Begin with descriptive
- Encourage databases such as C



Cecilia Dupecher

Notable Accomplishments in Genomic Medicine

The NHGRI Genomic Medicine Working Group has compiled a list of interesting advances in the realm of genomic medicine over the past three years.

JAMA. 2016;316(1):70-78.

Genetics in Medicine | ACMG PRACTICE GUIDELINES

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npj | Genomic Medicine

www.nature.com/npjgenmed

Genom Med 2016; 1:16019.

ARTICLE **OPEN**

Development and validation of a whole-exome sequencing test for simultaneous detection of point mutations, indels and copy-number alterations for precision cancer care

Hanna Rennert^{1,2}, Kenneth Eng^{1,3}, Tuo Zhang^{1,4}, Adrian Tan^{1,4}, Jenny Xiang^{1,4}, Alessandro Romanel⁵, Robert Kim^{1,2}, Wayne Tam², Yen-Chun Liu², Bhavneet Bhinder¹, Joanna Cyrt¹, Himisha Beltran^{1,6}, Brian Robinson^{1,2}, Juan Miguel Mosquera^{1,2}, Helen Fernandes^{1,2}, Francesca Demichelis⁵, Andrea Sboner^{1,2,3}, Michael Kluk^{1,2}, Mark A Rubin^{1,2,7} and Olivier Elemento^{1,3,7}

We describe Exome Cancer Test v1.0 (EXaCT-1), the first New York State-Department of Health-approved whole-exome sequencing (WES)-based test for precision cancer care. EXaCT-1 uses HaloPlex (Agilent) target enrichment followed by next-generation sequencing (Illumina) of tumour and matched constitutional control DNA. We present a detailed clinical development and validation pipeline suitable for simultaneous detection of somatic point/indel mutations and copy-number alterations (CNAs).

Many Thanks...

GMWG Programs Participants!

Ebony Bookman

Joy Boyer

Lisa Brooks

Erin Currey

Cecilia Dupecher

Alvaro Encinas

C. Fletcher-Hoppe

Eric Green

Jyoti Gupta

Lucia Hindorff

Carolyn Hutter

Jean Jenkins

Heather Junkins

Melpi Kasapi

Dave Kaufman

Rongling Li

Nicole Lockhart

Jean McEwen

Donna Messersmith

Kiara Palmer

Erin Ramos

Laura Rodriguez

Simona Volpi

Robert Wildin

Ken Wiley

Anastasia Wise

Carol Bult

Rex Chisholm

Geoff Ginsburg

Howard Jacob

Howard McLeod

Mary Relling

Dan Roden

Marc Williams

NHGRI Genomic Medicine Definition

August 2012

Genomic Medicine: *An emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision-making) and the other implications of that clinical use.*

- Purposefully narrow
- By ‘genomic,’ NHGRI means direct information about DNA or RNA; downstream products outside immediate view
- NHGRI recognizes dominant portion of its current portfolio appropriately supports the foundational research that will ultimately produce the discipline of genomic medicine
- Fourth and fifth NHGRI strategic plan domains capture research activities under umbrella of genomic medicine
- Metaphorically viewed as key ‘destination’ for attaining mission of improving health through genomics research

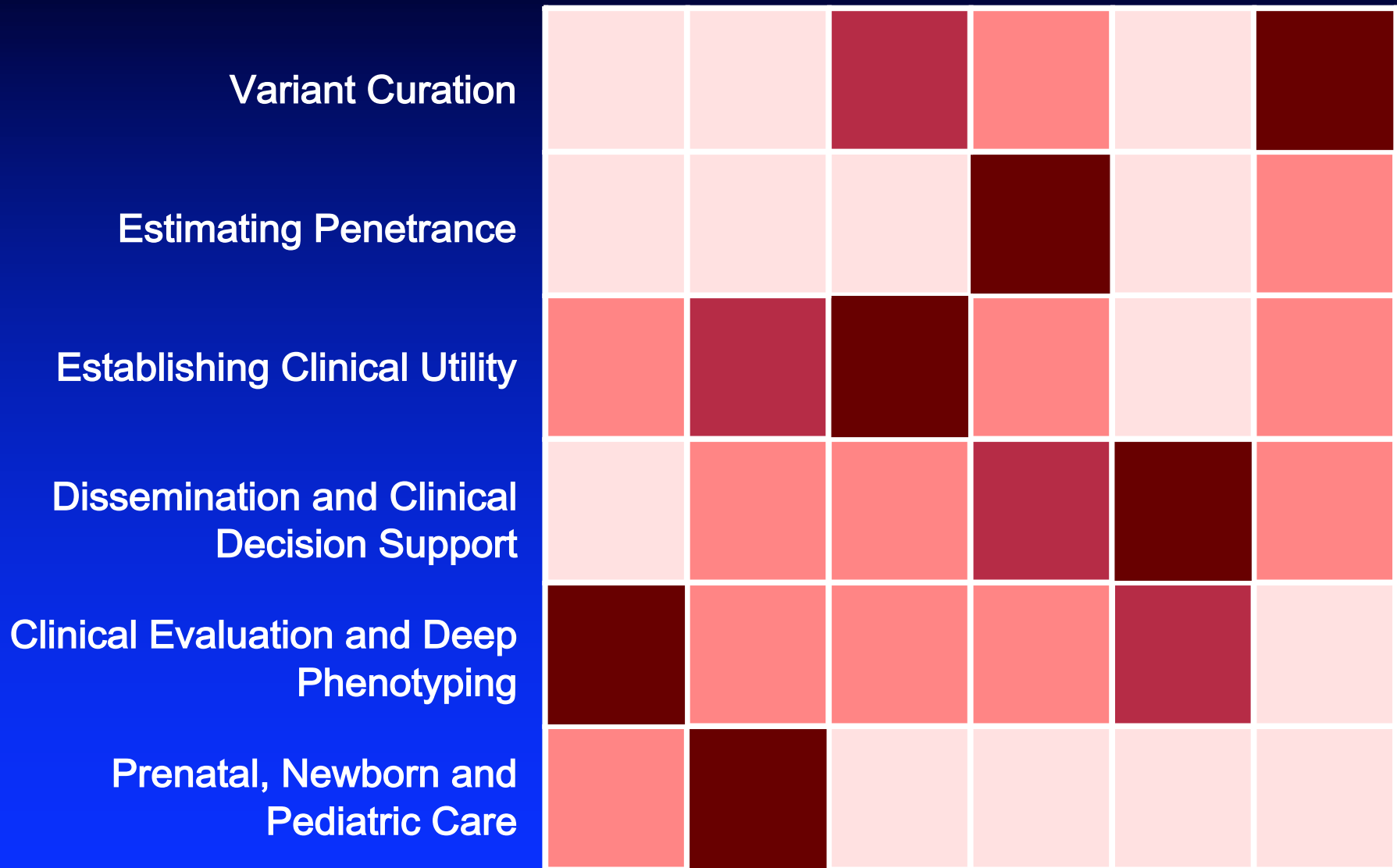
NHGRI's Genomic Medicine Research Program

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	28	FY13-17
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.

Emphasis Areas of Genomic Medicine Programs

UDN NSIGHT CSER2 eMERGE IGNITE ClinGen



Primary

Spectrum of Genomic Medicine Implementation: Intensity vs. Breadth

