The NIH Centers on Genomic Sequencing and Newborn Screening Disorders: Introduction and Overview

Advisory Committee on Heritable Disorders in Newborns and Children

August 25, 2016

Don Bailey, Ph.D.

Newborn **S**equencing **I**n **G**enomic medicine and public **H**eal**T**h (NSIGHT)

NBS is an evolving public health program that is constantly faced with new challenges and opportunities

- Advanced understanding of causes of diseases and treatments
- Challenges in getting evidence for presymptomatic treatment of rare disorders
- Advocacy efforts pushing for expanded screening
- Limited state budgets compromise capacity for screening and follow-up
- New technologies for screening, including the possibility of whole genome or whole exome sequencing

VIEWPOINT

Newborn Screening
Evolving Challenges in an Era of Rapid Discovery

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Newborn screening is designed for presymptomatic identification of serious conditions for which there are effective treatments. Because newborn screening programs in the United States are operated by states, there has historically been considerable cross-state variability in screened conditions and thus a need for a mechanism to guide states.

The Discretionary Advisory Committee on Heritable Disorders in Newborns and Children, which was ap- disease) and 2 (Pompe disease and mucopolysaccharidosis I) are still under consideration.

Eight conditions have been reviewed but not recommended (spinal muscular atrophy, Niemann-Pick disease, neonatal hyperbilirubinemia, Krabbe disease, hemoglobin H disease, Fabry disease, adrenoleukodystrophy, and 22q11.2 deletion syndrome). Even though a careful and deliberative process can be justified, a central question is whether this

JAMA The Journal of the American Medical Association

NIH 2010 meeting on NBS in the genomic era

- Experts from academia, industry, and federal agencies in the fields of newborn screening and genomics participated.
- Outcomes
  - Important to evaluate genomic data in newborns using newborn screening as a framework
  - Important to prioritize clinical validity and clinical utility; not just analytical validity
  - Important to address ethical, legal and social concerns

Recent articles on sequencing and NBS highlight many of the issues that need to be studied

ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Variants of uncertain significance in newborn screening disorders: implications for large-scale genomic sequencing

Alekhya Narravula, MSc[1], Kathryn B. Garber, PhD[1], S. Hussain Askree, PhD[1], Madhuri Hegde, PhD[1] and Patricia L. Hall, PhD[1]

Parental Views on Expanded Newborn Screening Using Whole-Genome Sequencing

Galen Joseph, PhD, Flavia Chen, MPH, Julie Harris-Wai, PhD, MPH,[a] Jennifer M. Puck, MD, Charlotte Young, BS, Barbara A. Koenig, PhD

Genet. Res., Camb. (2015), vol. 97, e21. © Cambridge University Press 2015
doi:10.1017/S0016672315000178

PERSPECTIVE

Challenges of using next generation sequencing in newborn screening

Ethical Issues with Newborn Screening in the Genomics Era

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J Genet Counsel (2015) 24:452–463
DOI 10.1007/s10897-014-9779-3

PROFESSIONAL ISSUES

Genetics Professionals' Opinions of Whole-Genome Sequencing in the Newborn Period

Elizabeth Ulm · W. Gregory Feero · Richard Dineen · Joel Charrow · Catherine Wicklund

Ethical Issues in DNA Sequencing in the Neonate

David P. Dimmock, MD*, David P. Bick, MD

EJHG Open

European Journal of Human Genetics (2015) 23, 1593–1600

www.nature.com/ejhg

POLICY

Whole-genome sequencing in newborn screening? A statement on the continued importance of targeted approaches in newborn screening programmes

Heidi Carmen Howard*[,1], Bartha Maria Knoppers[2], Martina C Cornel[3], Ellen Wright Clayton[4], Karine Sénécal[2] and Pascal Borry[5] endorsed by the European Society of Human Genetics; the P3G International Paediatric Platform; the Human Genome Organisation; and the PHG Foundation

RFA issued in 2012

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	*Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) National Human Genome Research Institute (NHGRI)
Funding Opportunity Title	**Genomic Sequencing and Newborn Screening Disorders (U19)**
Activity Code	U19 Research Program – Cooperative Agreements
Announcement Type	New
Related Notices	None
Funding Opportunity Announcement (FOA) Number	**RFA-HD-13-010**

Three overarching questions

Must address one or more of the following:

A.

For disorders currently screened for in newborns, how can genomic sequencing replicate or augment known newborn screening results?

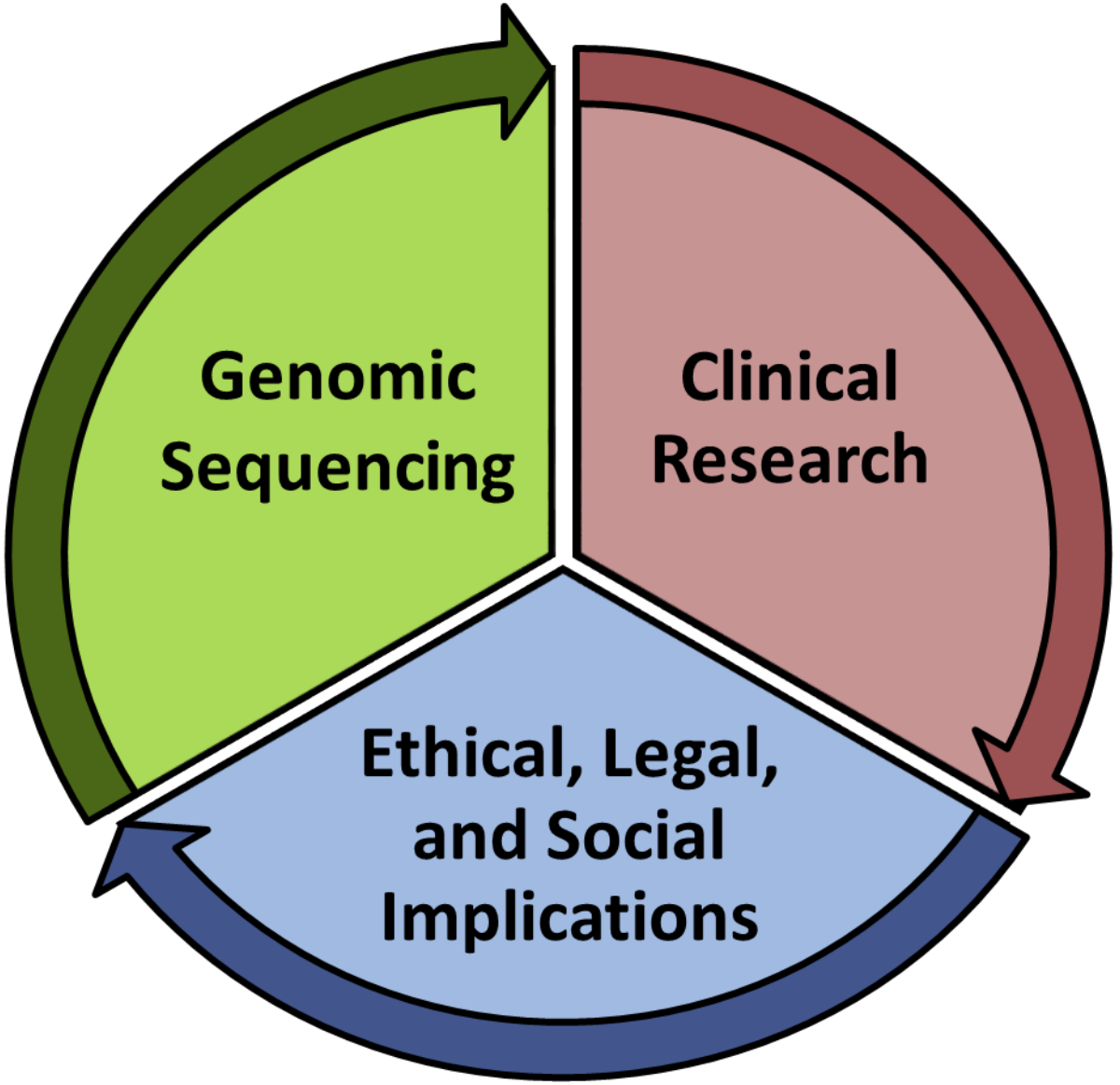
B.

What knowledge about conditions not currently screened for in newborns could genomic sequencing of newborns provide?

C.

What additional clinical information could be learned from genomic sequencing relevant to the clinical care of newborns?

Three required components for each center



Four awardees

- **Robert Green, M.D., and Alan Beggs, Ph.D.**
  Brigham and Women's Hospital, Boston
- **Stephen Kingsmore, M.D.**
  Children's Mercy Hospital, Kansas City, Mo.
  Rady Children, Hospital , San Diego, Ca
- **Jennifer Puck M.D., Barbara Koenig, Ph.D., Pui-Yan Kwok, PhD.**
  University of California, San Francisco
- **Cynthia Powell, M.D., M.S., and Jonathan Berg, M.D., Ph.D.**
  University of North Carolina at Chapel Hill
  RTI International

Post award collaboration

- Centers not originally funded as a network
- But through the cooperative agreement mechanism, NICHD and NHGRI have provided considerable support and encouragement for cross-center interactions and collaborations when appropriate
- For example:
  - Bi-weekly conference calls of all investigators
  - Working groups on ethical issues and common data elements
  - Annual meeting of center investigators to share findings and challenges
  - Other meetings coordinated with conferences on related topics
  - January 2016 *Pediatrics* supplement edited by John Lantos on Ethical Issues in Genomic Testing of Children
  - Jointly authored marker paper led by Jonathan Berg describing centers and activities has been provisionally accepted for publication in *Pediatrics* pending minor revisions

Goals for today

- Provide a very brief overview of each of the funded centers
- Give an example of a finding or process that would be of interest to this committee
- Allow time for questions and discussion by committee members