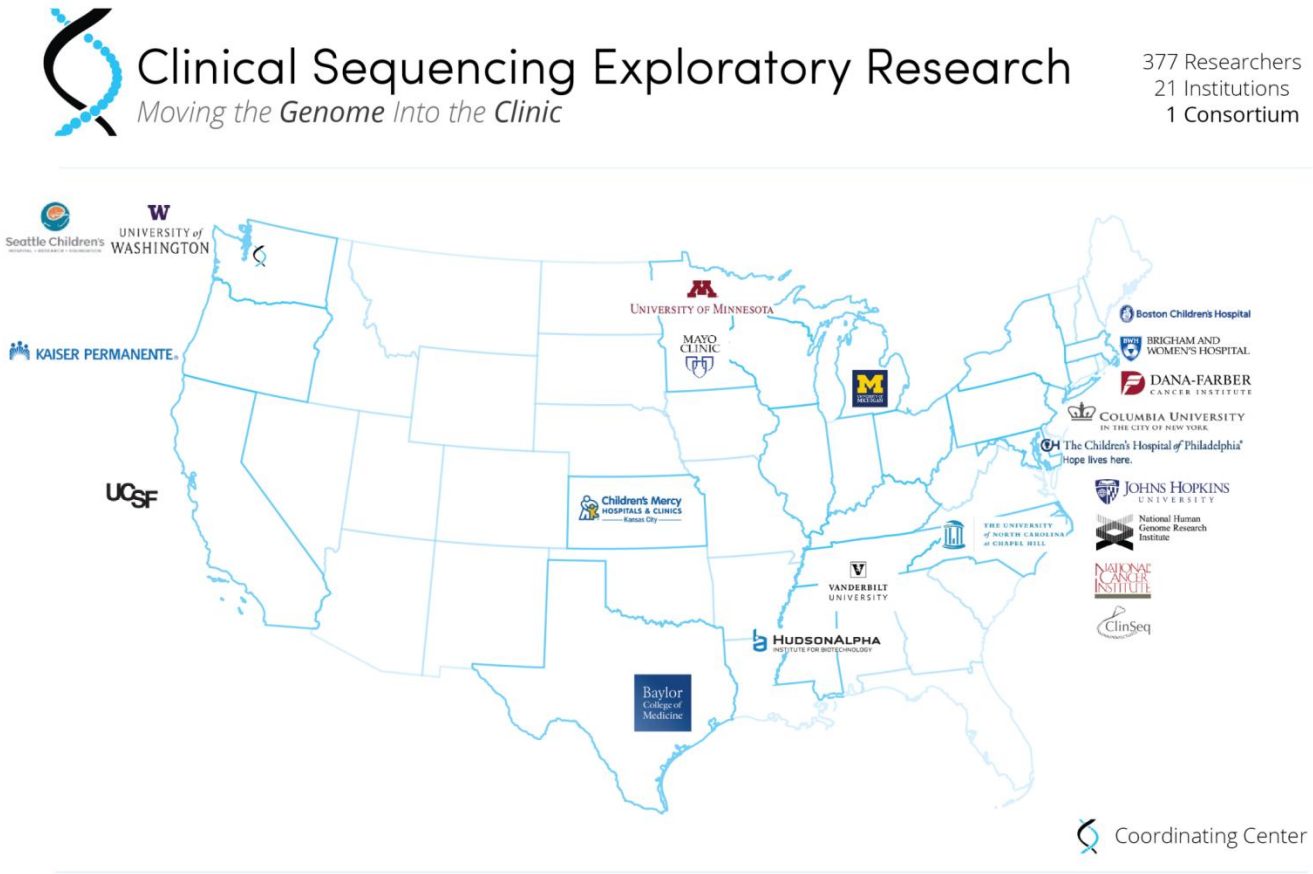


cser
Clinical Sequencing Exploratory Research

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

Future Opportunities for Genome Sequencing and Beyond

July 28-29, 2014, Rockville, MD

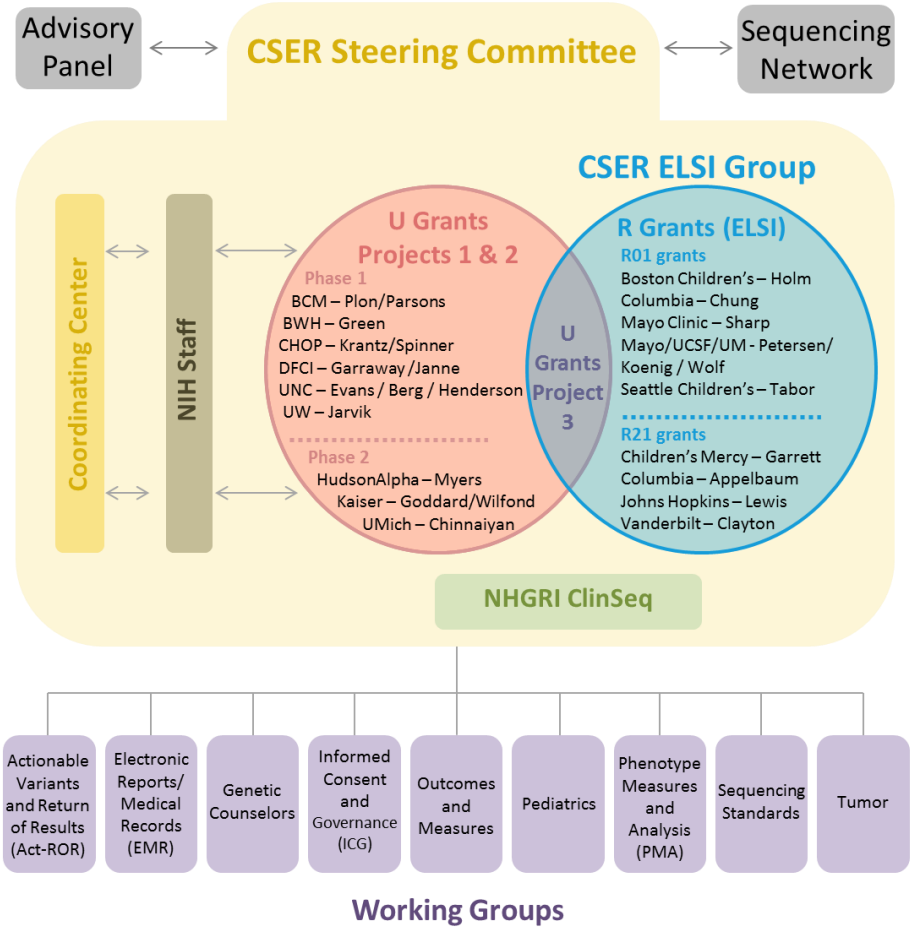
Contents

Clinical Sequencing Exploratory Research

Moving the Genome Into the Clinic

377 Researchers
20 Institutions
1 Consortium

NHGRI's Clinical Sequencing Exploratory Research (CSER) program supports multidisciplinary research to develop and share innovations and best uses of genomic sequencing in the clinical care of individual patients, including the ethical, legal, and psychosocial implications of returning genomic results.



- Funding: 9 U grants, $65M from FY11-FY16 ($56M from NHGRI, $9M from NCI). $15.5M NHGRI funds in FY14
- "U-grants" are described in RFAs HG-10-017, HG-12-010, and HG-12-015 and implement three integrated projects: 1) recruitment of patients and physicians in a clinical setting; 2) generation and interpretation of genomic sequence data in a clinically useful format; 3) ethical, legal, and psychosocial research
- "R-grants" are described in HG-11-003 and HG-11-004 and explore a broad range of ethical, legal, and psychosocial issues related to return of genomic results (originally funded as ELSI Return of Results Consortium)
- 118 publications to date (https://cser-consortium.org/publications)
- 9 Working Groups convened to identify and share common challenges and opportunities
- Identification of high priority cross-study projects (e.g. clinical exome coverage comparison; content analysis of informed consent documents; best practices in variant signout)

Summary of CSER U-grant Enrollment (June, 2014)

Racial / Ethnic Categories	Number Enrolled	Percentage
Total	1768	
White	1334	75.4%
Hispanic/ Latino	145	8.2%
Black or African American	124	7.0%
Asian	55	3.1%
American Indian / Alaska Native	30	1.7%
Native Hawaiian or Other Pacific Islander	3	0.2%
Not Reported	54	3.1%
More than One Race Selected	23	1.3%

	Germline	Tumor
Participants Sequenced	1035	331
Results Returned	137	242
Clinically Relevant Findings	69	166
ACMG Incidental Findings	33	N/A

Clinical Sequencing Exploratory Research Consortium

Executive Summary in preparation for the
NHGRI Future Opportunities for Genome Sequencing and Beyond Meeting
July 28-29, 2014

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RATIONALE FOR CSER

Our understanding of human genetic variation and its association with disease risk and with individual response to treatment continues to expand rapidly. Simultaneously, a revolution has occurred in genomic sequencing technologies, making it technically and economically feasible to consider the application and utilization of genomic sequence data in clinical care. Reports of whole genome and whole exome sequencing being applied to the medical care of individual patients are becoming more frequent, but much more work is needed before the use of sequence data in clinical care can become routine. The potential range of clinical applications and the specific diseases or individual susceptibilities most likely to be usefully addressed by a genomic sequencing approach have yet to be determined. The ethical, legal, and psychosocial implications (ELSI) of returning genomic data, including those related to technical uncertainties, incomplete knowledge, and unanticipated findings, remain incompletely understood.

The incorporation of comprehensive genomic sequence data into clinical care will require changes to institutional policies, standard procedures (including simplified analysis and interpretive tools and improved means for facilitating informed patient and family decision making), and the ability to integrate sequence information into the clinical workflow and electronic medical record (EMR). Implementation without an evidence base may result in harm or inefficiencies that then thwart future productive implementation.

PURPOSE

NHGRI initiated the Clinical Sequencing Exploratory Research (CSER) program to gather the necessary data to begin to develop best practices for clinical sequencing and to conduct the ELSI research required to learn how to responsibly apply personal genomic sequence data to medical care. The CSER Consortium was expanded in 2013 to include nine R award projects that formerly comprised the ELSI Return of Results Consortium. These studies explore a broad range of ethical, legal and social implications relating to the return of research results in both research and clinical settings. The Consortium of grantees cooperates to generate an evidence base for implementation in the rapidly advancing field of clinical sequencing and to disseminate Consortium findings to the clinical, genomic and bioethical communities. As common successes and challenges among the CSER sites become evident, CSER will be well poised to provide best practice recommendations, and to identify gaps and future opportunities to be addressed.

AIMS

1. Generate and interpret genomic sequence data on patients in a variety of clinical contexts;
2. Study the challenges of applying comprehensive genomic sequence data to the care of patients, including:
    a. generation and application of genomic sequence data in the clinical workflow and timeline,
    b. interpretation and translation of sequence data for the clinician, and
    c. communication of sequencing results to the patient and family
3. Examine the ethical, legal, and psychosocial implications of bringing sequence data into the clinic.

RESEARCH PROGRAM AND UNIQUE ATTRIBUTES

The CSER Consortium consists of 18 primary research grants (see Appendix A), a Coordinating Center and multiple collaborators across the U.S., covering a wide range of clinical and ethical applications of genomic science. The diversity of research domains and the collaborative nature of the Consortium enable the program to deliver informed and generalizable recommendations and resources to the wider research community. Investigators from NHGRI's intramural ClinSeq program also participate in CSER. The U award site-specific projects each individually contribute to CSER aims and both the U and R awardees actively contribute to Working Groups which develop Consortium-wide products.

The CSER Consortium is uniquely positioned among NHGRI programs to answer diverse clinical implementation questions incorporating the input of large numbers of practitioners of genomic medicine. The collective expertise of the 377 Consortium investigators at 31 institutions allows rapid advancement of knowledge about the implementation of genomic medicine and development of best practices.

MAJOR ACCOMPLISHMENTS AND ACTIVITES

The individual projects explore dimensions of clinical sequencing technology, its use in clinical care, and patients' and physicians' attitudes, as well as other ELSI issues. The Working Groups' efforts translate this expertise into expert guidance for genomic medicine implementation. The CSER Consortium is uniquely suited to study the productive usage and cost effectiveness of implementing whole genome and whole exome sequencing in a genomic medicine context. In addition to learning from each other, CSER work has attained high visibility within the clinical genetics and ELSI communities, including broad representation at meetings of the American College of Medical Genetics and Genomics (ACMG), American Society of Human Genetics (ASHG), American Society of Bioethics and Humanities (ASBH), American Association for Cancer Research (AACR), American Society of Clinical Oncology (ASCO), Pediatric Academic Societies (PAS), and National Society of Genetic Counselors (NSGC). Highlights of CSER accomplishments to date, including 118 publications, are summarized below.

Highlights of U01 Site-Specific Productivity

- BCM has completed clinical whole exome tumor and germline sequencing, from informed consent through disclosure of results, of over 100 sequentially diagnosed pediatric solid and brain tumor patients. Approximately 40% of patients will have a potential actionable somatic finding, cancer susceptibility mutation and/or medically actionable incidental finding.
- The MI-OncoSeq Project at the UM has recruited 224 patients. Observational data collection of precision medicine tumor boards, longitudinal patient surveys, and physician interviews have shown considerable challenges involving patient education and expectation of benefits.
- The MedSeq Project at Brigham & Women's Hospital has enrolled 161 patients. Investigators have been impressed with how well the enrolled primary care physicians and cardiologists have navigated their patients' family history information and Genome Reports.
- The Children's Hospital of Philadelphia (CHOP) has enrolled 121 patients. CHOP has validated their exome sequencing approach and standardized the variant calling and analysis pipelines.
- UW constructed a widely disseminated list of gene-disease pairs that are actionable in adults and estimated the rate of such incidental findings from 2000 exomes (Dorschner et al PMID: 24055113). UW is performing a randomized controlled trial of WES that includes cost and other outcomes.
- UNC developed a formal classification scheme for adjudication of genomic variants that incorporates the clinical context and nature of the variant and UNC has shown that diagnostic performance of WES varies considerably across patient categories. High diagnostic yields are found in certain patients, e.g., those with retinal disorders and neurological conditions, while WES demonstrates considerably less diagnostic power in suspected cancer predisposition syndromes.
- Construction of condition taxonomies for grouping disorders for return of results (UW, KPNW, UNC)
- Establishment of clinical sequencing pipelines and variant annotation/interpretation resources (all sites)
- Design & implementation of a recruitment, sequencing, analysis, medical record, and return of results pipeline with continuous refinement based in part on CSER experience (all sites)
- Generation of dynamic, curated in-house, publically available variant databases to aid in variant classification supported by review of gene-disease relationships and application of variant filters (all sites).
- Development and application of a clinical interpretation platform for somatic analysis (BCM, DFCI, UM)
- Dissemination of non-geneticist physician educational material (BCM, B&W,HA,UW)

Outreach and Dissemination of Lessons Learned

- Generation of publically available software tools or databases
    - TARGET: database of genes that, when somatically altered in cancer, are directly linked to a clinical action (DFCI)
    - PHIAL: heuristic algorithm for clinical interpretation for cancer genome sequencing data (DFCI)

- BCM has made publically available the software for their clinical exome pipeline, including their variant calling software (Atlas) and their in-house annotation engine (Cassandra)
- "Proband" is an iPad app that allows genetic counselors and other providers to digitally create and store human pedigrees while in a counseling session. Currently validating a phenotype-based gene prioritization algorithm "Phenomatics" and developing software "Varify" to facilitate analysis workflow (CHOP)

- ClinVar submission pending for reclassification of over 600 variants the HGMD classified as disease-causing, some 90% are not disease causing (UW CC, BWH, others)
- Working Group publications summarizing current CSER practices and lessons learned
  - **Bioinformatics |** Tarczy-Hornoch et al., A survey of informatics approaches to whole-exome and whole-genome clinical reporting in the electronic health record. *Genet Med.* 2013; 15(10):824-32. PMID: 24071794
  - **Actionability & Return of Results |** Berg et al., Processes and preliminary outputs for identification of actionable genes as incidental findings in genomic sequencing data in the CSER Consortium. Genet Med. 2013; 15(11):860-7.
  - **Pediatrics |** Clayton EW, McCullough LB, Biesecker LG, Joffe S, Ross LF, Wolf SM; Clinical Sequencing Exploratory Research (CSER) Consortium Pediatrics Working Group. Addressing the ethical challenges in genetic testing and sequencing of children. *Am J Bioeth.* 2014 Mar;14(3):3-9.
  - **Return of Results |** Jarvik et al., Return of Genomic Results to Research Participants: The Floor, the Ceiling, and the Choices in Between. *Am J Hum Genet.* 2014; 94(6):818-26. PMID: 24814192
  - **Outcomes & Measures |** Gray SW, Martins Y, Feuerman LZ, Bernhardt BA, Biesecker BB, Christensen KD, et al. Social and behavioral research in genomic sequencing: approaches from the Clinical Sequencing Exploratory Research Consortium Outcomes and Measures Working Group. *Genet Med.* 2014 Mar 13.
- Working Group papers in progress
  - **Bioinformatics |** Shirts et al., Optimal management of different types of genetic information in the Electronic Medical Record
  - **Sequencing Standards |** Buhay, Wagle et al., Comparison of poorly covered regions in whole exome and whole genome sequencing across 7 sequencing centers
  - **Pediatrics |** Brothers et al., When Research Participants Grow Up: Recontact and Reconsent at the Age of Majority
  - **Actionability & Return of Results |** Amendola et al., Challenges of variant classification: Pathogenicity classification from 6503 participant's exomes
  - **Actionability & Return of Results |** Rehm et al., Best Practices in Variant Sign-out: Experience from the CSER Consortium
  - **Genetic Counseling |** Amendola et al., Illustrative case studies in the return of genomic sequencing results
  - **Pediatrics | McCullough et al.,** Ethics of obtaining informed consent from parents for genomic scale clinical sequencing
- Sessions at high-visibility clinical genetic conferences, e.g. Exploring Clinical Sequencing: What Have We Learned? and Point/Counterpoint: Reporting of Incidental Findings Sessions. ACMG Meeting, 3/2014
- Upcoming presentations at high-visibility conferences: 1) CSER ELSI Panel at the 2014 ASHG conference, 2) Plenary Session at the 2014 National Society of Genetic Counselors conference, 3) Plenary Session at the 2014 European Society for Human Genetics
- Outreach as experts in genomic aspects of human subjects, including to IRBs; set up of clinical genomics labs; variant interpretation
- Annotated site-specific papers of high impact
  - Evans BJ, The First Amendment Right to Speak About the Human Genome, *University of Pennsylvania Journal of Constitutional Law* 2014;16(3):549-636. [This legal analysis suggests that a willing researcher has a First Amendment right to share non-CLIA genetic results with a willing participant.]

- Appelbaum PS, Parens E, Waldman CR, Klitzman RL, Fyer A, Martinez J, Price N, Chung WK. Models of consent to return of incidental findings in genomic research. *Hastings Cent Rep* 2014 In press. PMID: 24919982; NIHMS 563207. [Based on a survey of genetic investigators and interviews with researchers and participants, this paper suggests 4 models of informed consent for return of incidental findings, each with benefits and liabilities.]
- Parsons DW, Roy A, Plon SE, Roychowdhury S, Chinnaiyan AM. Clinical Tumor Sequencing: An Incidental Casualty of the American College of Medical Genetics and Genomics Recommendations for Reporting of Incidental Findings. J Clin Oncol. 2014 Jun 23. pii: JCO.2013.54.8917. [Epub ahead of print] PubMed PMID: 24958819. [This perspective article is an explanation to the oncology community of the implications of requiring the reporting of incidental findings in clinical tumor sequencing for patients, laboratories, and clinicians.]

Site-specific Best Practices Publications

CSER offers unique interactions and learning that benefit all projects and the community.

Published

- **Sequencing** | Biesecker LG, Green RC. Diagnostic clinical genome and exome sequencing. *The New England Journal of Medicine*. 2014;370:2418-2425. PubMed PMID: 24941179;
- **Genetic Counseling |** Facio et al., A Genetic Counselor's Guide to Using Next-Generation Sequencing in Clinical Practice *J Genet Couns.* 2013 Oct 24. PMID: 24151055
- **Informed Consent |** Henderson GE, Wolf SM, Kuczynski KJ, Joffe S, Sharp RR, Parsons DW, Knoppers BM, Yu JH, Appelbaum PS: The challenge of informed consent and return of results in translational genomics: empirical analysis and recommendations. *J Law Med Ethics* (In press); Appelbaum PS, Waldman CR, Fyer A, Klitzman RL, Parens E, Martinez J, et al. Informed consent for return of incidental findings in genomic research. *Genet Med* 2014;16:367-73. PMC3999314.
- **Return of Results |** McLaughlin et al. A physician-oriented approach to the return of results of potential medical relevance from whole genome sequencing. [Our concise, 5-6 page Genome Report featuring a single-page summary of results of potential medical relevance with additional pages containing structured variant, gene, and disease information along with supporting evidence for reported variants and brief descriptions of associated diseases and clinical implications, Submitted].
- **Tumor Sequencing |** Van Allen et al: Whole Exome Sequencing and Clinical Interpretation of FFPE Tumor Samples to Guide Precision Cancer Medicine. Nat Med 2014 (In press).

In Progress

- **Tumor |** Germline reporting in the context of clinical tumor sequencing (BCM)
- **Sequencing Standards |** Description of categorization of somatic variants in tumor specimens for clinical reporting (BCM)
- **Informed Consent |** Informed consent in the context of acute/chronic illness (BCM)
- **Clinical practice |** Gallego et al. Next generation sequencing panels for the evaluation of colorectal cancer and polyposis syndromes: a cost-effectiveness analysis (UW)

Coordination

- Establishment of infrastructure including Working Groups, meetings, publication policies, and outreach
- Past and ongoing collection, analysis, and presentation of Consortium-wide study metrics
- Partnering within and outside CSER to propose, establish, and support impactful CSER activities

CURRENT CHALLENGES BEING ADDRESSED

CSER continues to identify and address new challenges as they arise. Current examples are:

- Shifting the focus of next generation sequencing to predictive and preventative medicine

- Developing a framework for curating, classifying, and signing out variants; developing tiers of evidence and handling insufficient knowledge re disease association, penetrance, and expressivity
- Timely analysis, especially in setting of diseases with poor prognosis and short windows for action
- Construction of user-friendly reports for full range of users (providers to patients)
- Optimizing informed consent given inherent clinical time constraints
- Reducing participant expectations from genomic data

FUTURE OPPORTUNITIES

Selected opportunities where CSER is uniquely able to contribute to the field of genomic medicine are:

Clinical & Translational

- Identify and address barriers to implementing clinical sequencing at the scale of routine clinical care.
- Assess the clinical utility of genomic medicine on patient outcomes in a variety of ethnic, socioeconomic, and clinical contexts; including diverse and non-academic patient populations
- Define the evidence base, including clinical characteristics, that signal when genome-scale sequencing promises to be an effective tool in patient care - and when more targeted approaches may be more applicable. We can capitalize on the diversity of phenotypes represented in the CSER program, as well as the qualitatively different approaches taken by each site, to identify best use cases and best practices
- Generate outcome data that assess how, and in what situations genome-scale sequencing offers clinical utility and at what cost
- Increase the evidence base for genomic testing through longitudinally following up and evaluating the clinical utility, psychosocial impact, and economic costs and benefits of both primary and incidental germline findings on patients and their immediate family members
- Determine whether the addition of additional types of genomic information (e.g., transcriptome analysis) might offer additional clinical benefits in particular disease contexts
- Contribute to in the development of large-scale, dynamic, low-error databases and open-source bioinformatics tools for analyzing whole exome/genome sequence data
- Develop and disseminating best practices, including 1) Incorporating sequence data into the EMR and evaluating the outcomes in near real-time to facilitate quality improvement in a learning healthcare system and developing and implementing clinical decision support, 2) Developing and disseminating resources to better inform physicians and patients, 3) Training non-genetics medical professionals to handle/utilizing sequencing results in daily practice. 4) Coordinating downstream effects of care delivery

Analytical

- Systemically compare different analytical models to address the application of genome sequencing in varying clinical contexts
- Evaluate and refine the protocol for variant adjudication and interpretation in variant review boards as new resources become available
- Improve strategies for identifying non-coding variants with medical relevance

Legal & Ethical

- Explore recent amendments to HIPAA and CLIA requiring CLIA-compliant, HIPAA-covered laboratories to allow individuals access to the designated record set (“DRS”) maintained by a HIPAA-covered entity. Variant Call Format (VCF), .bam, and .fastq files may be returnable as part of the DRS.
- Address the cascade of information flowing from the initial patient sequenced to related individuals, including family and other downstream interests that arise (privacy, research, archiving, biobanking)
- Follow up after return of results to ascertain the extent to which the consent process prepared participants and their families for the information they received

Appendix A: U/R-Awards & Intramural Site

Institution	Lead PI(s)	Study population
U-Grants		
Baylor College of Medicine (BCM)*	Sharon Plon and D. Will Parsons	Childhood cancer patients with high-risk solid tumors and brain tumors
Brigham and Women's Hospital (B&W)	Robert C. Green	Generally healthy adults from primary care, cardiomyopathy patients
Children's Hospital of Philadelphia (CHOP)	Ian Krantz and Nancy Spinner	Pediatric patients with one of four conditions - intellectual disability, sudden cardiac arrest/death, hearing loss, or mitochondrial disorders
Dana-Farber Cancer Institute (DFCI)	Levi Garraway and Pasi Janne	Patients with advanced lung and colorectal cancer
University of North Carolina (UNC)	James P. Evans, Jonathan Berg and Gail Henderson	Patients from one of five domains - cancer, cardiology, dysmorphology, neurodevelopmental or ophthalmology
University of Washington, Seattle (UW)*	Gail Jarvik	Patients who have clinical indications for colorectal cancer/polyposis (CRCP) genetic testing
Hudson-Alpha Institute for Biotechnology (HA)†	Richard Myers	Children with intellectual disability and/or developmental delay
Kaiser Foundation Research Institute† (KPNW)	Katrina Goddard and Benjamin Wilfond	Women and their partners seeking pre-conception carrier testing
University of Michigan, Ann Arbor (UM) *†	Arul Chinnaiyan	Patients with advanced sarcoma or other rare cancers
University of Washington, Seattle †	Gail Jarvik, Deborah Nickerson, Wylie Burke, and Peter Tarczy-Hornoch	CSER Coordinating Center
NHGRI	Leslie Biesecker	ClinSeq study
R-Grants		
Cleveland Clinic	Richard Sharp	Presenting diagnostic results from large-scale clinical mutation testing
Columbia University (CU)	Paul S. Appelbaum	Challenges of informed consent in return of data from genomic research
Columbia University	Wendy K. Chung	Impact of return of incidental genetic test results to research participants in the genomic era
Children's Hospital Boston (CHB)	Ingrid A. Holm	Returning research results in children: Parental Preferences and Expert Oversight
Children's Mercy Bioethics Center (CMH)	Jeremy R. Garrett	The presumptive case against returning individual results in biobanking research
Johns Hopkins University (JHU)	Michelle Huckaby Lewis	Return of research results from samples obtained for newborn screening
Mayo Clinic, University of California, San Francisco (UCSF), University of Minnesota*	Gloria Petersen, Barbara Koenig, Susan Wolf	Disclosing genomic incidental findings in a cancer biobank: An ELSI experiment
Seattle Children's Hospital (SCH)	Holly K. Tabor	Innovative Approaches to Returning Results in Exome and Genome Sequencing Studies
Vanderbilt University (VU)	Ellen Wright Clayton	Returning research results of pediatric genomic research to participants

** Co-funded by the National Cancer Institute*

† Additional sites & Coordinating Center added in 2013

Appendix B: Publications to date

* NHGRI Intramural ClinSeq Program

1. Gallego CJ, Bennette CS, Heagerty P, Comstock B, Horike-Pyne M, Hisama FM, Amendola LM, Bennett RL, Dorschner MO, Tarczy-Hornoch P, Grady WM, Fullerton SM, Trinidad SB, Regier DA, Nickerson DA, Patrick DL, Jarvik GP, Veenstra DL. Comparative effectiveness of next generation genomic sequencing for disease diagnosis: Design of a randomized controlled trial in patients with colorectal cancer/polyposis syndromes. Contemporary Clinical Trials, Contemporary Clinical Trials, 2014 (In press).
2. Henderson GE, Wolf SM, Kuczynski KJ, Joffe S, Sharp RR, Parsons DW, Knoppers BM, Yu JH, Appelbaum PS: The challenge of informed consent and return of results in translational genomics: empirical analysis and recommendations. J Law Med Ethics 2014 (In press).
3. Van Allen EM, Wagle N, Stojanov P, Perrin DL, Cibulskis K, Marlow S, Jane-Valbuena J, Friedrich DC, Kryukov G, Carter SL, McKenna A, Sivachenko A, Rosenberg M, Kiezun A, Voet D, Lawrence M, Lichtenstein LT, Gentry JG, Huang FW, Fostel J, Farlow D, Barbie D, Gandhi L, Lander ES, Gray SW, Joffe S, Janne P, Garber J, MacConaill L, Lindeman N, Rollins B, Kantoff P, Fisher SA, Gabriel S, Getz G, Garraway LA: Whole Exome Sequencing and Clinical Interpretation of FFPE Tumor Samples to Guide Precision Cancer Medicine. Nat Med 2014 (In press).
4. Eckstein, Lisa and Garrett, Jeremy R. and Berkman, Benjamin E., A Framework for Analyzing the Ethics of Disclosing Genetic Research Findings (December 13, 2013). Journal of Law, Medicine and Ethics, Forthcoming.
5. Parsons DW, Roy A, Plon SE, Roychowdhury S, Chinnaiyan AM. Clinical Tumor Sequencing: An Incidental Casualty of the American College of Medical Genetics and Genomics Recommendations for Reporting of Incidental Findings. J Clin Oncol. 2014 Jun 23. pii: JCO.2013.54.8917. [Epub ahead of print] PubMed PMID: 24958819.
6. Ziniel SI, Savage SK, Huntington N, Amatruda J, Green RC, Weitzman ER, Taylor P, Holm IA. Parents' preferences for return of results in pediatric genomic research. *Public health genomics*. 2014;17:105-114. PubMed PMID: 24642506; PubMed Central PMCID: PMC4073487
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8. * Wright MF, Lewis KL, Fisher TC, Hooker GW, Emanuel TE, Biesecker LG, Biesecker BB. Preferences for results delivery from exome sequencing/genome sequencing. *Genetics in medicine : official journal of the American College of Medical Genetics*. 2014;16:442-447. PubMed PMID: 24310310;
9. Wang C, Gordon ES, Stack CB, Liu CT, Norkunas T, Wawak L, Christman MF, Green RC, Bowen DJ. A randomized trial of the clinical utility of genetic testing for obesity: Design and implementation considerations. *Clinical trials (London, England)*. 2014;11:102-113. PubMed PMID: 24216219; PubMed Central PMCID: PMC3946398
10. Wagner JK, Mozersky JT, Pyeritz RE. "Use it or lose it" as an alternative approach to protect genetic privacy in personalized medicine. *Urologic oncology*. 2014;32:198-201. PubMed PMID: 24445287; PubMed Central PMCID: PMC3970576
11. Vassy JL, Lautenbach DM, McLaughlin HM, Kong SW, Christensen KD, Krier J, Kohane IS, Feuerman LZ, Blumenthal-Barby J, Roberts JS, Lehmann LS, Ho CY, Ubel PA, MacRae CA, Seidman CE, Murray MF, McGuire AL, Rehm HL, Green RC. The medseq project: A randomized trial of integrating whole genome sequencing into clinical medicine. *Trials*. 2014;15:85. PubMed PMID: 24645908;
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