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Alzheimer's Disease: A History of Progress and Challenges Toward Discovery of a Cure

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ABSTRACT

Neurodegenerative Diseases like Alzheimer's Disease (AD) have puzzled researchers and scientists for decades. Through the years, though, advancements in technology and our understanding of biology itself have brought us closer to the end goal of a cure. This review takes a deep dive through the last 30 years of progress and challenges faced by those working on diagnosing and curing this bleak disease, from the initiation of the Human Genome Project to the emergence of genetics testing companies to some of the most recent, promising studies and clinical trials. While researchers and scientists have achieved several important milestones and developed many crucial technologies, the process of diagnosing and treating Alzheimer's has not come without a long history of legal, ethical, and discriminatory issues, which will be discussed. The discovery of a cure, though, ultimately dismisses these issues, and as of right now, gene therapy seems to be the most promising path to that cure.

Introduction

For decades, both the causes and therapies for neurodegenerative diseases like Alzheimer's Disease have perplexed scientists who remain committed to finding solutions. With no known cure, these diseases progressively degrade the human brain to a diminished state, presenting dire consequences for individuals and their families. The question remains: how should scientists and clinicians go about pursuing treatment and therapies?

Real progress toward understanding and potentially curing neurodegenerative diseases and many other health maladies came from the work done for the Human Genome Project (HGP), which was completed in 2003. During this monumental project, scientists and researchers around the world attempted to map and sequence the entire human genome, which meant pinpointing where each gene for each trait was located on the chromosomes and figuring out the specific base sequence for each gene, respectively.[1] Some believers, like President Bill Clinton, even promised that the research would "revolutionize the diagnosis, prevention, and treatment of most if not all, human diseases," in 2000.

One tangential consequence of the completion of the HGP was the creation of direct-to-consumer (DTC) genetics testing companies like 23andMe. These companies gave consumers access to the knowledge and benefits of the newly discovered genetic information. Although a lot of the tests were light-hearted and fun, what was more important—and certainly more controversial, was the widespread ability of 23andMe to test for specific incurable diseases, including Alzheimer's.[2] This became possible in 2017 as computational technology for sequencing continued to advance and geneticists increasingly understood the complex genetic and inherited causes of Alzheimer's and other neurodegenerative diseases.

[1] "Human genome fact sheet," genome.gov, 2024, https://www.genome.gov/about-genomics/educational-resources/fact-sheets/human-genome-project.
[2] "DNA Reports List," 23andMe.com, 2024, https://www.23andme.com/dna-reports-list/.

The controversy over these tests resulted from the sensitive information they could disclose since diseases like Alzheimer's are life-threatening and have no cure. Effective communication and healthy reactions to nuanced test results became a challenge, contributing to the overall legal, ethical, and discriminatory issues of testing. Also in question was the true accuracy of these tests, which had gotten 23andMe into legal trouble before with the Food and Drug Administration (FDA) in 2013, nearly causing a company shutdown.[3]

Where to search for a cure has therefore been the prevailing question for many scientists. The answer may come in the form of gene therapy. Gene therapy is conducted by using viral vectors, which are deactivated viruses, to carry therapeutic genes into the cells of the body. These genes contain information to either silence or replace disease-causing genes.[4] Currently, scientists all around the world are running studies and clinical trials to find different approaches toward a cure for diseases like AD using gene therapy. The early results seem promising.

The Human Genome Project and its Impact on Neurodegenerative Diseases

The idea of the Human Genome Project, the mapping and sequencing of the 22 autosomes and 2 sex chromosomes that make up the human genome, originally began in the mid-1980s. It was initiated by leading biologists including UC Santa Cruz Chancellor Robert Sinsheimer, Salk Institute researcher Renato Dulbecco, and the Department of Energy's (DOE) Charles DeLisi.[5] Since its inception, critics have questioned the HGP based on its feasibility and the various ethical problems it raises.

Early opponents ridiculed the immense projected cost and its potential to divert funding from smaller-scale scientific projects, which made up the majority of biological research at the time. Government agencies established several committees to study the feasibility of the HGP, including the Office of Technology Assessment and the National Research Council. The resulting reports addressed those concerns, calling for a strategic division of sequencing efforts and funding for the sequencing of additional nonhuman "model" organisms, such as mice.[6]

In 1988, with such parameters in place, both the DOE and the National Institutes of Health (NIH) signed a memorandum of understanding[7] coordinating an official launch date of the HGP on October 1, 1990, intending to finish in 2005. In the years before 1990, the DOE set up three genome centers, and the NIH started a university grant-based system for research. David Smith, an embryologist, and James Watson, one of the founders of molecular biology and co-discoverer of the structure of DNA, headed the efforts of the DOE and NIH, respectively.[8] Soon the project gained international attention, with several countries, including the U.K., France, Germany, Japan, and China joining the effort.[9] Mapping techniques and more efficient, cost-effective sequencing techniques were also developed at this time.

In 1990, the NIH and DOE released a five-year plan to set standards for mapping, sequencing, and the development of technology to help the project.[10] The plan was updated in 1993 to account for progress, which remained in effect until 1998. During this time, scientists made steady advances, with the more achievable mapping-phase goals having been met in 1996. Sequencing would prove more difficult, so the smaller genomes of less complex model

[3] Erika Hayden, "The rise and fall and rise again of 23andMe," Nature 550, 2017, 174-177 https://doi.org/10.1038/550174a.
[4] "Gene Therapy," Pennmedicine.org, 2024, https://www.pennmedicine.org/research-at-penn/gene-therapy.
[5] Lisa Gannett, "The Human Genome Project," Stanford Encyclopedia of Philosophy, September 14, 2023, https://plato.stanford.edu/archives/fall2023/entries/human-genome/.
[6] Gannett, "The Human Genome Project."
[7] "Human genome project timeline," Genome.gov, 2022, https://www.genome.gov/human-genome-project/timeline.
[8] Gannett, "The Human Genome Project."
[9] "Human genome fact sheet," Genome.gov.
[10] Tian Zhu and Tito Carvalho, The Human Genome Project (1990-2003), May 6, 2014, https://hdl.handle.net/10776/7829.

organisms would be sequenced as scientists awaited technological progress in computational speeds before tackling much of the human genome.[11] Thus, by 1997, only three percent of the human genome had been sequenced.

Later, in 1998, the HGP faced an unexpected challenge from the private sector. Frustrated by the cost and how long the HGP was taking, J. Craig Venter's Celera Genomics announced plans to sequence the entire human genome faster and cheaper using "whole-genome shotgun" (WGS) sequencing. The "shotgun" method consisted of breaking up DNA into pieces, sequencing them, and reassembling them. While HGP scientists had restricted the shotgun method only to cloned fragments already mapped to specific chromosome regions because of fears of reassembly accuracy, Celera would now apply it to the whole genome by breaking the entire genome into millions of DNA pieces, sequencing each of them using new capillary model machines, and re-assembling the sequences with a modern supercomputer.[12] While HGP scientists downplayed the idea of a sequencing "race," they undoubtedly felt the pressure of the private sector potentially scooping the achievement in the process.

In 1998, the DOE and the National Human Genome Research Institute (NHGRI) of the NIH published a second five-year plan, which moved the completion date forward to 2003.[13] The plan aimed to achieve this by delaying the finishing process and abandoning its clone-to-clone shotgun and reassembling processes. The agencies also continued to call for improved technology with higher sequencing capacities and cheaper rates.

By 1999, HGP scientists at the Sanger Center, along with their partners at several universities, hailed the first completed sequenced chromosome, the relatively small chromosome 22.[14] By the end of spring in 2000, 90 percent of the human genome had been sequenced to within 99.9% accuracy. Finally, in April 2003, the HGP leaders deemed the project officially completed, two years earlier than expected and considerably under budget.

Having passed this milestone, scientists created an instruction book for understanding the genetic basis of human life. The impact of the HGP was revolutionary, and it promised many pharmaceutical and biomedical applications. Twenty years later, countless studies and scientific researchers still use the HGP as the basis of their work and barely scratch the surface of its potential.[15] Research done for and from the HGP has allowed many complex diseases, like Alzheimer's Disease, to be attributed to specific genes on specific chromosomes, and variants in the genome can now be attributed to various effects. The HGP and ever-improving technology have also given rise to the feasibility of very detailed commercial genetic testing, which involves the sampling of DNA in a person's blood or saliva to estimate their risk of contracting specific diseases.

Genetic Testing for Alzheimer's and Other Neurodegenerative Diseases

Genetic testing has fundamentally advanced our understanding and ultimately our clinical approach to neurodegenerative diseases. It has allowed us to diagnose several diseases, determine familial inheritance risk, and predict the development of a disease or the influence of a drug.[16] With the development over the past 20 years of techniques including whole genome sequencing, scientists have also been able to improve both the speed and accuracy of their diagnoses.

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[11] James Watson, "The Human Genome Project: Past, Present, and Future," April 6, 1990, pg. 44-49.
[12] Gannett, "The Human Genome Project."
[13] Francis Collins et al, "New goals for the U.S. Human Genome Project: 1998-2003," Science 282, 1998, 682–689, https://doi.org/10.1126/science.282.5389.682.
[14] I. Dunham et al, "The DNA sequence of human chromosome 22," Nature 402, 1999, 489-495, https://doi.org/10.1038/990031.
[15] Ed Cara, "The Human Genome Project Turns 20: Here's how it altered the world," MIT Department of Biology, April 14, 2023, https://biology.mit.edu/the-human-genome-project-turns-20-heres-how-it-altered-the-world/.
[16] InformedHealth.org, "In brief: What does genetic testing involve?," Institute for Quality and Efficiency in Health Care, 2023, https://www.ncbi.nlm.nih.gov/books/NBK367582/.

It is important to note that Alzheimer's is a polygenic disease, meaning it has several genetic risk factors that interact to trigger it.[17] AD can also be triggered by a multitude of non-genetic lifestyle factors, such as exercise and dietary habits.[18] These circumstances make it incredibly hard for scientists to identify a definitive cause for AD. Despite this, there are some widely agreed-upon genetic risks for the disease. Scientists established back in the 1990s that mutations of the genes Presenilin 1 + 2 and the APP gene, located on chromosomes 14, 1, and 21 respectively, were a cause of early-onset Alzheimer's Disease (EOAD), the rarer and earlier-appearing version of AD.[19] Regarding late-onset Alzheimer's Disease (LOAD), which is the much more common version affecting adults over 65, scientists identified the presence of the APOE ε4 allele as an established genetic risk factor in 1993.[20] Other neurodegenerative diseases with established genetic causes include Huntington's and Parkinson's disease.

With these risk factors established, the subsequent question was how to effectively and judiciously test for these diseases. When predictive tests for Huntington's Disease (HD), the first genetic condition for which a test was offered, arrived in 1993, leaders at research societies focused on Huntington's both domestic and international developed a strict testing protocol.[21] They were motivated by the knowledge that the information revealed in these genetic tests was powerful: it could provide crucial information to patients about their neurological condition, but it could also cause extreme distress in thinking about their future, given the limited treatment options for this devastating disease. These protocols included multiple in-person clinic visits with a genetic counselor and evaluations by mental health professionals to determine their psychological readiness. The counseling addresses the benefits, risks, and limitations of testing, and results are disclosed typically in person with supportive medical professionals often on hand.[22] With the HD model firmly established, these extensive procedures have now become the model for the clinical testing of other neurodegenerative diseases and hereditary cancer syndromes.[23]

With continued advances in genetics testing technology and analysis of the HGP, it was only a matter of time before someone capitalized on this new, revolutionary capability. The first and most famous case was Anne Wojcicki's company 23andMe, which appeared in 2006. Her goal was to widen access to genetic testing and to provide customers with information about their health, disease risks, and ancestry.[24] These tests would be administered through a direct-to-consumer (DTC) model, where testing kits were sold directly to consumers from the company, bypassing both clinics and counseling. The company also planned to sell access to the valuable genetic database built by their consumers and tests to increase research and profits. With such a plan in place, 23andMe developed several testing kits in its first decade, ranging from the popular testing for ancestry tracing to those that could test for serious, incurable diseases, like Alzheimer's, in 2017.[25] Despite the many advantages the DTC model offers, it would prove vulnerable to a range of legal and ethical criticisms.

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[17] Xiaopu Zhou et al, "Deep learning-based polygenic risk analysis for Alzheimer's disease prediction," Communications Medicine 3, April 6, 2023, https://doi.org/10.1038/s43856-023-00269-x.

[18] Lana Arab and Marwan Sabbagh, "Are certain lifestyle habits associated with lower Alzheimer disease risk?," Journal of Alzheimer's Disease: JAD 20, 2010, 785-794, https://doi.org/10.3233/JAD-2010-091573.

[19] Adnan Awada, "Early and late-onset Alzheimer's disease: What are the differences?," Journal of neurosciences in rural practice, 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4481819/.

[20] J. Scott Roberts et al, "Genetic testing for neurodegenerative diseases: Ethical and health communication challenges," Neurobiology of disease, 2020, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311284/.

[21] Roberts et al, "Genetic testing for neurodegenerative diseases…"

[22] Huntington's Disease Society of America, "Genetics Testing Protocol for Huntington's Disease," 2016, http://hdsa.org/wp-content/uploads/2015/02/HDSA-Gen-Testing-Protocol-for-HD.pdf.

[23] Kimberly Quaid, "Genetics testing for Huntington disease," Handbook of Clinical Neurology 144, 2017, 113-126, https://doi.org/10.1016/B978-0-12-801893-4.00010-9.

[24] Hayden, "The rise and fall and rise again of 23andMe."

[25] "DNA Reports List," 23andMe.

Legal and Ethical Issues for Testing

Regulators and critics have expressed the most concern with the ethics of practicing the DTC model. More specifically, they fear the possible deleterious interpretations of, and reactions to, the results of tests for incurable diseases. This is reflective of the fact that the DTC model used for 23andMe's tests bypasses established protocols, like those established for the HD clinical tests. Many consumers lack the health literacy and quantitative abilities required to fully understand the nuanced and probabilistic information that the tests offer because AD and many other diseases have many diverse triggers, as mentioned previously.[26] Although consumers do have to provide informed consent before buying tests, which aims to educate them on the benefits, risks, and limitations of what at-home genetic testing can offer, most customers are still left on their own to deal with the complex and often heartbreaking results.

Nonetheless, tests like 23andMe's 2017 genotyping test for the APOE ε4 allele are of high interest to at-risk family members trying to plan their future or to cope with uncertain risk status. These circumstances have left a negative psychological impact on many testees, especially those who have witnessed diseases like AD devastate the lives of their older relatives, who now know of their increased risk as well. Even before 23andMe made testing widely available, some at-risk individuals have taken drastic, often unnecessary actions upon discovering and misinterpreting their risk of contracting an incurable disease. These ranged from patients putting themselves on strict diets to taking extra vitamins and supplements to adjusting the terms of their lifetime insurance plans.[27] [28] Often, company recommendations to "ask your doctor" about test results have also put unnecessary burdens on primary care providers who already have limited time and health care resources to give patients.[29]

Given all the overactive measures and mental harm from misinterpretation, the question remains: exactly how accurate are these tests? As noted above, many diverse factors contribute to the development of complex diseases, and therefore different tests have different efficacy rates. Although predictive testing is relatively straightforward and accurate for conditions like HD and EOAD/autosomal dominant AD, tests for known risk factors of LOAD, like 23andMe's test for the APOE ε4 allele, have at best modest predictive value because of their polygenic nature and other contributing factors.[30]

The question of accuracy for DTC tests has placed 23andMe in legal jeopardy before. In 2013, the FDA became concerned about people taking drastic measures after receiving false positives, and the agency sent a strong letter to 23andMe demanding a halt to marketing operations after communications had broken off. The FDA was seeking evidence proving the accuracy of 23andMe's tests and the mental well-being of their customers.[31] Despite this multi-year setback, the tests of 23andMe are now FDA-approved, and they have restored their relationship with the agency. Incidents of false positives do remain, however, and their impact cannot be understated.

Regardless of the accuracy of tests, effective communication of testing results is of utmost importance. Researchers have undertaken significant efforts to study the best methods to deliver information. Recommendations include the use of plain language as opposed to medical terms, the conveyance of absolute risks across clear time

[26] Institute of Medicine Committee on Health Literacy "Health Literacy: A Prescription to End Confusion," National Academies Press, 2004, https://pubmed.ncbi.nlm.nih.gov/25009856/.
[27] Jacqueline Vernarelli et al., "Effect of Alzheimer disease genetic risk disclosure on dietary supplement use," The American journal of clinical nutrition 91, 2010, 1402–1407, https://doi.org/10.3945/ajcn.2009.28981.
[28] Donald Taylor et al, "Genetic testing for Alzheimer's and long-term care insurance," Health affairs 29, 2010, 102-108, https://doi.org/10.1377/hlthaff.2009.0525.
[29] Amy McGuire and Wylie Burke, "An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons," JAMA 300, 2008, 2669–2671, https://doi.org/10.1001/jama.2008.803.
[30] Roberts et al, "Genetic testing for neurodegenerative diseases…"
[31] Hayden, "The rise and fall and rise again of 23andMe."

periods, and the inclusion of visual aids to show quantitative figures.[32] A hybridized model of the DTC system, the so-called consumer-directed testing concept, also appeared in the late 2010s.[33] In this system, consumers still initiate the request for a genetic test (often influenced by DTC advertisements), but a physician orders the test and also offers genetic counseling. This, in theory, provides the best of both worlds of DTC and clinical tests, retaining the widespread accessibility of the DTC model, but also ensuring the availability of professional guidance, and that testing occurs in a clinically certified laboratory.

Although the shortcomings of the DTC model have been well-documented, polls have indicated that the actual damage to customers is relatively minimal, which has enabled these products to stay on the market. There has been no documented widespread psychological or social harm from DTC tests for AD and other health conditions. Only two percent of people have seriously regretted their decision to purchase a DTC test and only one percent have reported harm.[34] In general, those ordering tests are doing so voluntarily, and ultimately, their decisions must be honored.

Other issues also exist outside the immediate reception of test information. Consumers unsure about ordering a test have also had concerns about genetic discrimination, the act of discriminating against an individual in a social, healthcare, or work setting based on their medical records and data. Although companies like 23andMe affirm that they do not disclose personal genetic data to insurers or employers without explicit consent from a testee, many prospective testees have declined to test, have paid to test without insurance money, or even have tested under an alias because of concerns about data privacy. They do this with good reason: a survey for at-risk individuals for HD in Canada revealed that around a third of those polled experienced genetic discrimination of some form, citing insurance costs as the most common factor.[35] Fortunately, in the US, the 2008 Genetic Information Nondiscrimination Act (GINA) outlaws health insurers and employers from using personal genetic information, including family health history, to inform their decisions. However, this protection neither extends to military personnel, nor does it affect the acquisition of life, disability, or long-term care (LTC) insurance.

As for AD, receiving a positive diagnosis can often prompt individuals to purchase LTC insurance or add to their current insurance plans, with the hope that insurers will not find out about their risk for an incurable disease and inevitably increase premiums. Confirmed cases of insurance discrimination against AD are rare, but there is currently little data suggesting to what extent life, disability, and LTC insurers are using personal genetic information as a factor in coverage plans. Nevertheless, the expansion of testing and the demographics of an aging population may prompt the need for legislation to extend protection to these other fields of insurance.

The Future: Gene Therapy

The ongoing plight of Alzheimer's Disease and other neurological conditions has raised many questions and difficulties for millions of people worldwide. Although no current cures exist, gene therapy currently shows a very promising path. Current therapies for AD and other neurological conditions can only provide symptomatic relief rather than addressing the underlying pathology; namely, the faulty DNA in an affected patient that causes the condition in the

[32] Angela Fagerlin et al. "Helping patients decide: ten steps to better risk communication," Journal of the National Cancer Institute 103, 2011, 1436-1443, https://doi.org/10.1093/jnci/djr318.
[33] Erica Ramos and Scott Weissman, "The dawn of consumer-directed testing," American journal of medical genetics. Part C, Seminars in medical genetics 178, 2018, 89-97, https://doi.org/10.1002/ajmg.c.31603.
[34] J. Scott Roberts et al. "Direct-to-Consumer Genetic Testing: User Motivations, Decision Making, and Perceived Utility of Results," Public health genomics 20, 2017, 36-45, https://doi.org/10.1159/000455006.
[35] Yvonne Bombard et al. "Perceptions of genetic discrimination among people at risk for Huntington's disease: a cross sectional survey," BMJ 338, 2009, https://doi.org/10.1136/bmj.b2175.

first place.[36] Gene therapy works to address the DNA part: it uses viral vectors, which are deactivated viruses, to deliver new genes that can either replace a diseased gene with a healthy one, silence a diseased gene, or introduce a modified gene to train the immune system.[37] These viral vectors attempt to transverse the blood-brain barrier, which is a selective semipermeable defense layer, to deliver treatments without causing significant side effects.

The promise of gene therapy relies on a diverse set of approaches that tackles the many root causes of AD and other neurodegenerative diseases. In one 2023 clinical trial at the University College London (UCL), Dr. Catherine Mummery used gene silencing therapy to decrease levels of the harmful tau protein, a protein that helps stabilize nerve cell skeletons in the brain and is known to cause AD when it accumulates and tangles together. The drug tested, known as BIIB080, is made up of pieces of RNA that have complementary sequences to the mRNA template for the MAPT gene, which encodes for tau proteins. When introduced to the body, the base sequences of the drug and mRNA pair together, just like a DNA double helix would, and, subsequently, the mRNA is deactivated and destroyed by the cell. This leaves the MAPT gene unaffected, while the mRNAs that signal it to produce tau proteins are destroyed, substantially reducing the production and accumulation of tau.

This specific gene-silencing approach has shown promise. In the clinical trial done by UCL, of the 46 patients, 34 received BIIB080 and 12 received a placebo. None had serious side effects, and those receiving the highest dose of the drug had an over 50% reduction in tau levels over 24 weeks. But Mummery cautions that further research needs to be done to see if the drug can slow down the progression of physical symptoms. Although the clinical use of this drug is still some time away, the results from the trial do provide hope for the future course of therapies.[38]

Another promising approach studied by Dr. Yoke Peng Loh at the NIH's Intramural Research Program involves protecting the neurons in the brain from the buildup of tau proteins. Instead of silencing the MAPT gene to slow tau production, as executed by Mummery and her team, Loh and her lab aimed to treat AD by making the neurons more resistant to the overwhelming entanglements of tau. They intended to achieve this resistance by boosting the numbers of a molecule called neurotrophic factor alpha-1 (NF-alpha-1) in cells through the use of a viral vector that would deliver extra copies of the gene producing this molecule to neurons. NF-alpha-1 helps keep neurons alive in situations when they would otherwise perish.

The team tested this approach on male mice, all of which had 3 of the same genetic mutations that put humans at risk of developing AD. Without treatment, the mice should have developed full Alzheimer's symptoms by 6 months old. At 2 months old, they injected the gene therapy into the hippocampus of the mice, an area of the brain crucial for memory function. This resulted in a 50-80% increase in NF-alpha-1 levels in the hippocampus of the mice. This also allowed the mice to perform with significantly better results five months later in the Morris Water Maze, a learning and memory test. Upon examining the brain specimens, they saw that the treated mice had more neurons surviving in the hippocampus and fewer precursors to the tau tangles. The gene therapy also seemed to have positive influences on keeping the mitochondria of the neurons alive, which is central to neuron activity. The treatment ultimately slowed the development of AD in the mice, suggesting that it could very well be beneficial to at-risk individuals who have not yet developed significant symptoms.[39]

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[36] Vivek Sudhakar and R. Mark Richardson, "Gene Therapy for Neurodegenerative Diseases," Neurotherapeutics: The Journal of the American Society for Experimental NeuroTherapeutics 16, 2019, 166-175 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6361055/.

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[38] National Health Service, "Clinical trials show promise for first 'gene silencing' treatment for Alzheimer's disease," NHS England, January 26, 2024, https://www.genomicseducation.hee.nhs.uk/blog/clinical-trials-show-promise-for-first-gene-silencing-treatment-for-alzheimers-disease/.

[39] Brandon Levy, "Gene Therapy Protects Neurons From Alzheimer's Disease," National Institutes of Health, December 12, 2023, https://irp.nih.gov/blog/post/2023/12/gene-therapy-protects-neurons-from-alzheimers-disease; Lan Xiao et al. " Hippocampal delivery of neurotrophic factor-α1/carboxypeptidase E gene prevents

However, just as in the case of the UCL clinical trial, this study is still only at the proof of concept stage. Loh and her team plan to improve their delivery methods and investigate whether their treatment can also help mice that already have shown symptoms. Nevertheless, Loh remains hopeful. Even if the treatment cannot completely halt the progression of AD, if it can suspend patients to a stage where they can still live and function on their own without the need for special care. This alone would be a great accomplishment. These two cases are only part of the many studies scientists and researchers are conducting trying to harness the potential of gene therapy to crack the treatment for AD and other neurodegenerative diseases. As these efforts indicate, the eventual discovery of a cure hinges on scientists and researchers around the world trying different and innovative approaches.

Conclusion

As scientists continue their quest to discover a cure for Alzheimer's and other neurodegenerative diseases, gene therapy will become an increasingly important field of focus. Although the long-sought-after breakthrough cure may still be some time away, several recent clinical trials and studies have shown promise in this general approach. It is a great legacy in the history of genomics that none of this would be possible without the research and collaboration that went into the completion of the HGP. Being able to understand and sequence one's genome allowed for the rise of precision medicine, of which gene therapy is a central component. Much of our drug experiments today are run on model organisms like mice, whose genomes scientists simultaneously sequenced with humans as part of the overall goals of the Human Genome Project. Understanding modern medicine and biological breakthroughs requires an understanding of the HGP's history and importance, as it acts as the main resource across the range of life science research.

Curing diseases like AD is only one part of the equation. Accurate diagnostics is the other. As sequencing technology and our understanding of AD and other diseases have improved through the last decade, sensitive DTC genetic tests have hit the market, increasing accessibility but also raising numerous complex and nuanced ethical and legal issues surrounding the interpretation of results and genetic discrimination. With an aging global population and the increasing availability of testing, the field must find ways to address these concerns with greater education for the public and training for professionals.

Ideally, a cure for AD and similar diseases would end all such concerns. After all, these tests are so sensitive solely because at-risk testees have no cure available to them for a disease of Alzheimer's magnitude. Such a cure would be revolutionary: knowing a reliable treatment exists, hesitant individuals would become more willing to test, and DTC options would be able to facilitate this demand without the current range of concerns. A cure, however, will arrive only with the continued collaboration and innovation of scientists and researchers as a global effort.

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