Testimony on behalf of the American Society of Human Genetics, Submitted to the House Appropriations Subcommittee on Labor, Health, and Human Services, Education, and Related Agencies, Anthony Wynshaw-Boris, MD, PhD, President

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). The $2.6 billion increase provided for Fiscal Year (FY) 2020 reinforces our nation's commitment to the health and well-being of all Americans by investing in biomedical research and scientific innovation. **ASHG urges the Subcommittee to appropriate $44.7 billion for NIH in FY 2021.**

My name is Tony Wynshaw-Boris. I am a professor and chair of the Department of Genetics and Genome Sciences at Case Western Reserve University. My laboratory studies the biology, specifically the genetics, of the development and function of the brain.

A Breakthrough Year in Genetics and Genomics

Seeking to understand the human body and diseases in service of the public is an underlying imperative of genetics and genomics research. A recent poll conducted by ASHG and Research!America indicated that 74% of Americans support increased federal funding for genetics research[1]. Indeed, thanks to sustained federal investment in basic and translational research, we are now seeing the transformative impact of genetics research with greater insight about diseases, innovative diagnostic technology and new treatments.

My laboratory studies the pathophysiological mechanisms of human neurogenetic disorders, using animal models and more recently inducible pluripotent

stem cell (iPSC) models. These studies have started with an understanding of brain development with a focus on how normal development is affected in these disorders, and in some cases, this has provided targets that could lead to novel therapies. My research underscores the importance of basic research and its application to human diseases.

Building on scientific knowledge and an enhanced understanding of disease gleaned from years of federally funded research, new treatments are now available for patients suffering from devasting diseases who previously lacked options. In the past year alone, the FDA has approved several new drugs and gene therapies for rare diseases: Duchenne muscular dystrophy (DMD)[2], spinal muscular atrophy (SMA)[3], sickle cell disease[4], and a drug that targets the most common mutation (90%) causing cystic fibrosis[5]. The FDA also approved the first-ever personalized therapy, Milasen, for a fatal neurodegenerative disease: supported in part by NIH funding, the research and clinical team took a remarkably short ten months to go from identifying the genetic defect to designing the drug[6].

In addition, there are numerous promising therapies currently undergoing clinical trials. This includes a gene therapy for X-linked severe combined immunodeficiency (SCID-X1), known as the “bubble boy” disease. For children suffering from this disease, common infections can be life-threatening. However, infants enrolled in the study have functioning immune systems and are living normal lives as toddlers[7].

Basic research on the human genome and biology is fundamental to this clinical progress. For example, the naturally occurring “CRISPR-Cas9” system was discovered through federally funded basic research investigating the immune systems of bacteria[8].

Scientists are now harnessing it as a research and clinical tool to edit the human DNA code, and numerous clinical trials are underway studying its therapeutic utility for a variety of cancers, blood disorders, and congenital blindness[9]. Creative new tools based on CRISPR-Cas9 are also being explored for cancer screening[10] and rapid diagnostics for infectious diseases such as COVID-19[11].

Genetics-based research and technology is advancing knowledge across all areas of life science research. About 20 years ago, the National Human Genome Research Institute (NHGRI) was funding over 90 percent of human genomics research at the NIH; today, NHGRI only accounts for about 15 percent, and nearly every NIH institute and center supports research on the human genome[12]. This reflects the increased use of genetics and genomics approaches for investigating diseases suffered by millions of Americans, such as cancer, cardiovascular diseases, and mental health.

For example, the Pan-Cancer Project, a large-scale study aimed at understanding cancer that involved over a thousand researchers around the globe, sequenced and analyzed the complete genomes of 38 types of cancer. A significant new discovery from this study is that mutations that occur decades before diagnosis can contribute to the onset of cancer in humans[13].

Researchers are also exploring analytical approaches providing novel insights on how the human genome is connected with disease. Research groups are developing polygenic risk scores (PRS), a predictive value of a person's risk for disease based on multiple genes for a variety of complex diseases including cardiovascular disease, diabetes, Alzheimer's, autism, and many more[14]. The potential of PRS in health care as an early intervention tool may help improve outcomes and tailor clinical care.

Genetics research also impacts other scientific disciplines and federal agencies. For example, a collaboration between NIH and NASA-funded researchers published a landmark study last year, describing genetic, physiological and other changes resulting from spaceflight. The study provides a foundation for understanding how astronauts' body and health may be affected in space[15].

NIH-funded Activities: Return on Investment

Besides the immeasurable value of improving the quality of life and health of the public, NIH research funding can be quantified as a driver of economic activity. For FY 2019, NIH funding supported over 475,000 jobs across the nation and stimulated about $81 billion in economic activity. The economic gain in 29 states exceeded $500 million[16].

An overwhelming majority of Americans believe more research is needed in human genetics and support increased federal funding for research. To echo the public's need and sentiment, the Society's vision—people everywhere realize the benefits of human genetics and genomics research—is achievable with sustained and robust funding for the NIH. ASHG joins the Federation of American Societies for Experimental Biology (FASEB), and the Ad Hoc Group for Medical Research in recommending a $44.7 billion budget for NIH for FY 2021.

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, academicians, clinicians, laboratory practice professionals, genetic counselors, nurses and others who have a

special interest in the field of human genetics.

[1] https://www.ashg.org/discover-genetics/public-views-of-genetics-survey/

[2] https://www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-first-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation

[3] https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-gene-therapy-treat-pediatric-patients-spinal-muscular-atrophy-rare-disease

[4] https://www.fda.gov/news-events/press-announcements/fda-approves-novel-treatment-target-abnormality-sickle-cell-disease

[5] https://directorsblog.nih.gov/2019/10/31/dare-to-dream-the-long-road-to-targeted-therapies-for-cystic-fibrosis/

[6] Kim, J., *et al*. 2019. Patient-Customized Oligonucleotide Therapy for a Rare Genetic Disease. *N.Engl.J.Med.* 381:1644-1652; https://directorsblog.nih.gov/2019/10/23/one-little-girls-story-highlights-the-promise-of-precision-medicine/

[7] Mamcarz, E., *et al.* 2019. Lentiviral Gene Therapy Combined with Low-Dose Busulfan in Infants with SCID-X1. *N.Engl.J.Med.* 380:1525-34; https://www.nih.gov/news-events/news-releases/gene-therapy-restores-immunity-infants-rare-immunodeficiency-disease

[8] https://www.genome.gov/dna-day/15-ways/genome-editing

[9] https://clinicaltrials.gov/

[10] Gootenberg, JS., *et al.* 2017. Nucleic acid detection with CRISPR-Cas13a/C2c2. *Science*. 356:438-442.

[11] https://www.broadinstitute.org/files/publications/special/COVID-19%20detection%20(updated).pdf

[12] https://www.genome.gov/sites/default/files/media/files/2020-02/NHGRIFY2021CJ.pdf

[13] https://directorsblog.nih.gov/tag/pan-cancer-analysis-of-whole-genomes-consortium/

[14] https://www.genome.gov/Health/Genomics-and-Medicine/Polygenic-risk-scores

[15] Garrett-Bakelman, FE., *et al*. 2019. The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. *Science*. 364:eaau8650; https://directorsblog.nih.gov/2019/04/23/nasa-twins-study-reveals-health-effects-of-space-flight/

[16] https://www.unitedformedicalresearch.org/wp-content/uploads/2019/04/NIHs-Role-in-Sustaining-the-US-Economy-FY19-FINAL-2.13.2020.pdf