Emerging Research Issues

In an effort to ensure that ELSI research keeps pace with the rapidly evolving field of genomics, the National Advisory Council for Human Genome Research (NACHGR), in consultation with NHGRI staff and other experts in the research and policy communities, regularly reviews the ELSI research priorities and identifies emerging genomic research issues that require attention from the ELSI research community. These "emerging issues" fall within the existing ELSI research priorities found in the Program Announcements (PAs), but relate to new developments in genomic research that were not specifically addressed when the PAs were released in November 2007. It is hoped that as a result of this effort to highlight emerging issues, the ELSI research community will be stimulated to learn more about the genomic science involved and will develop research proposals that address their ethical, legal and social implications.

All research grant applications should be submitted either under the November 2007 Regular Research grant (R01) or Small Research grant (R03) ELSI Program Announcement. You are encouraged to discuss your proposal with ELSI Research Staff before preparing your application.

Natural selection in the human genome

Positive natural selection--the phenomenon that accounts for the increase in the prevalence of advantageous traits in a population--has played an important role in our development as a species. When populations are subject to very different environmental, disease, or cultural pressures, natural selection may change the frequencies of alleles in one population relative to another. Large differences in allele frequencies between populations may thus signal places in the genome that have undergone selection--in some cases very recently. Other signals of recent positive selection include long haplotypes and reduced allelic variation in the regions around the selected variants.

The characterization of signatures of recent positive selection in genes that are of adaptive significance in humans can have great medical relevance, by helping to identify functionally significant variants that play a role in health and disease. However, research on recent positive selection in the human genome is fraught with methodological challenges and has significant ethical and social implications. The results of studies that attribute differences in allele frequencies between populations to recent positive natural selection may challenge past understandings about human history and the way that we think about differences. Where the frequencies differ substantially between populations (as defined by ancestral geography), these findings may affect the way we think about differences (both real and perceived) between people from various ancestral backgrounds.

Possible Research Questions Include:

! How similar or different are the ethical, legal, and social implications of studies that hypothesize recent positive natural selection in humans, depending on whether the trait claimed to be under selection:

- varies between populations, within populations, or both;
- relates to the physical environment, the cultural environment, or other types

of environments;
- is associated with a selection tradeoff;
- is seen as generally advantageous in all environments or as one that confers an advantage for people with some genotypes or in certain environments but not for or in others;
- is still under selection in a particular geographic area, versus not being under selection in a different geographic area?

! How do studies that hypothesize recent positive natural selection in humans as an explanation for group allele frequency differences (whether within or between populations): 1) define the populations and phenotypes they study; 2) account for the possible effects of demographic events other than natural selection and other non-genetic factors on the traits they study; 3) quantify or otherwise operationalize the selective forces hypothesized as an explanation for group allele frequency differences; and 4) ascribe function to a particular gene when there may be several genes in a region showing signals of selection?

! Are there particular characteristics of the social environment that may influence the degree to which researchers attribute group allele frequency differences to recent positive natural selection as opposed to other demographic events that may influence populations' histories?

! How has the popular press historically reported on studies that purport to find evidence of recent positive natural selection in humans? How have they reported on studies that posit other explanations for group allele frequency differences?

! How do members of the public understand and interpret research findings and stories in the press that suggest recent positive natural selection in humans as a possible explanation for group allele frequency differences and individual differences? About the mutability or immutability of these differences?

Direct to Consumer Personal Genomics

As technologies have improved and the costs of genome sequencing and genotyping have plummeted, services offering direct to consumer genetic testing have emerged. These services offer to provide, for a fee, information on an individual's genomic makeup with varying levels of detail and interpretation. Some of these services also provide individuals with the ability to search online databases that contain information on existing, new and emerging genetic associations so that they can explore on an ongoing basis what this genomic information might mean to them, in terms of health and disease, ancestral origins, and traits and behaviors.

The ability to obtain genomic information directly from a laboratory or private company has many implications for individuals, their families and society. It has the potential to provide health information for geographically isolated or underserved populations. It also may allow individuals more direct access to and control over their health information and may lead to healthier life style choices based on possible genetic susceptibilities. However, there also are potential risks in obtaining complex and ambiguous genetic and genomic information in this manner. The relationships between particular genetic variations and the presence or absence of specific diseases or traits are often tenuous and the interpretation of the findings

can change over time. This makes the communication of clear and accurate genetic information challenging, even in ongoing face-to-face clinical settings. It is not known how individuals, and society more broadly, might understand and interpret this information when it is provided directly to individual consumers. Further, little is known about how the availability of this information only to those individuals with sufficient funds or technological access will affect disparities in health care access and outcomes. These issues require further exploration if we are to understand and address the risks and take full advantage of the benefits of this new approach to obtaining and communicating genomic information.

Possible Research Questions Include:

- What impact will genomic information provided directly to consumers have on 1) individual health behaviors; 2) individual levels of psychological relief or distress; 3) individual and societal concepts of health and illness; and 4) individual, familial, cultural and societal concepts of identity and relatedness?

- Assuming that more and more genomic information and testing services will be provided is this manner, what are the safest and most effective ways to communicate this information?

- How will the information be handled within families? Will family members be consulted prior to participation? Will test results be shared among family members? How will the information affect family relationships?

- How will the availability and use of direct to consumer genetic testing services to convey potentially health-relevant information affect the provider/patient relationship and the overall provision of health care? (e.g. Will individuals share this information with their health care providers? How will these providers interpret and use it?)

- What impact will the cost of this service have on the ability of individuals from all social and economic strata of society to participate and make use of the potential benefits of this information? How will this affect views about the value and accessibility of genomic information among diverse populations and communities?

- Will the availability of these services have an impact—either positive or negative—on current disparities in access to and use of health care services? Will it have an affect on disparities in health outcomes?

- Do current privacy and security policies adequately protect the information being generated and communicated by these services? If not, what policies will need to be instituted?

- Since it is unlikely that these services will be provided within a research context, how can data on positive outcomes or adverse events be tracked and evaluated?

- What types of regulatory models might be developed for these services, and what are the advantages and disadvantages of these models?

- Will the public availability of phenotypic and genotypic information from well known individuals affect current approaches to maintaining the confidentiality and privacy of personal genomic information in research, medical and non-medical settings?