On November 16, 2005, the Policy and Program Analysis Branch (PPAB) of the National Human Genome Research Institute (NHGRI) convened a roundtable to examine what core policy issues the NHGRI should work on to help ensure that our greatly expanding knowledge of human genomics is translated into improved health care. The NHGRI Policy Roundtable brought together 19 representatives from government, research, advocacy, health care, insurance, industry, and academia.

One of the NHGRI's major goals is to enhance health care in the USA through the integration of genomic medicine into mainstream medical practice. Genomic medicine is a powerful way to tailor health care at the individual level by using patients' genomic information. By identifying the genetic factors associated with disease, it is possible to design more effective drugs; to prescribe the best treatment for each patient; to identify and monitor individuals at high risk from disease; and to avoid adverse drug reactions. Various NHGRI research programs are already helping to realize the promise of genomic medicine, but many important advances in genomic medicine will only occur if we effectively address matters of public policy.

In tandem with important scientific advances, the NHGRI is already addressing many policy issues related to genomic medicine. The institute continues to advocate for comprehensive federal protections from genetic discrimination by employers or health insurance providers for all: NHGRI believes that such protections are essential to protect Americans from potential abuse of genomic medical information. The NHGRI is also monitoring intellectual property practices related to genomic medicine. Responding to widespread concerns that a "thicket of patents" may slow the incorporation of genomics into the clinical setting, the NHGRI commissioned the National Academies of Sciences to examine the impact of intellectual property [nationalacademies.org] on advances in genomic medicine and is currently planning how best to respond to the report's recommendations. The NHGRI is also working with other interested parties to draw up guidelines regarding the direct marketing of genetic tests to the public. The Roundtable was convened to discuss what further action PPAB should take on these and other issues.
Morning Session

The session began with opening remarks from Francis Collins, NHGRI Director, and Tim Leshan, Chief of PPAB. Participants then role-played a hypothetical scenario in which 'Brad,' a young Biotech executive in the year 2015, visits his doctor and has his genome sequenced to analyze whether he is predisposed to heart disease. Moderator Eric Green, the Director of the NHGRI Division of Intramural Research, revealed the scenario in stages: describing how Brad got his genome sequenced through a referral to a genetic counselor; how he found out that he had three alleles predisposing him to an increased risk of heart disease at a young age; how he was recruited to a drug trial testing the drug "Relaxin," designed to reduce the risk of a heart attack in people with his genetic profile; and how, through taking Relaxin, he lived to old age. At each stage, the moderator challenged participants to offer their perspectives about a wide range of policy issues from the viewpoints of their own professions.

Afternoon Session

Moderator Kathy Hudson, Director of the Genetics and Public Policy Center, invited the roundtable participants and members of the audience to comment on the themes that had emerged during the morning session. The group discussed which policy issues are most crucial for the future of genomic medicine. Participants agreed that the NHGRI, together with other agencies, has an important role to play in shaping policies related to the integration of genomic medicine into clinical practice. They identified several issues that would benefit from NHGRI leadership or participation. The discussions provided substantive analysis to help the NHGRI determine its policy focus priorities and the best means to accomplish its goals.

Discussion Themes from the Morning Session:

- Currently, the public is not fully aware of the importance of family medical history, and many doctors are not clear about how to interpret the family history of a patient who has had the initiative to collect it. Similarly, it is not clear how a doctor would treat patients differently based upon access to their genome sequences. Greater scientific expertise is needed to convey accurate and complete genomic information to individuals and to the general public. An increased public awareness and more scientifically aware policy makers would allow for more thoughtful and complete analyses of important science and health care issues.

- We may be able to have our genomes sequenced for $1000 in 10 years time. Uptake of this type of technology may be slowed without legal protections, as privacy and
discrimination concerns may cause patients to be resistant to genomic technology. For example, genetic information could have negative consequences for a patient's health care insurance, particularly if they are seeking individual coverage rather than coverage through their employer's group coverage. This potential for abuse may cause doctors to feel opposing pressures to omit sensitive medical information from medical records to protect their patient and also to include such information in the medical records to protect themselves from liability. Passing federal legislation prohibiting genetic discrimination is essential to the future development and utility of genomic medicine. Even with such legislation, results from genome sequencing may still affect the ability of individuals to acquire life, long-term care, and disability insurance.

- The different responsibilities of the primary care physician, genetic counselor, and medical geneticist need to be examined and perhaps redefined. Currently, there are only ~ 2,000 genetic counselors in the United States. If genetic counselors are to play a central role as genomic medicine is integrated into clinical practice, there is a need for more genetic counselors. At the same time, other health care providers will need to learn more genomics so they can better inform and treat their patients. The standard practice of care for doctors with regard to genomic medicine needs to be defined. And, if patients are expected to make lifestyle changes based on information about their genetic risk factors, appropriate support needs to be in place to help them.

- A "thicket of patents" for gene mutations related to disease also threatens either to derail progress or to allow biotechnology companies in other countries to develop products more rapidly than US. companies.

- Our ability to enable health care providers to interpret the results of genome sequence, and recommend preventative treatments, is also likely to lag behind our ability to develop methods to generate accurate genomic sequence cheaply. However, insurance is unlikely to cover such sequencing in the absence of clinical utility. Even if there is clear clinical utility, insurance may still be reluctant to bear the coverage costs. Government payments for genome sequencing or incentives for insurance companies to provide coverage are possible remedies.

- Regulating individualized genome sequencing is new ground for the FDA. The FDA has to design regulations for many different biomarkers with varying levels of clinical utility. Whether FDA even regulates this activity will be dependent upon whether the sequencing is performed by clinical research laboratories or by private companies.

- Pharmacogenomics companies face many challenges. They must comply with Institutional Review Board requests, develop products that are only marketable to a subset of the public, and, possibly, have to develop and market products without patent protections. There are 5000 biotech companies, but to date only 200 have launched a product. Policymakers need to address how to provide incentives that enable product development.

- The estimates of patients' risk of disease based on their genomic profiles will change as research advances, and will be greatly complicated by the eventual availability of low-cost whole genome sequencing. It will be challenging to communicate these changes in estimated risk to patients.

- The communication of genome sequencing results to patients raises ethical
difficulties. If health care providers order genome testing to assess risk for one
disease, the results may also have information about risk for other diseases. It is
unclear how much of this information they should communicate to patients. Should they only give information for which there is clinical utility, or is it unethical to withhold any information related to patient health? Perhaps the patient only wishes to know information directly related to the reason for his or her genome sequencing. The responsibility of the sequencing laboratory to draw attention to gene variants associated with increased risk of disease is unclear, and the threshold for the clinical validity of an association between a gene variant and disease risk is undefined.

- Institutional Review Boards that oversee large cohort studies involving genomics face many challenges and concerns. Such studies often involve institutions spread across the U.S. Each state has different laws and its own IRB system. Some laws relate to HIPAA and some do not. It is, therefore, very challenging to approve these large studies. But these population-based studies are essential to determine associations between gene variants and diseases, and to examine the efficacy of integrating genomics into medicine.

**Possible NHGRI activities:**

1. **Intellectual Property:** The ever-increasing number of patents related to mutations associated with disease threatens to prevent routine patient genome sequencing from becoming a reality. An "anti-commons land-grab" approach threatens to limit the advance of personalized medicine. The NHGRI needs to develop recommendations that overcome the issues associated with the "thicket of patents."

2. **Regulation of genetic tests:** For companies to develop genetic tests and associated medicines, they need to understand the regulations that will govern FDA approval for their clinical use. The NHGRI should encourage greater dialogue between agencies to clarify the current approval procedure, and to recommend changes appropriate for genomic medicine products.

3. **Privacy and consent:** The NHGRI should collaborate with others to draw up guidelines for Institutional Review Boards overseeing large cohort studies and banking of genetic material, and for the informed consent of subjects of such studies. They should also work with other agencies to publish "duty to inform" recommendations to guide researchers on which information to tell research participants, and which to withhold.

4. **Economics of genomic medicine:** The NHGRI needs to work with health economists to understand better the economic factors that will determine whether and how genomics is translated into clinical practice. What will be financial costs and societal benefits of integration of genomics into health care? Will society ultimately save money through increased productivity of a healthier population? How can we ensure that all benefit from genomic medicine and that it is not exclusive?

5. **Reevaluating the health care paradigm in genomic medicine:** The NHGRI should engage with other agencies to evaluate what changes to the current health care system would optimize the benefits of genomic medicine for the American people, and to define roles for different health care providers. Genomic medicine will demand that patients make informed decisions about whether to have a genetic test, whether to take a genomic based drug, and
what lifestyle changes to make to reduce their risks of contracting a disease. Currently, it is not clear whose responsibility it is to help them make those choices. Most health care professionals have insufficient knowledge about genomic medicine and there are too few geneticists and genetic counselors.

6. Genetic non-discrimination: The NHGRI should continue to advocate for federal legislation that prevents genetic discrimination by employers and health insurance providers. It should also fund ELSI grants to study current state legislation, which currently represents the only protection against genetic discrimination. NHGRI should fund research to study the use of genetic information in life and disability insurance and its impact on coverage for individuals.

7. Non-medical applications of genomics: Genomics is being used for purposes other than the advance of medicine. The NHGRI should examine the scope and ethics of such uses, and assess the impact on genomic medicine.

8. Reimbursement by health insurers: The NHGRI should examine the issue of reimbursement by health insurance companies for clinical genomics services including genetic testing. Should clinical utility be the benchmark for whether health insurance should pay? How would clinical utility of whole genome sequencing be defined? Does government have a role in contributing to coverage of sequencing services?

9. Design of large cohort studies, validation of tests and products: The NHGRI should issue guidelines for the design of disease association studies that identify genetic markers linked to specific diseases. It should also issue guidelines for the validation of a test or product related to genomics.

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