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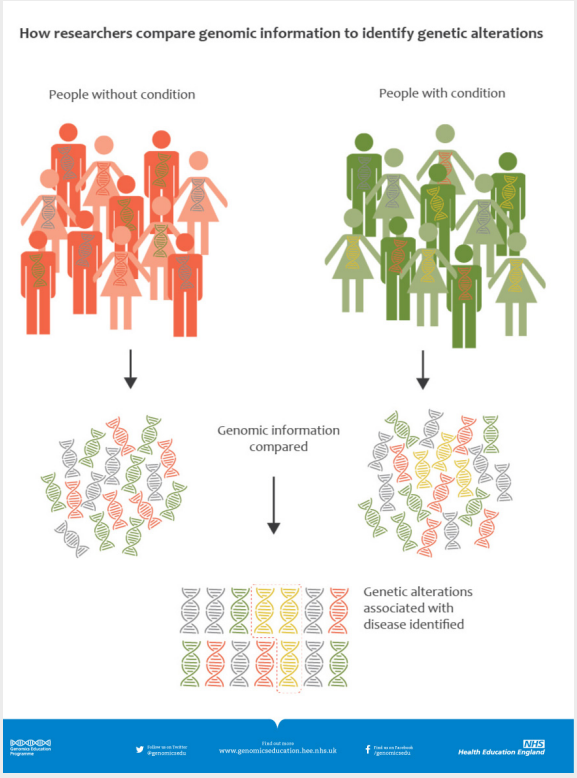
Success Stories
in Human Genetics and Genomics Research

NEUROGENETICS

Federally funded basic research is driving progress toward understanding the genes involved in a large number of neurological and psychiatric disorders. About 40% of more than 5,000 genetic disorders with a known molecular basis are associated with the nervous system.[1] Improvements in sequencing technology and other genetic tools have enabled the identification of genes involved in many brain disorders and provided new insights into their role in disease. These advances, along with recent breakthroughs in gene therapy, have already translated research discoveries into treatments for previously incurable diseases.

Big Ideas and Collaborative Science

The majority of common neurologic diseases are caused by the summation of small effects from many genetic mutations.[2] The significant impact of neurological disorders, including mental and substance use disorders, on public health drives the need for greater understanding of the nervous system and the biological underpinnings causing disease. To that end, the National Institutes of Health (NIH) has been at the leading edge of funding large-scale consortiums aimed at rapid discovery and innovation through collaborations across disciplines and expertise.



The NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN)® Initiative supports research developing new tools to study the brain, including genetic tools to characterize, map, and monitor cells.[3] Large, international consortia, partially funded by NIH, have conducted genome-wide association studies, to discover genetic risk factors for some of the most common neurologic disorders. These include Alzheimer's disease, for which more than 20 genes associated with risk have been identified[4] , and Parkinson's disease, for which there are about 90 known risk variants.[5] Researchers, part of the PsychENCODE Consortium, found common genetic patterns among autism, schizophrenia, bipolar disorder, depression, and alcoholism. Understanding the contribution of genetics in the risk of developing mental disorders may lead to new diagnostics and treatment.[6]

Advances in Diagnostics

Today, several hundred childhood and adult neurological disorders can be diagnosed by a simple DNA blood test. These include cognitive and developmental disabilities, inherited ataxias, muscular dystrophies, epilepsies, and familial degenerative disorders.[7] A molecular diagnosis can guide clinical management, enable targeted therapies, and provide families with the option of genetic counseling.[8]

"The ability to translate new understanding at the molecular level to treat patients – what we really mean by precision medicine – that's why we do what we do" [9]

—Elliot Sherr, MD, PhD, UC San Francisco

Genetic testing can also identify rare mutations underlying little-known disabilities and provide clues for novel treatments. For instance, genetic tests recently revealed that a severely developmentally delayed teenager had a mutation in a gene involved in how neurons in the brain communicate, although there was no previous evidence linking the gene to cognitive challenges. This discovery led neurologists to try a drug already in use to boost neuronal signaling in multiple sclerosis. Within weeks, the patient's cognitive and emotional capacities improved.[9]

Novel Treatments

New treatment options for certain neurological diseases include RNA silencing or interference, and gene therapies.[10] Recently, gene replacement therapies have been developed to treat some previously uncurable neurological diseases. In May 2019, the U.S. Food and Drug Administration (FDA) approved a gene replacement therapy to treat pediatric patients with spinal muscular atrophy, a rare disease and leading genetic cause of infant mortality. Previously, most children with this disease did not survive past early childhood due to respiratory failure. Now, one intravenous injection can deliver a fully functional copy of the mutated gene into motor neuron cells, leading to improvements in muscle movement and function and improved survival of children with spinal muscular atrophy.[11]

How Congress Can Support Neurogenetics Research

Strong preclinical science is essential to the ultimate success of translating scientific discoveries to clinical application. Studies of model organisms such as mice and fruit flies have advanced our knowledge of neurobiological diseases and led to insights that are helping human patients. Recent gene discoveries, in animal models as well as humans, have expanded our understanding not just of neurological diseases, but of normal brain development and function, as well.

With sustained NIH support, basic research, human genomics data, and technological developments will continue to create advances in patient-targeted therapies, pharmacogenetics, and precision health. Congress can support further advances in neurogenetics with sustained and robust NIH funding, which will lead to more therapeutic options and cures for neurological diseases.

Additional Resources

Neurology. Clinical Practice: doi.org/10.1212/CPJ.0b013e31823c0f5f.

The Lancet. Neurology: doi.org/10.1016/S1474-4422(19)30033-X.

Neuron: *doi.org/10.1016/j.neuron.2010.10.015*

References: *ashg.org/advocacy/fact-sheets/*