

**Testimony on behalf of the American Society of Human Genetics (ASHG),  
Bruce D. Gelb, MD, President**

**Submitted to the House Appropriations Subcommittee on  
Labor, Health and Human Services, Education, and Related Agencies,  
Fiscal Year 2025 Funding for the National Institutes of Health**

**May 2, 2024**

The American Society of Human Genetics (ASHG) thanks the Subcommittee for its continued strong support and leadership in funding the National Institutes of Health (NIH). Congress' continued support for human genetics and genomics research is essential for continued progress in the field and reinforces our nation's commitment to the health and well-being of all Americans at a time when the need for investing in biomedical research and scientific innovation continues to increase. **ASHG urges the Subcommittee to appropriate at least \$51.3 billion for NIH's base budget in FY 2025. This amount would allow NIH's base budget to keep pace with the biomedical research and development price index (BRDPI) and allow meaningful growth of five percent.**

*Extraordinary Progress in Human Genetics & Genomics Research*

Federal funding for human genetics and genomics research is enabling new insights into the structure of and variation in the human genome, and leading to new discoveries in preventing, diagnosing, and treating disease. Recent advances in genetic research and the application of genomic information have led to improved diagnostic testing of critically ill infants and diagnosis of rare syndromes, enhanced our understanding of genetic predisposition to adverse drug events, and revolutionized treatment with the success of the first CRISPR-Cas-9-based gene therapy approved for sickle cell disease.<sup>1</sup> Understanding the genomic contribution to disease enables improved diagnosis and treatment, subsequently reducing healthcare costs and improving well-being.<sup>2</sup> Continued federal funding to support research exploring the genetic underpinning of cancer has led to better techniques for early detection and prevention of cancerous tumors, leading to increased survival,<sup>3</sup> and the creation of a national ecosystem for sharing and analyzing cancer data to ensure more efficient collaboration, increasing the potential for novel discoveries driven by human genetics and genomics research.<sup>4</sup> NIH funding

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<sup>1</sup> Manolio *et al.* "Genomic Medicine in Review: 2023." <https://pubmed.ncbi.nlm.nih.gov/38065071/>

<sup>2</sup> *Impact on Health Care and Public Health*. National Academies Press (US); 2010.  
<https://www.ncbi.nlm.nih.gov/books/NBK209648/>

<sup>3</sup> <https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.34479>;

<sup>4</sup> <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative>

for human genetics and genomics has directly unleashed the power of precision medicine to improve health and well-being of all Americans and people throughout the world. By leveraging the diverse data shared by nearly 250,000 participants in the NIH-funded *All of Us* Research Program, researchers have uncovered over 275 million previously unreported genetic variants, half of which are from non-European genetic ancestry.<sup>5</sup> This extensive pool of variants provides unprecedented insights into the genetic influences on health and disease, particularly among historically underrepresented communities. This research has already led to significant findings expanding our knowledge of genetic-related disease, fostering a future where scientific discovery is more inclusive and beneficial for all. Notably, investigators funded by the Electronic Medical Records and Genomics (eMERGE) multicenter consortium utilized *All of Us* genomic datasets to develop and apply ten polygenic risk scores (PRS) – estimates of an individual’s risk for a disease or trait based on their genes – for common diseases across diverse genetic ancestry groups.<sup>6</sup> Without consideration of diversity, these scores may lead to inaccurate results, perpetuating inequities, and ineffective treatments. The inclusion of diverse data from *All of Us* ensures the relevance and fairness of these prediction scores for all Americans. Through initiatives like the NIH *All of Us* Research Program, continued robust federal funding demonstrates a commitment to advancing precision medicine, ultimately leading to more tailored and effective healthcare interventions for all people.

Human genetics and genomics research is also delivering hope for the millions of people in the United States living with neurodegenerative diseases. Decades of work funded by NIH have led to unprecedented insights into the biological causes of Alzheimer’s disease (AD), dementia, amyotrophic lateral sclerosis (ALS), and other related diseases, paving the way for better prediction, prevention, and treatment.<sup>7</sup> By analyzing genetic data from over 100,000 Alzheimer’s patients and nearly 700,000 cognitively healthy individuals, NIH-funded researchers have identified dozens of new genetic risk factors, implicating key pathways to neurodegenerative disease development and developing improved PRS that integrate the effects of multiple genes to better predict an individual’s likelihood of developing Alzheimer’s.<sup>8</sup> Collectively, these efforts are illuminating the complex genetic architecture of Alzheimer’s and related dementias, suggesting novel targets for drug development, and laying the foundation for a precision medicine approach to protecting brain health. Therefore, adequate NIH funding is essential to build on this progress and translate genomic discoveries into meaningful outcomes for the millions of people affected by AD.

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<sup>5</sup> The All of Us Research Program Genomics Investigators. “Genomic data in the All of Us Research Program.” *Nature* **627**, 340–346 (2024). <https://doi.org/10.1038/s41586-023-06957-x>

<sup>6</sup> Lennon *et al.*, “Selection, Optimization and Validation of Ten Chronic Disease Polygenic Risk Scores for Clinical Implementation in Diverse US Populations,” *Nat Med* **30**, 480–487 (2024). <https://www.nature.com/articles/s41591-024-02796-z>

<sup>7</sup> Kunkle *et al.* “Genetic meta-analysis of diagnosed Alzheimer’s disease identifies new risk loci and implicates A $\beta$ , tau, immunity and lipid processing.” *Nat Genet* **51**, 414–30 (2019). <https://doi.org/10.1038/s41588-019-0358-2>

<sup>8</sup> Clark *et al.* “Polygenic Risk Scores in Alzheimer’s Disease Genetics: Methodology, Applications, Inclusion, and Diversity.” *Journal of Alzheimer’s Disease* **89**: 1–12 (2022). <https://doi.org/10.3233/JAD-220025>.

In addition, federal funding has leveraged advances in genomics tools and research to uncover the mechanisms underlying rare diseases and conditions, which collectively impact approximately 25 million Americans. For example, funding for NIH’s Undiagnosed Diseases Network (UDN) that established a nationwide network of researchers and clinicians has improved the ability for patients suffering from undiagnosed conditions to receive the clarity of a diagnosis and has contributed to major advances in therapies (*e.g.*, gene and cell therapy) that can be used to treat both rare and common genetic diseases. Knowledge gained from the study of rare genetic diseases will also impact our approach to treating common diseases. Critically, these advances are driven by NIH’s robust support for fundamental research to better understand disease mechanisms.

*Genetics & Genomics: Striving for Health Equity and Research Cohort Diversity*

Genetic science can advance health equity through the deliberate, meaningful inclusion and participation of individuals from diverse groups in human genetics and genomics research. While human beings are 99.9% identical in our genetic makeup, the variation in the remaining 0.1% can influence a person’s risk of disease or how the body responds to medications, stress, or environmental factors. Participation in genetics and genomics research must reflect humanity’s diversity so that we can gain a fuller understanding of the genetics of health and disease, so all people can enjoy its benefits, and genetic discoveries can be equitably applied in healthcare. Specifically, prioritizing the inclusion of diverse ancestries in genomic studies improves diagnostic accuracy and helps us understand the differences in drug responses when developing new drugs.

While human genetics and genomics research has advanced biomedical research and improved the lives of patients, the field has historically failed to account for the rich diversity of patients that the research should be designed to serve. For example, because most individuals participating in genetic research are of European ancestry, PRS tools are more effective for assessing disease risk in people of European ancestry than for individuals with Hispanic, South Asian, East Asian, or African ancestry.<sup>9</sup> Recently, scientists have taken a step to improve the accuracy of these genetic scores for a broader population by creating a new method called PRS-CSx.<sup>10</sup> This approach incorporates population-level differences in DNA patterns to make PRS even more useful for more people in clinical contexts. However, despite technical advances like PRS-CSx, issues around scientific mistrust, miscommunication, and barriers that make it challenging for individuals to participate in genetics and genomics research still contribute to a lack of meaningful engagement with underrepresented communities in this necessary research.

PRS tools like single-nucleotide polymorphisms (SNPs) are another way for scientists to reduce disparities in genetics research. Scientists can study SNPs in large population groups to identify

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<sup>9</sup> Goodson *et al.* “Opportunities and counterintuitive challenges for decentralized clinical trials to broaden participant inclusion.” *NPJ Digit Med* 5: 58 (2022). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9072305/>

<sup>10</sup> Ruan *et al.* “Improving Polygenic Prediction in Ancestrally Diverse Populations.” *Nat Genet* 54(5): 573–580 (2022). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9117455/>

SNPs that, while common in the population, are also associated with increased risk of disease. This approach is known as a genome-wide association study (GWAS).<sup>11</sup> Recent emerging studies have begun to analyze more diverse population groups, performing multi-ethnic GWAS through initiatives funded by the NIH, like the Population Architecture using Genomics and Epidemiology (PAGE) study.<sup>12</sup> This landmark study funded by the National Human Genome Research Institute (NHGRI) identified ancestry-specific, shared determinants of blood cell traits, which are used to predict the risk of cardiovascular disease and cancers in diverse populations.

ASHG was pleased to see that the *Consolidated Appropriations Act 2024* included language urging the NHGRI to build on these successes and establish a community engagement program to support efforts to increase the participation of individuals historically underrepresented and hesitant to participate in human genetics and genomics research. Congress should continue to support NIH Institutes and Centers to develop specific programs that emphasize diversity in research and clinical trials in ways that address the distinct needs of vulnerable populations.

#### *Broad Data Sharing: Essential for Human Genetics and Genomics Research*

The funding provided by the U.S. government to the NIH is instrumental in promoting the health and stability of the United States, and its benefits extend globally. Broad sharing of human genome data from NIH-funded research drives cutting-edge innovations worldwide and is essential for advancing science, maximizing the public's return on investment in biomedical research, and maintaining the United States' leadership and global competitiveness. Furthermore, the genetics and genomics research community is a leader in developing best practices for sharing data while protecting individuals' privacy.<sup>13</sup>

#### *Summary*

**ASHG joins the Ad Hoc Group for Medical Research in recommending at least a \$51.3 billion base budget for NIH for FY 2025. This funding level would allow NIH's base budget to keep pace with inflation, specifically the biomedical research and development price index, and support crucial research on human genetics and genomics across all of the NIH's 27 Institutes and Centers.**

*The American Society of Human Genetics (ASHG), founded in 1948, is the primary professional membership organization for human genetics specialists worldwide. The Society's nearly 8,000 members include researchers, clinicians, genetic counselors, nurses, and others who have a special interest in the field of human genetics.*

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<sup>11</sup> Uffelmann, E., Huang, Q.Q., Munung, N.S. *et al.* "Genome-wide association studies." *Nat Rev Methods Primers* 1, 59 (2021). <https://doi.org/10.1038/s43586-021-00056-9>

<sup>12</sup> Hu, Yao *et al.* "Multi-ethnic genome-wide association analyses of white blood cell and platelet traits in the Population Architecture using Genomics and Epidemiology (PAGE) study." *BMC genomics* vol. 22,1 432 (2021). <https://doi.org/10.1186/s12864-021-07745-5>

<sup>13</sup> American Society for Human Genetics. (2021). Perspectives: Research and Privacy [Fact sheet]. <https://www.ashg.org/wp-content/uploads/2021/08/Factsheet-DataPrivacy.pdf>