Ethical, Legal and Social Implications (ELSI) Program

National Human Genome Research Institute
National Institutes of Health

Jean E. McEwen, J.D., Ph.D.

Overview

- Background of the program
- Strategic plan for “Genomics and Society”
- Current priority topic areas
- Methodological approaches
- Funding mechanisms and approaches
- Centers of Excellence in ELSI Research (CEER) Program
- Tensions and challenges

Background

- Established in 1990
- Mission: To anticipate and address the ethical, legal, and social implications of genetic and genomic research
- 5% of NHGRI Extramural Research budget
- FY2012: $19M
- More than 1000 publications over 21 years
- Largest funder of bioethics research in the world

PERSPECTIVE

doi:10.1038/nature09764

Charting a course for genomic medicine from base pairs to bedside

Eric D. Green[1], Mark S. Guyer[1] & National Human Genome Research Institute*

There has been much progress in genomics in the ten years since a draft sequence of the human genome was published. Opportunities for understanding health and disease are now unprecedented, as advances in genomics are harnessed to obtain robust foundational knowledge about the structure and function of the human genome and about the genetic contributions to human health and disease. Here we articulate a 2011 vision for the future of genomics research and describe the path towards an era of genomic medicine.

Since the end of the Human Genome Project (HGP) in 2003 and the publication of a reference human genome sequence[1,2], genomics has become a mainstay of biomedical research. The scientific community's foresight in launching this ambitious project[3] is evident in the broad range of scientific advances that the HGP has enabled, as shown in Fig. 1 (see rollfold). Optimism about the potential contributions of genomics for improving human health has been fuelled by new insights about cancer[4–7], the molecular basis of inherited diseases (http://www.ncbi.nlm.nih.gov/omim and http://www.genome.gov/GWAStudies) and the role of structural variation in disease[8], some of which have already led to new therapies[9–13]. Other advances have already changed medical practice (for example, microarrays are now used for clinical detection of genomic imbalances[14] and pharmacogenomic testing is routinely performed before administration of certain medications[15]). Together, these achievements (see accompanying paper[16]) document that genomics is contributing to a better understanding of human biology and to improving human health.

As it did eight years ago[17], the National Human Genome Research Institute (NHGRI) has engaged the scientific community (http://www.genome.gov/Planning) to reflect on the key attributes of genomics (Box 1) and explore future directions and challenges for the field. These discussions have led to an updated vision that focuses on understanding human biology and the diagnosis, prevention and treatment of human disease, including consideration of the implications of those advances for society (but these discussions, intentionally did not address the role of genomics in agriculture, energy and other areas). Like the HGP, achieving this vision is broader than what any single organization or country can achieve—realizing the full benefits of genomics will be a global effort.

This 2011 vision for genomics is organized around five domains extending from basic research to health applications (Fig. 2). It reflects the view that, over time, the most effective way to improve human health is to understand normal biology (in this case, genome biology) as a basis for understanding disease biology, which then becomes the basis for improving health. At the same time, there are other connections among these domains. Genomics offers opportunities for improving health without a thorough understanding of disease (for example, cancer therapies can be selected based on genomic profiles that identify tumour subtypes[18,19]), and clinical discoveries can lead back to understanding disease or even basic biology.

The past decade has seen genomics contribute fundamental knowledge about biology and its perturbation in disease. Further deepening this understanding will accelerate the transition to genomic medicine (clinical care based on genomic information). But significant change rarely comes quickly. Although genomics has already begun to improve diagnostics and treatments in a few circumstances, profound improvements in the effectiveness of healthcare cannot realistically be expected for many years (Fig. 2). Achieving such progress will depend not only on research, but also on new policies, practices and other developments. We have illustrated the kinds of achievements that can be anticipated with a few examples (Box 2) where a confluence of need and opportunities should lead to major accomplishments in genomic medicine in the coming decade. Similarly, we note three cross-cutting areas that are broadly relevant and fundamental across the entire spectrum of genomics and genomic medicine: bioinformatics and computational biology (Box 3), education and training (Box 4), and genomics and society (Box 5).

Understanding the biology of genomes

Substantial progress in understanding the structure of genomes has revealed much about the complexity of genome biology. Continued acquisition of basic knowledge about genome structure and function will be needed to illuminate further those complexities (Fig. 2). The contribution of genomics will include more comprehensive sets (catalogues) of data and new research tools, which will enhance the capabilities of all researchers to reveal fundamental principles of biology.

Comprehensive catalogues of genomic data

Comprehensive genomic catalogues have been uniquely valuable and widely used. There is a compelling need to improve existing catalogues and to generate new ones, such as complete collections of genetic variation, functional genomic elements, RNAs, proteins, and other biological molecules, for both human and model organisms.

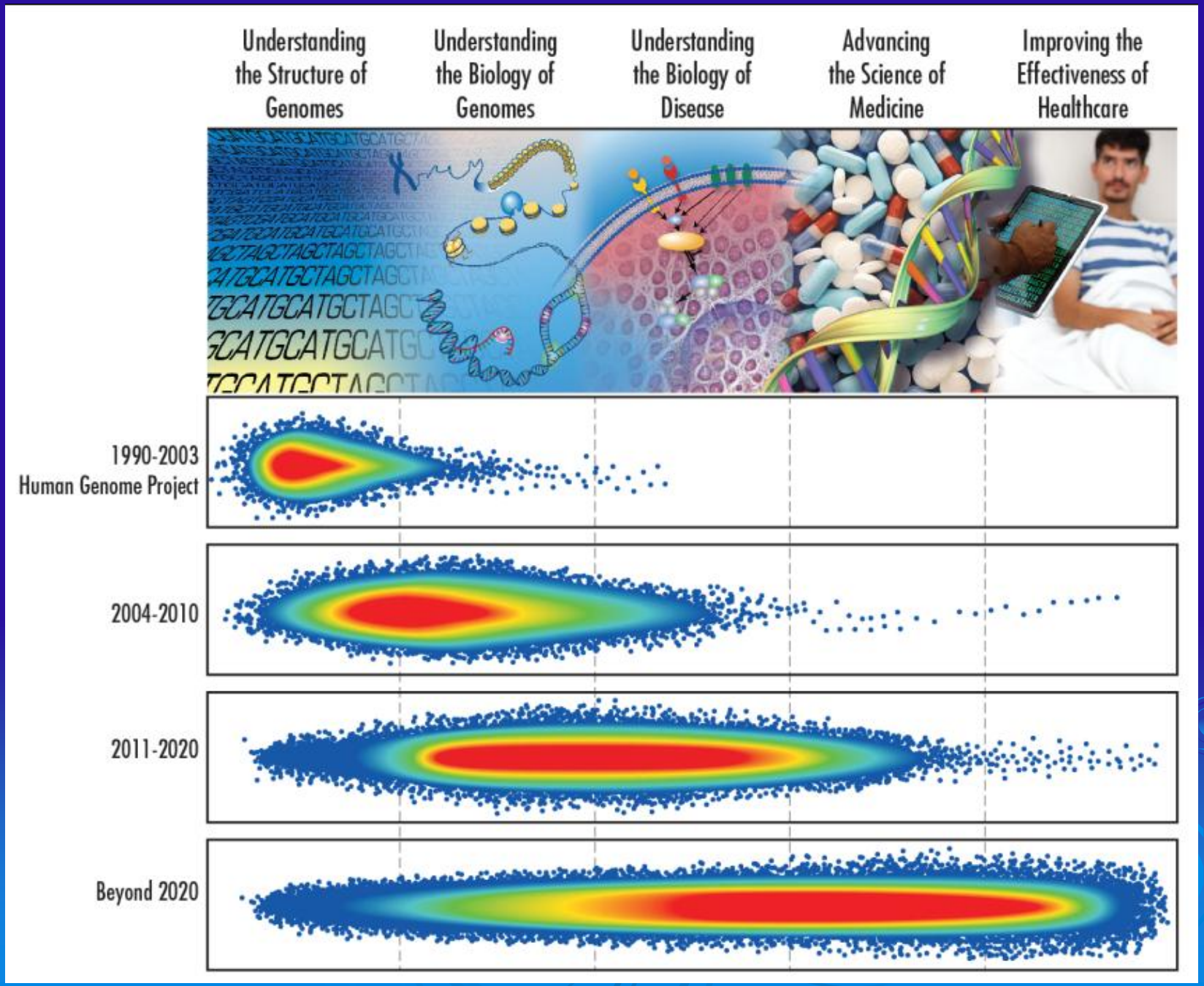
Genomic studies of the genes and pathways associated with disease-related traits require comprehensive catalogues of genetic variation, which provide both genetic markers for association studies and variants for identifying candidate genes. Developing a detailed catalogue of variation in the human genome has been an international effort that began with The SNP Consortium[20] and the International HapMap Project[21] (http://hapmap.ncbi.nlm.nih.gov), and is ongoing with the 1000 Genomes Project[22] (http://www.1000genomes.org).

Over the past decade, these catalogues have been critical in the discovery of the specific genes for roughly 3,000 Mendelian (monogenic) diseases

Figure 1 | Genomic achievements since the Human Genome Project (see accompanying rollfold). ▶

[1]National Human Genome Research Institute, National Institutes of Health, 31 Center Dr., Bethesda, Maryland 20892-2152, USA.
*Lists of participants and their affiliations appear at the end of the paper.

genome.gov/sp2011


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
1990-2003 Human Genome Project
2004-2010
2011-2020
Beyond 2020

Genomics and Society

- Psychosocial and ethical issues in genomics research
- Psychosocial and ethical issues in genomic medicine
- Legal and public policy issues
- Broader societal issues

Psychosocial and Ethical Issues in Genomics Research

- Protection of research participants
- Perceptions of risks and benefits
- Diversity of research cohorts
- Role of race and ethnicity
- Community engagement

Psychosocial and Ethical Issues in Genomic Medicine

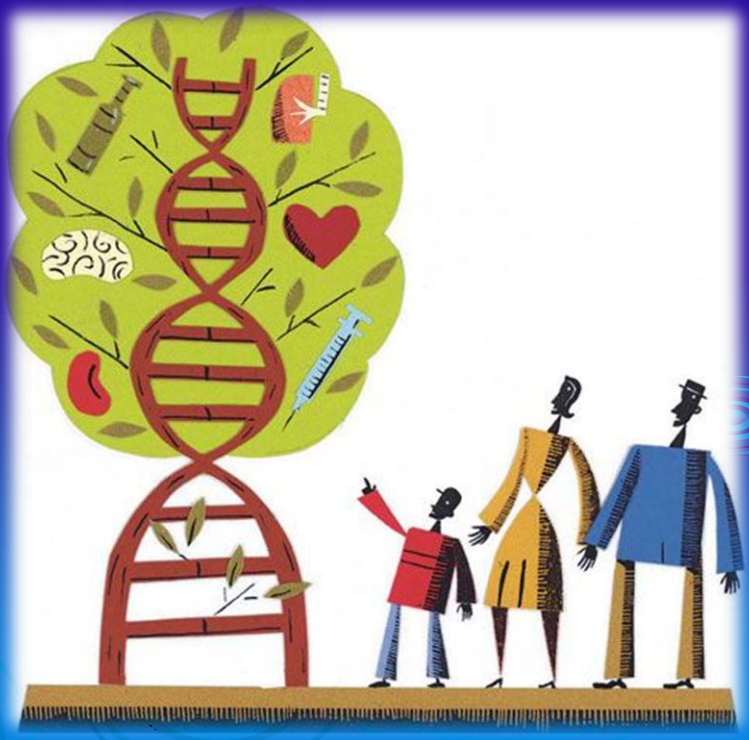
- Genomic uncertainty
- Direct-to-Consumer (DTC) tests
- Fair access
- Effectiveness of diagnostics, therapeutics and behavioral change
- Pre-implantation, prenatal and postnatal genetic diagnoses
- Constructs of race and ethnicity

Legal and Public Policy Issues

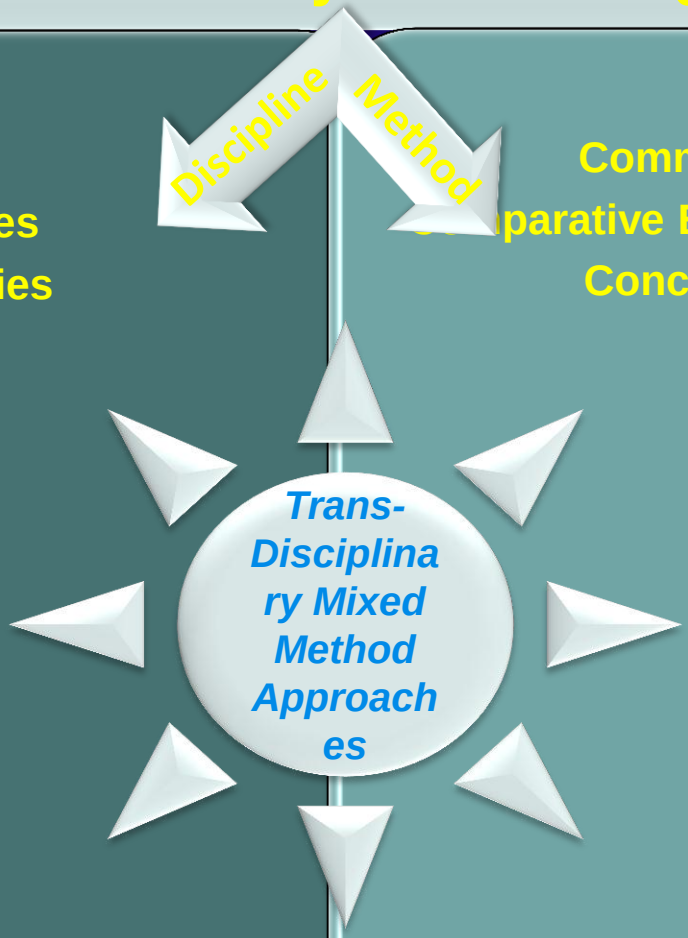
- Intellectual property
- Insurance reimbursement
- Regulation of genetic testing, DTC testing, pharmacogenomics and therapeutics
- Genetic discrimination/stigmatization
- Applications of genetic information in non-medical settings

Broader Societal Issues

- Concepts of health and disease
- Individual and group identity
- Insights on human origins
- Genetic determinism, free will and individual responsibility



Genomics & Society Research Question



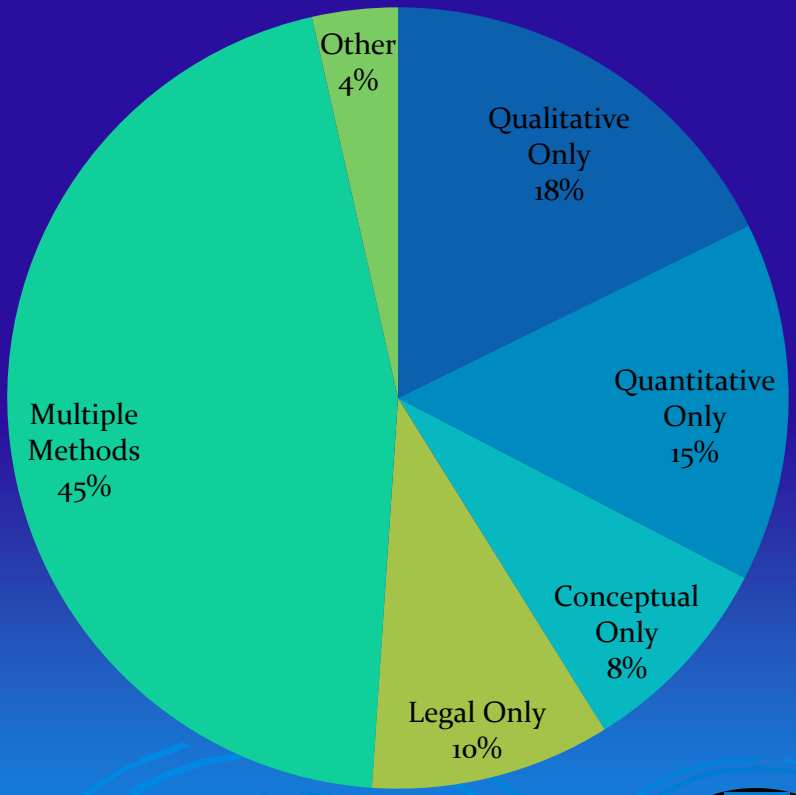
- Anthropology
- Communication Sciences
- Cross-disciplinary studies
- Economics
- Ethics
- Health Services
- History
- Law
- Literature & the Arts
- Philosophy
- Political Science
- Psychology
- Public Health
- Public Policy
- Sociology

- Archival Research
- Community Based Research
- Comparative Effectiveness Research
- Conceptual/Critical Analysis
- Content Analysis
- Simulation Modeling
- Ethnography
- Focus Groups
- Legal Analysis
- Network Analysis
- Oral History
- Quasi-experimental
- Experimental Trials
- Structured Interviews
- Survey methods
- Textual Interpretation
- Time series analyses

Output

- Basic Knowledge
- Tools & Methods
- Validated Interventions
- Research Guidance
- Practice Guidance
- Public Policy

Representation of Methods in ELSI Grants Awarded in Fiscal Years 2005-2010

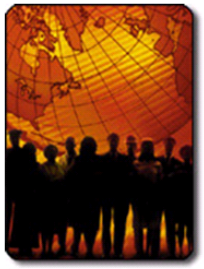


N = 141 Awards

ELSI Research Program Abstracts and Activities Database

Ethical, Legal and Social Implications (ELSI) Research Program Abstracts and Activities Database

ELSI Research Program ⁞ ELSI Planning and Evaluation History ⁞ **ELSI Abstracts and Activities Database** ⁞
ELSI Grant Publications & Products ⁞ ELSI Program Reports



The Ethical, Legal and Social Implications (ELSI) Research Program funds and manages projects that conduct research and education on ELSI issues. ELSI also supports other program activities such as workshops, research consortia and policy conferences related to these issues.

What's Included in the Database

The ELSI Research Program Abstracts and Activities Database organizes the abstracts for all ELSI projects and activities by the last name of the principle investigator (PI). Each entry also includes, and can be searched by using:

- A specific topic - or search term - related to an ELSI issue, (i.e., discrimination, genetic testing or privacy)
- The type of grant (i.e., education, research or conference).
- The grant number.
- The name of the principal investigator.
- The name of the institution where the research was conducted.
- The actual grant period or a year contained within the grant period.

Note: To see ALL abstracts and activities, click on the **Search** button below without typing anything into the search fields.

See Also:

Grants Home

ELSI Funding Opportunities

Applying for an NHGRI Grant

Grants Policies and Guidelines

Funded Grants and Grant History

NHGRI/NIH Active Grants

NHGRI Funding Opportunities E-Mail List

Related Offices and Areas

Policy & Ethics Home

Office of Policy, Communications and Education

Social and Behavioral Research Branch

A Range of Funding Mechanisms

- Regular research grants (R01)
- Small research grants (R03)
- Conference grants (R13)
- Exploratory research grants (R21)
- Post-doctoral traiing grants (F32)
- Career development grants (K99/R00)
- Administrative supplements (including minority supplements)

A Mix of Funding Approaches

- Investigator-initiated grants
- ELSI RFAs funded to address important emerging issues; organization of related consortia (e.g., CF, Cancer Genetics, Genetic Variation, Return of Results)
- ELSI RFAs funded in parallel with genomic projects (e.g., HMP, H3Africa)
- ELSI components of genomic projects (e.g., eMERGE, Clinical Sequencing)

CEER Program

Department of Health and Human Services

Participating Organizations
National Institutes of Health (NIH) (http://www.nih.gov/)

Components of Participating Organizations
National Human Genome Research Institute (NHGRI) (http://www.genome.gov/)

Title: Centers (P50) and Exploratory Grants for Centers (P20) for Excellence in Ethical, Legal and Social Implications (ELSI) Research (CEERs)

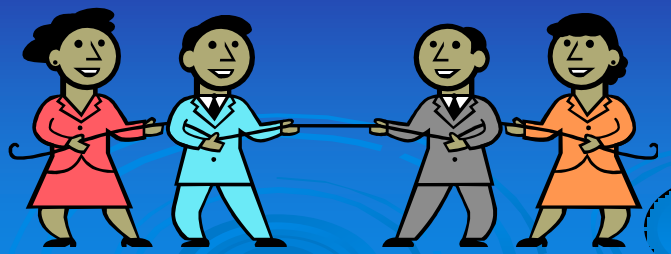
Announcement Type
This is a reissue of RFA-HG-03-005.

Request For Applications (RFA) Number: RFA-HG-09-003

- Launched in 2004
- Goals:
  - Foster *trans-disciplinary* research
  - Facilitate *translation* of research into health, research and public policies/practices
  - *Train* next generation of ELSI researchers
- Currently supporting 6 CEERs (P50) and 2 Exploratory CEERs (P20)
- 1/3 total program budget allocated to CEERs

Persistent “Tensions”

- Basic Research and Translation
- Investigator-initiated and Program-initiated Research
- Consultation and Research
- Integration and Objectivity



Challenges for the Future

- Re-envision inherent tensions as opportunities
- Address priority setting in a climate of uncertain funding
- Expand and integrate ELSI research

Questions?

Jean E. McEwen, J.D., Ph.D.
Program Director
Ethical, Legal, and Social Implications Program
NIH/NHGRI
Email: jm522n@nih.gov
Tel: (301) 402-4997