National Human Genome Research Institute

National Institutes of Health

U.S. Department of Health and Human Services

Update: Genomic Medicine Working Group

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 9, 2013

Genomic Medicine: On the Threshold?

- Identify risk
- Prevent disease
- Improve diagnostics
- Improve treatments
- Increase access

- Making genomics-based diagnostics routine
- Defining genetic components of disease
- Characterizing cancer genomes
- Developing clinical genomic informatics
- Defining role of microbiome in health and disease

Imperatives for genomic medicine

Opportunities for genomic medicine will come from simultaneously acquiring foundational knowledge of genome function, insights into disease biology and powerful genomic tools. The following imperatives will capitalize on these opportunities in the coming decade.

Making genomics-based diagnostics routine. Genomic technology development so far has been driven by the research market. In the next decade, technology advances could enable a clinician to acquire a complete genomic diagnostic panel (including genomic, epigenomic, transcriptomic and microbiomic analyses) as routinely as a blood chemistry panel.

Defining the genetic components of disease. All diseases involve a genetic component. Genome sequencing could be used to determine the genetic variation underlying the full spectrum of diseases, from rare Mendelian to common complex disorders, through the study of upwards of a million patients; efforts should begin now to organize the necessary sample collections.

Comprehensive characterization of cancer genomes. A comprehensive genomic view of all cancers[4–7] will reveal molecular taxonomies and altered pathways for each cancer subtype. Such information should lead to more robust diagnostic and therapeutic

to build on these first revelations and to investigate approaches for manipulating the microbiome as a new therapeutic approach.

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

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

Domain 5: Improving the Effectiveness of Healthcare

- Delivering genomic information to clinicians and patients
- Demonstrating effectiveness
- Educating healthcare professionals, patients and the public
- Increasing access to genomic medicine
  - Increasing role of non-geneticist healthcare providers
  - Increased use of telemedicine
  - Enhanced genomics education for future healthcare providers

Genomic Medicine Working Group of National Advisory Council on Human Genome Research

- Plan Genomic Medicine meetings, 2-3 per yr
- Provide guidance to NHGRI in other areas of genomic medicine implementation, such as:
  - Outlining infrastructural needs for adoption of genomic medicine
  - Identifying related efforts for future collaborations
  - Reviewing progress overall in genomic medicine implementation

NACHGR Genomic Medicine Working Group Members

Rex Chisholm	Northwestern
Geoff Ginsburg	Duke
Howard Jacob	Med Coll Wisconsin
Pearl O'Rourke	Partners
Mary Relling	St. Jude
Dan Roden	Vanderbilt
Marc Williams	Geisinger
Eric Green	Brad Ozenberger
Teri Manolio	Laura Rodriguez

NHGRI Genomic Medicine Meetings, 2011

- GM Colloquium, June 2011, Chicago IL
  - Define landscape, identify commonalities
  - Develop implementation roadmap to share experiences and facilitate adoption
  - Identify common infrastructure and research needs

Genomic Medicine Colloquium Report June 2011, Chicago, IL

REVIEW | Genetics inMedicine

Open

Implementing genomic medicine in the clinic: the future is here

Teri A. Manolio, MD, PhD[1], Rex L. Chisholm, PhD[2], Brad Ozenberger, PhD[1], Dan M. Roden, MD[3], Marc S. Williams, MD[4,5], Richard Wilson, PhD[6], David Bick, MD[7], Erwin P. Bottinger, MD[8], Murray H. Brilliant, PhD[9], Charis Eng, MD, PhD[10], Kelly A. Frazer, PhD[11], Bruce Korf, MD, PhD[12], David H. Ledbetter, PhD[5], James R. Lupski, MD, PhD[13], Clay Marsh, MD[14], David Mrazek, MD[15], Michael F. Murray, MD[16], Peter H. O'Donnell, MD[17], Daniel J. Rader, MD[18], Mary V. Relling, PharmD[19], Alan R. Shuldiner, MD[20], David Valle, MD[21], Richard Weinshilboum, MD[22], Eric D. Green, MD, PhD[1] and Geoffrey S. Ginsburg, MD, PhD[23]

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, intervening, and following up genomic findings. Key infrastructure needs

Genet Med 2012; 15:258-67.

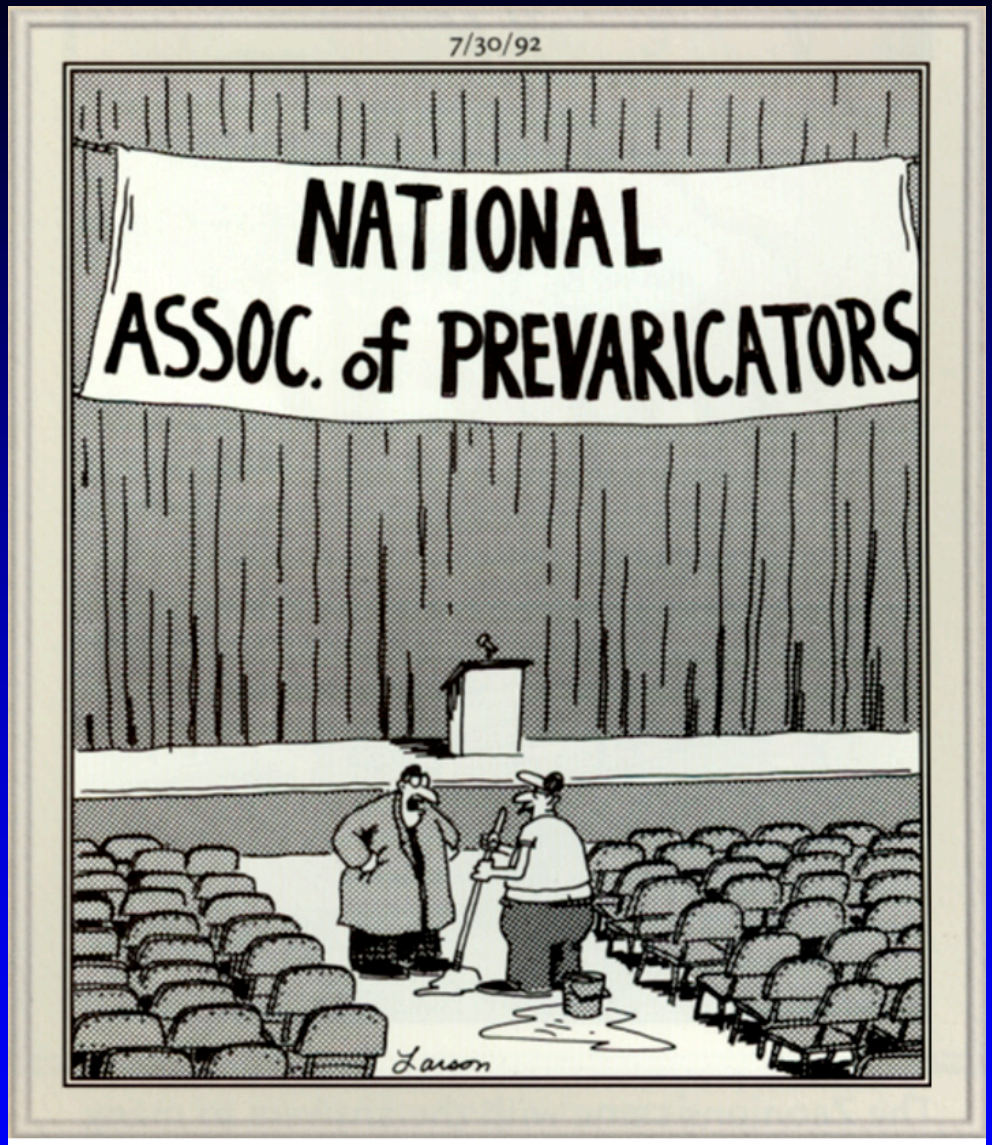
NHGRI Genomic Medicine Meetings, 2011

- GM Colloquium, June 2011, Chicago IL
  - Define landscape, identify commonalities
  - Develop implementation roadmap to share experiences and facilitate adoption
  - Identify common infrastructure and research needs
- ClinAction, December 2011, Bethesda MD

  Consider processes and resources needed to:
  - Identify clinically relevant variants
  - Decide whether they are actionable and what the action should be

NHGRI Genomic Medicine Meetings, 2011-2012

- GM II, December 2011, Bethesda MD
  - Identify potential collaborative projects
  - Explore requirements for adoption with institutional leaders
- GM III, May 2012, Chicago IL
  - Review early progress from pilot project working groups
  - Explore implementation barriers and solutions with payers and other stakeholders
- Payers' Meeting, October 2012, Bethesda MD
  - Identify potential for collaborative research and joint funding



"Yesterday? I was told the meeting was *today!*"

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

Genomic Medicine Funding Opportunities

Department of Health and Human Services

Part 1. Overview Information

Department of Health and Human Services

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Part 1. Overview Information

Participating Organization (s)	National Institutes of Health (NIH)
Components of Participating Organizations	This Funding Opportunity Announcement (FOA) is developed as a Common Fund initiative (http://commonfund.nih.gov/) through the NIH Office of the NIH Director, Office of Strategic Coordination (http://dpcpsi.nih.gov/osc/). The FOA will be administered by the National Human Genome Research Institute (NHGRI/NIH) (http://genome.gov) on behalf of the NIH.
Funding Opportunity Title	**Coordinating Center for an Undiagnosed Diseases Network (UDN) (U01)**
Activity Code	U01 Research Project – Cooperative Agreements
Announcement Type	New
Related Notices	• August 7, 2013 - See Companion RFA-RM-13-018. DNA Sequencing Core for an Undiagnosed Diseases Network (UDN) (U01).

Undiagnosed Diseases Network: RFAs RM-12-020, 13-003, 13-004, 13-018

Department of Health and Human Services

Part 1. Overview Information

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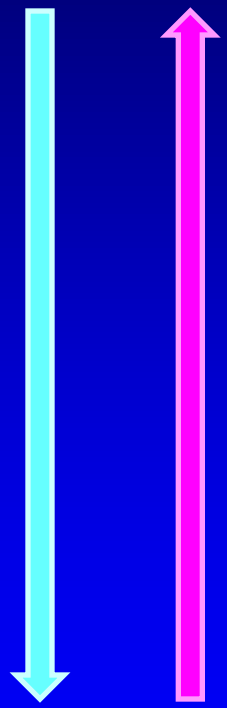
Funding Opportunity Title	**DNA Sequencing Core for an Undiagnosed Diseases Network (UDN) (U01)**
Activity Code	U01 Research Project – Cooperative Agreements
Announcement Type	New
Related Notices	• August 21, 2013: Removed reference to ASSIST in section IV.3, since ASSIST is currently only available for multi-project applications.
Funding Opportunity Announcement (FOA)	**RFA-RM-13-018**

eMERGE-PGRN Partnership

PGRN Pharmacogenomics Research Network

- State of art PGx array
- Ability to update
- Drug-gene guidelines
- CLIA standards and QC



- Privacy concerns
- Electronic phenotyping
- Large pt base
- Less PGx-focused labs

The *eMERGE* Network
electronic Medical Records & Genomics

Genomic Medicine IV, Jan 28-29, 2013
Educating Physicians in Genomic Medicine

Accreditation Council for Graduate Medical Education

Accreditation Council for Continuing Medical Education

American Academy of Pediatrics

American College of Cardiology

American College of Medical Genetics and Genomics

American College of Physicians

American College of Obstetrics and Gynecology

American Heart Association

American Society of Clinical Oncology

Association of Professors of Human Medical Genetics

Areas of General Consensus

- Present genomics to physicians as gradual evolution rather than “revolution”
- Embed genomics education at point of care with adequate clinical decision support technologies
- Share genomics education materials already produced by many societies
- Utilize other educational resources such as checklists, ethical guidelines, case studies
- Incorporate genomics into certifications and licensing, emphasizing appropriate competencies
- Allow subspecialty-tailored training rather than general programs requiring rare syndromes and dysmorphologies

Inter-Society Coordinating Committee for Practitioner Education in Genomics

Charge: To facilitate interactions among societies that will enhance their efforts to increase the understanding and expertise of practitioners in applying genomic results to clinical care.

Structure

- One representative from professional societies and one from interested NIH ICs
- Co-chaired by a professional society representative and an NIH person
- Meet at 6-month intervals with conference calls between meetings
- Design a 3- to 5-year work plan with potential for additional years if needed

Initial Working Groups and Products

Competencies: Review surveys and other sources, work with societies to identify appropriate competencies

Educational products: Collect existing products from ISCC societies, identify new educational needs and develop appropriate resources

Engagement of Specialty Boards: Determine extent specialty boards have genomics in their certification processes, support further integration

Use Cases: Develop general and society-specific use cases, create educational materials to support them

How to Spell Success?

Inter-society communications are free-flowing and useful, and there are documented improvements in appropriate use of genomic strategies by physicians.

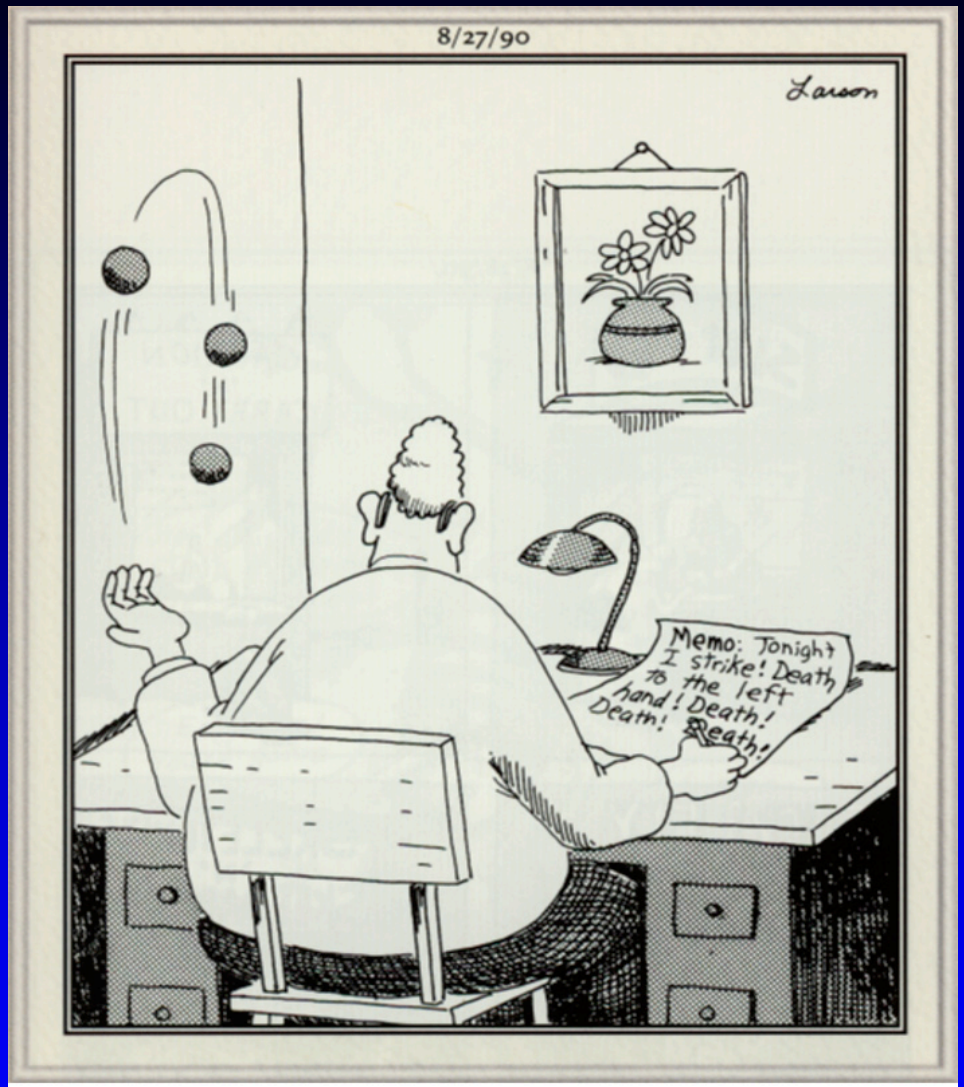
Specific process metrics might include:

- Educational best practices identified and disseminated
- Physician competencies generated
- Estimates of physician use
- Professional society guidelines documents reviewed and improved
- Interactions with other relevant efforts and other provider group educational activities

ISCC as of September 5, 2013

Accred Counc Grad Med Ed
Accred Council Cont Med Ed
Am Acad Family Physicians
Am Acad Pediatrics
Am Assoc Clin Chem
Am Board Medical Genetics
Am Board Medical Specialties
Am Coll Cardiology
Am Coll Med Genet Genom
Am Coll Obstet Gynecol
Am Coll Physicians
Am Heart Assoc
Am Med Assoc
Am Soc Clin Oncol
Am Thoracic Soc
Assoc Molec Pathology
Assoc Prof Human Med Genet
Coll Am Pathologists
Counc Med Specialty Soc
Soc Gen Internal Medicine

NCI
NCBI/NLM
NHLBI
NIAAA
NIAID
NIAMS
NICHD
NIDA
NIDCD
NIDCR
NIGMS
NIMH
NINDS



Innocent and carefree, Stuart's left hand didn't know what the right was doing.

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

NHGRI Genomic Medicine Meetings, 2012-2013

- GM V, May 28-29, 2013, Bethesda MD
  - Engage federal agencies to discuss potential overall US strategies for gm implementation
  - Explore current activities, needs, obstacles
  - Identify common interests and opportunities, plans for collaboration and strategy development

Agencies Participating in GM V

- Direct medical care efforts
  - Department of Veterans Affairs
  - US Air Force, US Army, US Coast Guard, US Navy
- Reimbursement and regulatory efforts
  - Centers for Medicare and Medicaid Services
  - Food and Drug Administration
  - Agency for Healthcare Research and Quality
  - Blue Cross/Blue Shield
- Supportive and facilitative efforts
  - Centers for Disease Control and Prevention
  - Patient-Centered Outcomes Research Institute
  - Office of the Assistant Secretary for Health
  - Office of the Assistant Secretary for Planning and Eval
  - Institute of Medicine Genomics Roundtable

Key Components of GM Implementation Strategies

Component	AHRQ	CDC	CMS	FDA	NHGRI	ASH	PCORI	USAF/ DOD	VHA
Equitable Access	X	X	X		X	X	X	X	X
Bioinformatics infrastructure for relating clinical characteristics to variants		X		X	X			X	X
Data sharing in accessible research databases	X	X			X	X			X
Standardized phenotypic, patient, variant, and reference information		X		X	X			X	X
Assessment of health economics and cost-effectiveness		X	X		X			X	X
Evidence of clinical validity and utility	X	X	X	X	X	X		X	X
Consent model		X			X	X		X	X
Ethical and legal framework to protect against potential abuses		X			X	X		X	X
Engaging public and building awareness		X			X	X		X	X

Exploring Projects in Evidence Development

- Possible joint project with military medical services, DVA, NIH Clinical Center (Sept 2013)
  - Identify potential collaborative projects
  - Define obstacles to implementation and collaboration
  - Engage scientific/clinical content experts in project design and selection
  - Explore funding sources
- NIH-wide efforts in GM implementation (Oct 2013)
  - Demonstrate opportunities
  - Identify current efforts
  - Explore challenges and common needs
  - Define opportunities for collaboration

Key Components: International/Other

Component	UK	Canada	Italy	ESF	CAP	IOM	AMA
Service delivery infrastructure for requesting and receiving genomic results	X		X	X	X		
Bioinformatics infrastructure for relating clinical characteristics to variants	X	X	X	X	X	X	X
Data sharing in accessible research databases	X			X	X		X
Standardized phenotypic, patient, variant, and reference information	X			X	X	X	X
Assessment of health economics and cost-effectiveness	X	X	X		X	X	X
Evidence of clinical validity and utility	X	X	X	X	X	X	X
Training/workforce development	X		X	X	X		
Ethical and legal framework to protect against potential abuses	X	X			X		X
Engaging public and building awareness	X	X	X	X			
Equitable access	X		X	X			X

NHGRI Genomic Medicine Meetings, 2013-2014

- GM V, May 28-29, 2013, Bethesda MD
  - Engage federal agencies to discuss potential overall US strategies for gm implementation
  - Explore current activities, needs, obstacles
  - Identify common interests and opportunities, plans for collaboration and strategy development
- GM VI, Jan 8-9, 2014, Bethesda MD
  - Engage international agencies
  - Explore current activities, needs, obstacles
  - Identify common research gaps to ensure evidence only need be generated once
  - Develop plans for international collaboration

Genomic Medicine VI, Jan 8-9, 2014
International Collaborations in Genomic Medicine

Canada (CIHR)

Canada (GenomeCanada)

Belgium (Europ Comm)

Belgium (U Liege)

Germany (EPMA)

Luxembourg (Ctr Syst Biomed)

Sweden (Swed Res Council)

UK (Wellcome Trust)

Israel (Hadassah U)

Kuwait (Genom Med Ctr)

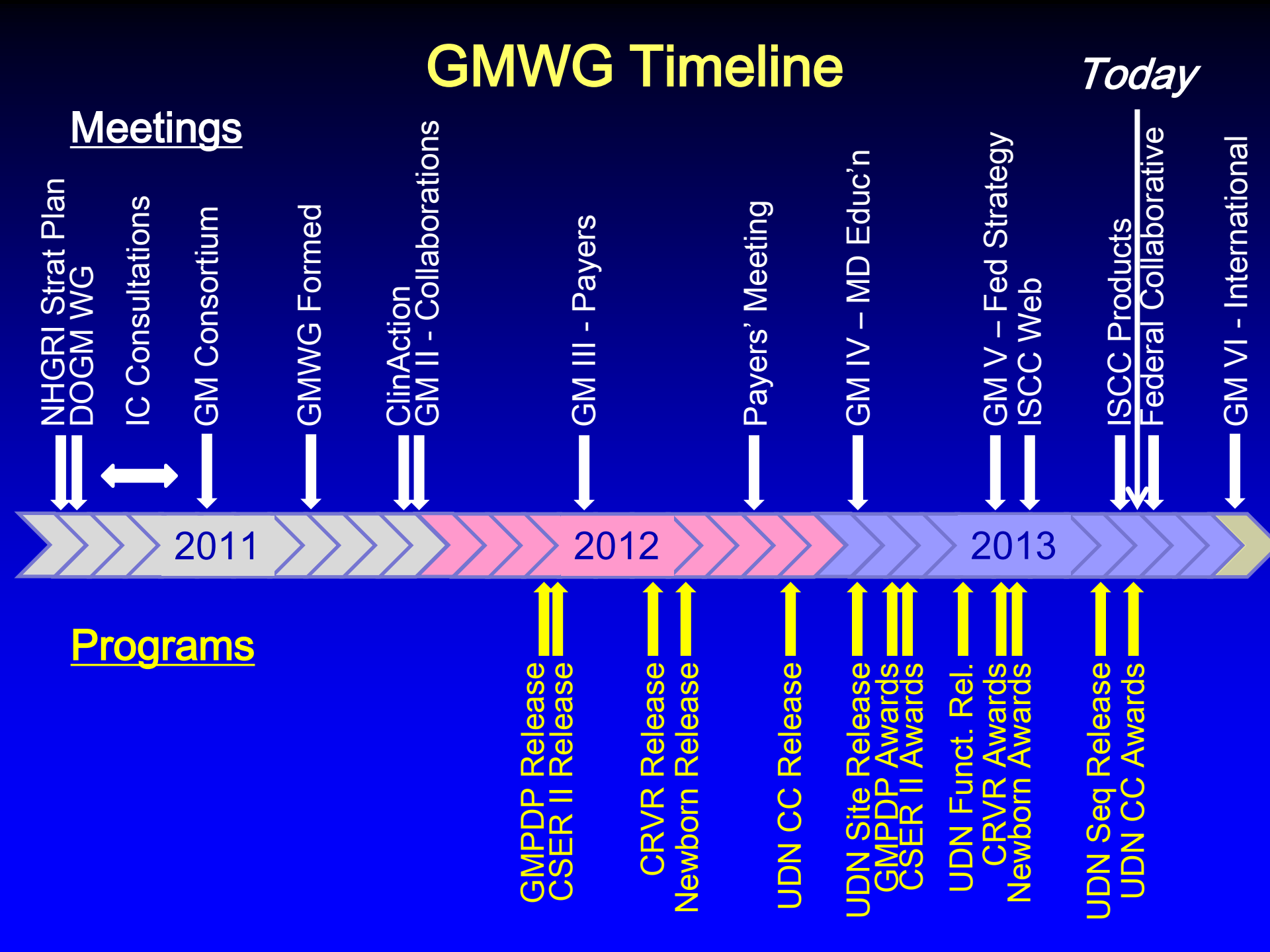
Japan (U Tokyo)

Korea (Korean NIH)

Singapore (National U)

Thailand (Health Ministry)

Australia (MRC)


GMWG Timeline
Today
Meetings
NHGRI Strat Plan
DOGM WG
IC Consultations
GM Consortium
GMWG Formed
ClinAction
GM II - Collaborations
GM III - Payers
Payers' Meeting
GM IV – MD Educ'n
GM V – Fed Strategy
ISCC Web
ISCC Products
Federal Collaborative
GM VI - International
2011
2012
2013
Programs
GMPDP Release
CSER II Release
CRVR Release
Newborn Release
UDN CC Release
UDN Site Release
GMPDP Awards
CSER II Awards
UDN Funct. Rel.
CRVR Awards
Newborn Awards
UDN Seq Release
UDN CC Awards

NHGRI's Genomic Medicine Research Program

Program	Goal	Σ $M	Years
eMERGE II	Use biorepositories with EMRs and GWA data to incorporate genomics into clinical research and care	32.4	FY11-14
eMERGE-PGx	Apply PGRN's validated VIP array for discovery and clinical care in ~9,000 patients	8.0	FY12-14
CSER	Explore infrastructure, methods, and issues for integrating genomic sequence into clinical care	61.8	FY12-16
RoR*	Investigate whether/when/how to return individual research results to ppts in genomic research studies	8.7	FY12-15
CRVR	Develop and disseminate consensus information on variants relevant for clinical care	14.0	FY13-16
GMPDP	Develop and disseminate methods for incorporating patients' genomic findings into their clinical care	24.8	FY13-16
Newborn Sequencing	Explore possible uses of genomic sequence information in the newborn period	10.0	FY13-16
UDN	Diagnose both rare and new diseases by expanding NIH's Undiagnosed Diseases Program	(67.9)	FY13-17

* Includes ELSI Set-Aside Funds. Seven-year average NHGRI = $23M/year or 6-7% extramural budget

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Nicole Lockhart
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Brad Ozenberger
Gene Passamani
Erin Ramos
Laura Rodriguez
Kathy Sun
Simona Volpi
Anastasia Wise
Rosanne Wise

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GMWG!