National Advisory Council for Human Genome Research

May 18, 2020

Concept Clearance for RFA

Investigator-Initiated Research on Genetic Counseling Processes and Practices

Purpose:
This is a new initiative to support investigator-initiated research on genetic counseling processes and practices. Research is needed to optimize the counseling process in the context of limited resources. To this end, grants would assess, innovate, scale, and/or research the implementation of novel counseling practices to address the need for more healthcare professionals trained in genetic counseling; the uneven access to in-person counseling across U.S. health care systems; and the challenges of effective and efficient communication of genomic findings to clinicians, patients, and families.

Background:
As medicine shifts to include genetics and/or genomics in its clinical testing, and clinical genetics pipelines simultaneously move to include genomic sequencing and treat growing numbers of patients, investigator-initiated research to assess, innovate, scale, and refine genetic counseling processes and outcomes could have significant impact on the field. Counseling processes often include education of patients about the risks and benefits of genetic/genomic tests, including how results may affect patients and their families; negotiation with payers; interpretation of laboratory reports; return of a growing array of results; communication of appropriate content; negotiation of boundaries between research and clinical care; and patient referral and family follow-up. However, the practice of genetic counseling has received little explicit research attention. Current research often focuses on either what results to return or downstream health outcomes. Understanding how to optimize the genetic counseling process for genomic testing, particularly in the context of limited resources, is important to study. In addition, the resources necessary for counseling may vary by who returns the results (e.g., genetics specialist vs. non-genetics provider), when disclosure occurs during the process of clinical care, and in what mode results are returned (e.g., face-to-face, online, or tele-counseling). Just as clinical sequencing and annotation processes have been studied as they transition to genomic approaches, this key part of the clinical genomic pipeline may benefit from evidence-based study and innovation.

The substantial growth of genomic medicine relative to the limited increase of professionals trained in genetic counseling also suggests that research on alternative, less labor-intensive methods of genetic counseling (e.g. automated triage, chatbots, health professionals training, telemedicine) may be important and timely. Research is needed to explore whether and in what contexts these methods may have benefit. Genetic counseling may involve a variety of healthcare providers, such as genetic counselors, nurses, nurse practitioners, or primary care physicians. In addition, specialized tools and methods may improve the counseling process for patients with specific needs (e.g. lower literacy, non-English-speaking, differing cultures or values, clinically urgent settings). Finally, further examination of the post-test period is needed to understand how patients comprehend and potentially act on information conveyed through counseling.

Investigator-initiated research focused on genetic counseling practices and processes in genomics will generate innovative and improved methods adaptable to multiple settings,

institutions, and types of healthcare providers. The research should facilitate a broader integration of genomic medicine into clinical care.

Proposed Scope and Objectives:
This initiative would support investigator-initiated research on genetic counseling practices and processes in support of genomic medicine. Responsive applications would include research personnel with substantial experience identifying and overcoming challenges in genetic counseling. This could include studies of genetic counseling practiced by a range of healthcare providers, such as genetic counselors, nurses, nurse practitioners, or primary care physicians. Projects would be broadly applicable to genomic medicine as a field; projects studying a specific disease or disease area would have to yield generalizable findings. Applications would include a plan to validate and disseminate methods shown to optimize the counseling process to enable wide distribution and implementation.

Examples of research topics that could be pursued under this initiative include, but would not be limited to, the following:

- Develop and evaluate innovative or automated processes to triage communication of clinical genomes to clinicians and patients. This includes systems that differentiate between levels of genetic counseling needed for different genetic variants, such as limited counseling for some findings (e.g., pharmacogenonmics) and very extensive for others (e.g. untreatable monogenic diseases)
- Implement and assess alternatives to in-person, one-on-one counseling that might address the shortage and uneven geographical distribution of genetic counselors, including evaluation of proposed technical solutions
- Assess the need for, develop, test, or measure efficacy of methods to increase capacity for genetic counseling in underserved areas
- Evaluate and improve strategies for communicating complex genomic findings (e.g. multiple genomic findings at once, *de novo* findings, gene-environment interactions, non-Mendelian risks, polygenic risk scores, pleiotropic effects, incomplete penetrance, and variants of unknown significance) and updating patients and families when variant interpretations change
- Evaluate and improve communication of genomic results to patients and families, including strategies for cascade screening in a variety of settings
- Understand the needs of patients and relatives in the communication of genomic information and the potential impact of genetic counseling processes on patient outcomes
- Evaluate, improve, and implement processes for follow-up care after communication of genomic results to patients and families
- Evaluate and research implementation strategies for including genetic counseling processes in both the clinical and research workflows, including the training and involvement of health professionals other than genetic counselors such as nurses, nurse practitioners, and primary care physicians

To increase synergy, an annual meeting of grantees to share research findings will be funded either as a small supplement to one of the grants each year, or organized as a satellite meeting at a professional conference (e.g. National Society of Genetic Counselors, American Society of Human Genetics, or American College of Medical Genetics and Genomics).

Relationship to Ongoing Activities:
Some of NHGRI's genomic medicine consortia (ClinGen, CSER, eMERGE, UDN), have Working Groups which are relevant to counseling practices for genomics. The ClinGen Consent and Disclosure Recommendations (CADRe) Working Group provides communication

strategies and recommendations for genetic testing consent and disclosure discussions. The CADRe working group has developed a preliminary framework to triage the counseling of genomic results based on the severity and risk of disease. The eMERGE Return of Results Working Group develops and identifies categories and thresholds of actionability, assesses ways to address the dynamic nature of genetic knowledge, and assesses the ethical, legal, and social implications of returning results. The CSER Education and Return of Results Working Group investigates patient and provider satisfaction, family-related factors relevant for return of results, and information-seeking. The UDN Genetic Counseling and Testing Working Group has focused on family empowerment. NHGRI program staff will ensure that research efforts are complementary and findings are disseminated to these consortia.

Looking across NIH, NCI has supported research (RFA-CA-20-006) related to genetic counseling and cancer risk communication and research (RFA-CA-17-041 & RFA-CA-19-017) related to genetic counseling and testing strategies to improve inherited cancer syndrome case ascertainment among cancer and primary care patient populations. However, the NCI-supported research is exclusively focused on individuals who have an inherited susceptibility to cancer and may not be broadly generalizable. The ascertainment RFAs (RFA-CA-17-041 & RFA-CA-19-017) include projects focused on risk identification and counseling and/or testing for cancer syndromes prior to cancer onset. The *All of Us* Research Program recently funded a Genetic Counseling Resource to provide genetic counseling services to enrolled study participants. While the *All of Us* Genetic Counseling Resource will likely be an important innovator in genetic counseling, generalizable research on the practice and process of counseling in the clinical setting is not a key part of their mission. NHGRI and *All of Us* Research Program staff will continue to discuss opportunities to share common resources or approaches between the two efforts, including holding joint meetings when feasible.

Mechanism of Support:
Three complementary RFAs are proposed, one to solicit R01 applications, the second to solicit R21 applications, and the third to solicit R41/R43 applications. The R01 mechanism will allow larger projects which require more time to complete. The R21 mechanism will encourage investigators to apply who are interested in smaller-scale projects or do not have preliminary data. The R43/R44 mechanism will allow for small businesses to participate in the research and development of innovative genetic counseling processes.

Funds Anticipated:
NHGRI will commit up to $5M total costs annually to fund 5-7 R01 and R21 awards and 2-3 R43/R44 awards (see below). If a greater proportion of R21s are awarded, then the cost in the later years may be lower. The total cost of this initiative could be flexible as to the number and size of awards depending on the funds available. Each RFA would include two receipt dates with the second receipt allowing resubmissions to address initial review concerns.

- R01 (Research Project) up to $500,000 direct costs/year; project period of up to 4 years
- R21 (Exploratory/Developmental Research) up to $200,000 direct costs/year; maximum of $400,000 for grant; project period of up to 3 years
- R41/43 (Small Business Technology Transfer/Small Business Innovation Research Awards) up to $200,000 direct costs for up to 1 year; project period of up to one year