Clinical Sequencing Exploratory Research (CSER) Program

Lucia A. Hindorff, PhD, MPH

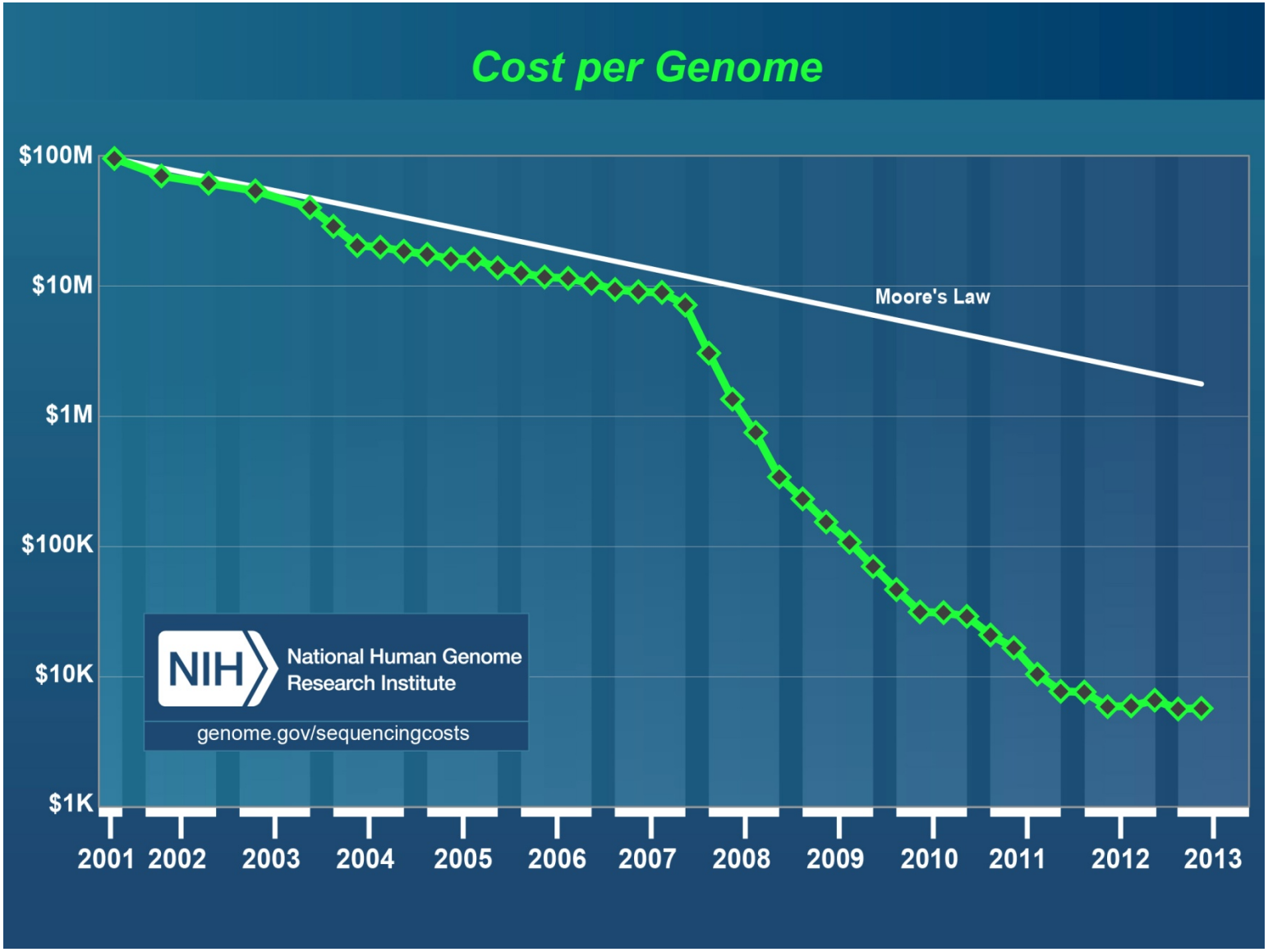
Division of Genomic Medicine, NHGRI

Global Leaders in Genomic Medicine

Washington, DC

January 9, 2014

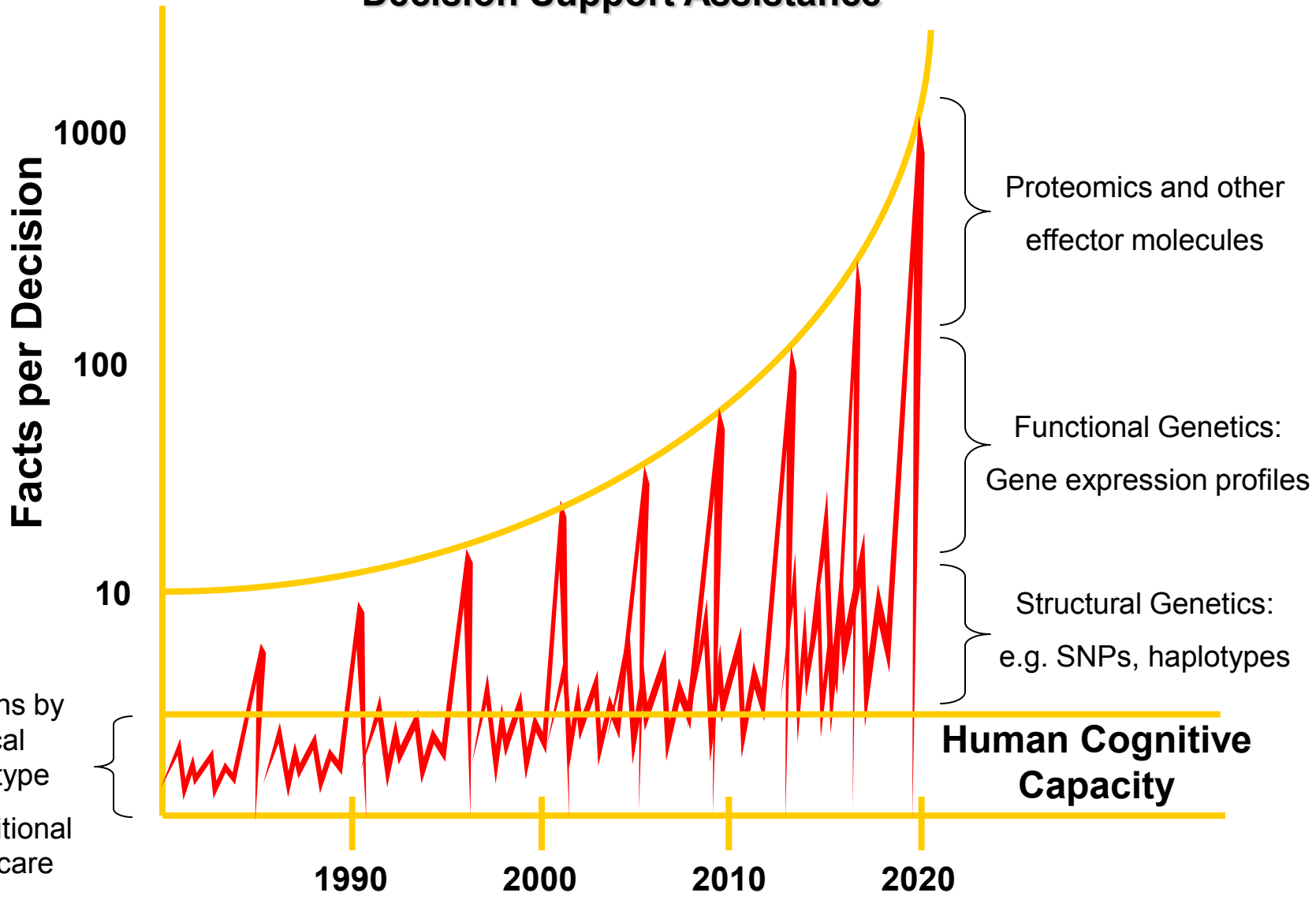
National Human Genome Research Institute



cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

The Need for Patient- and Physician-Specific Decision Support Assistance



cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

Courtesy Dan Masys

RFA HG 10 -017, HG 12-009

Clinical Sequencing Exploratory Research

- Research the challenges to applying comprehensive genomic sequence data to the care of patients:
  - generation and application of genomic sequence data in the clinical workflow and timeline,
  - interpretation and translation of the data for the physician,
  - communication to the patient.
- Examine the ethical and psychosocial implications of bringing broad genomic data into the clinic.

CSER Project Structure

cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

CSER sites (U awards)

	Institution	Principal Investigator(s)	Disease Focus
2011	Baylor College of Medicine* *Houston, TX*	Sharon Plon, Will Parsons	Cancer (Pediatric)
	Brigham and Women's Hospital *Boston, MA*	Robert Green	Healthy; Cardiomyopathy
	Children's Hospital of Philadelphia *Philadelphia, PA*	Ian Krantz, Nancy Spinner	Pediatric Diseases
	Dana-Farber Cancer Institute / Broad Institute *Boston, MA*	Levi Garraway, Pasi Janne	Cancer
	University of North Carolina *Chapel Hill, NC*	James Evans, Jonathan Berg, Gail Henderson	Multiple
	University of Washington* *Seattle, WA*	Gail Jarvik	Cancer (Colorectal polyposis)
2013	HudsonAlpha Institute for Biotechnology *Huntsville, AL*	Richard Myers	Pediatric intellectual and developmental disability
	Kaiser Foundation Research Institute *Portland, OR*	Katrina Goddard, Benjamin Wilfond	Pre-conception genetic screening
	University of Michigan*	Arul Chinnayan	Cancer (sarcoma)

*co-funded by NCI

cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

CSER sites (R Grants)

PI	Title
Paul Appelbaum *Columbia University*	Challenges of informed consent in return of data from genomic research
Wendy Chung *Columbia University*	Impact of return of incidental genetic test results to research participants in the genomic era
Ellen Wright Clayton *Vanderbilt University*	Returning research results of pediatric genomic research to participants
Jeremy Garrett *Children's Mercy Hospital*	The presumptive case against returning individual results in biobanking research
Ingrid Holm *Boston Children's Hospital*	Returning research results in children: Parental preferences and expert oversight
Barbara Koenig *Mayo Clinic*	Disclosing genomic incidental findings in a cancer biobank: An ELSI experiment
Michelle Lewis *Johns Hopkins*	Return of research results from samples obtained for newborn screening
Richard Sharp *Cleveland Clinic*	Presenting diagnostic results from large-scale clinical mutation testing
Holly Tabor *Seattle Children's Hospital*	Innovative approaches to returning results in exome and genome sequencing studies

CSER Coordinating Center
University of Washington

PI's	Areas of expertise	Key activities
Gail Jarvik, Wylie Burke, Deborah Nickerson, Peter Tarczy-Hornoch	Biostatistics, bioethics, cancer, clinical informatics, diagnostic testing, health care outcomes, medical genetics, neonatology, sequencing technology	• Facilitate Working Group and cross-consortia collaborations • Coordinate, initiate, lead high priority CSER projects • Synthesize site-specific variant pathogenicity data, gene lists • Coordinate logistics for CSER Steering Committee, ELSI Committee, and working groups • Help raise consortium visibility

CSER Working Groups

- **Informed Consent & Governance**
  Chairs: Paul Appelbaum and Joon-Ho Yu
- **Actionable Variants and Return of Results**
  Chairs: Laura Amendola, Wendy Chung
- **Psychosocial Outcomes and Measures**
  Chairs: Stacy Gray and Christine Rini
- **Sequencing Standards**
  Chair: Donna Muzny and Nick Wagle
- **Electronic Reports/Medical Records**
  Chair: Peter Tarczy-Hornoch and Brian Shirts
- **Phenotype Measures and Analysis**
  Chairs: Ian Krantz and Peter White
- **Pediatrics**
  Chairs: Kyle Brothers and Ben Wilfond
- **Genetic Counseling**
  Chairs: Sarah Scollon and Denise Lauterbach

cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

CSER recruitment
December, 2013

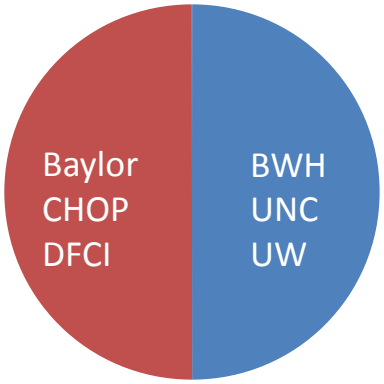
Patients/Participants			Physicians Enrolled
Contacted	Consented	Sequenced	
1,157	472	64 germline 114 tumor	116

cser
Clinical Sequencing Exploratory Research

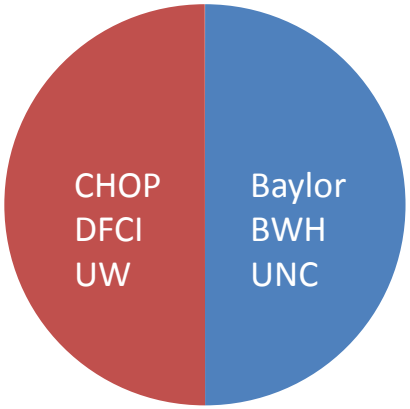
www.genome.gov/CSER
www.cser-consortium.org

Reporting Incidental Findings

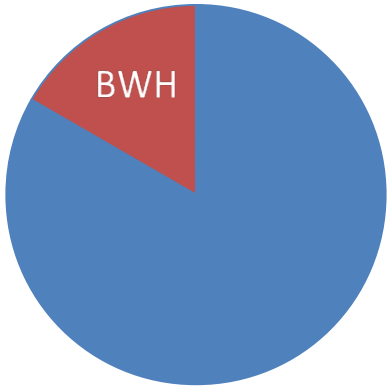
- All six CSER projects report incidental findings
- Half include IFs in their primary indication report, half have a separate report
- Half of sites allow opt out of medically actionable IFs
- 5/6 allow opt out of non-MA IFs



Separate Report
Combined Report



Can Opt-Out of MA IFs? Yes



Can Opt-Out of Non-MA IFs? Yes
Can Opt-Out of Non-MA IFs? No

cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

from H Rehm

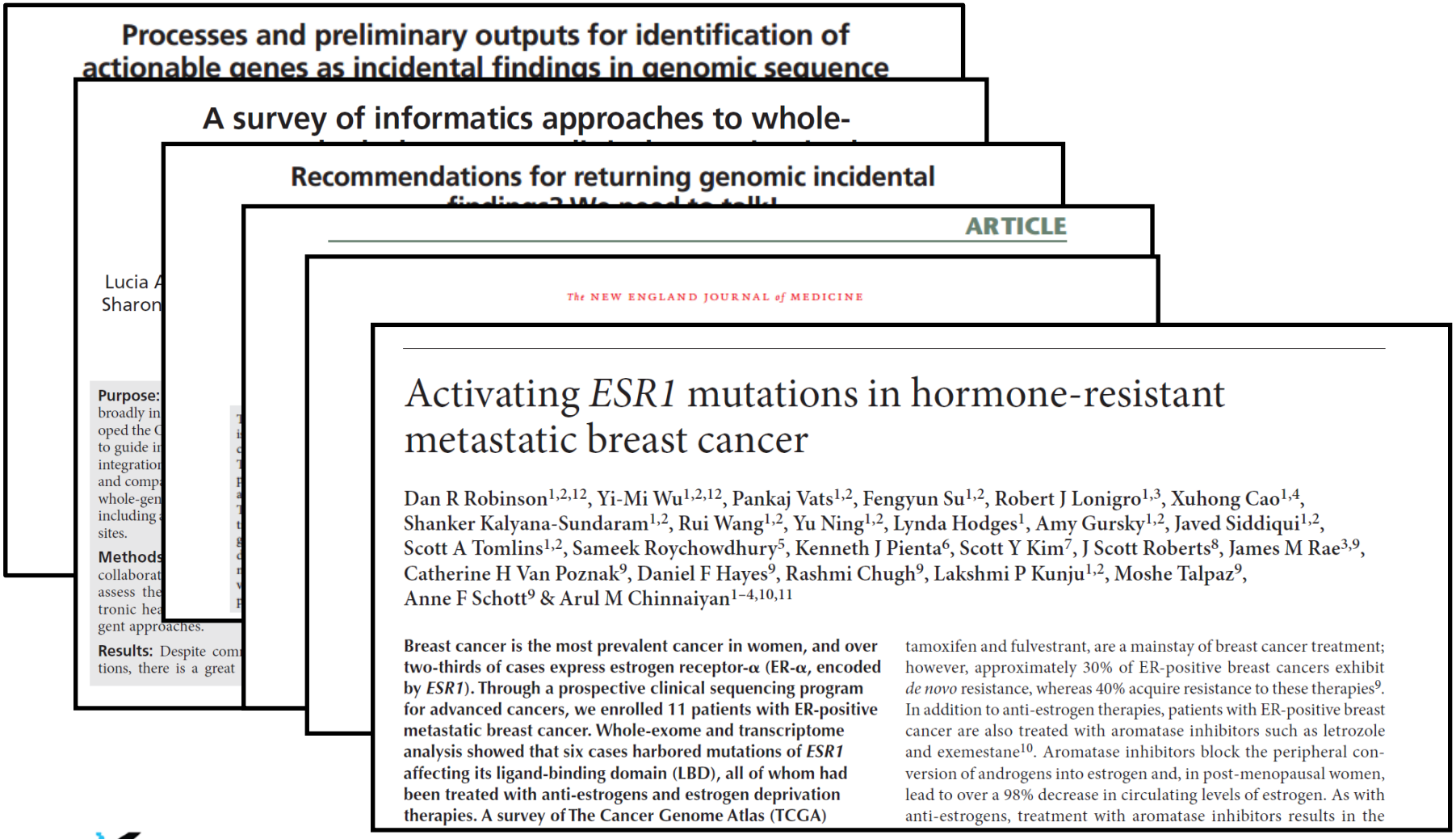
Variant Classifications Reported

- Generally, groups intend to return:
  - Pathogenic and VUS for primary indication
  - Pathogenic variants for IFs

- Biggest challenge:
  - What is sufficient evidence for pathogenicity?
    - Common evidence issues: “reported as pathogenic”; “segregates with disease in a family”

from H Rehm

Recent work



cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org

Clinical Sequencing Exploratory Research

*Moving the **Genome** Into the **Clinic***

377 Researchers
20 Institutions
1 Consortium

NCGenes

Jim Evans
Jonathan Berg
Gail Henderson

CanSeq

Levi Garraway

MedSeq

Robert Green

NEXT

Gail Jarvik

PEDISEQ: The CHOP Pediatric Genetic Sequencing Project

Ian Krantz
Nancy Spinner

BASIC3 — BCM Advancing Sequencing Into Childhood Cancer Care

Sharon Plon
Will Parsons

NexTGen — Understanding the impact of genome sequencing for reproductive decisions

Katrina Goddard
Benjamin Wilfond

HudsonAlpha

Rick Myers

MI-ONCOSEQ

Arul Chinnaiyan

R Grantees

Ingrid Holm
Paul Appelbaum
Wendy Chung
Jeremy Garrett
Michelle Lewis
Rich Sharp
Holly Tabor
Barbara Koenig, Gloria Peterson, & Susan Wolf
Ellen Clayton & Bartha Knoppers

NHGRI

Jean McEwen
Carolyn Hutter
Kathie Sun
Teri Manolio
Brad Ozenberger (now at WUSTL)

NCI

Charlisse Caga-Anan
Sheri Schully

cser
Clinical Sequencing Exploratory Research

www.genome.gov/CSER
www.cser-consortium.org