Alzheimer's Disease and Regenerative Medicine

Overview

Alzheimer's Disease (AD) is the most common form of dementia (the general term for loss of memory and intellectual abilities) that attacks neurons in the brain, resulting in memory loss, cognitive impairment and behavioral changes. The disease disrupts the brain's communication network, eventually destroying neuronal synapses and killing neurons altogether. There are an estimated 5.4 million Americans suffering from the disease, and the prevalence doubles every five years beyond the age of 65.[1] As of 2010, there are 35.6 million people living with the disease, and it is the sixth-leading cause of death in the United States.[2] While the majority of people with the disease are 65 and older, about five percent of the people afflicted have early-onset Alzheimer's which can occur when a patient is in their 40s and 50s.[3] AD is not a part of the normal aging process. Symptoms get progressively worse over time and can include confusion with time and place, struggles to complete familiar tasks and changes in mood and personality.

The disease is characterized by two types of abnormal lesions that build up around neurons in the brain including beta-amyloid plaques (clumps of protein fragments and cellular material) and neurofibrillary tangles (insoluble twisted fibers composed of the Tau protein). It is not certain whether these lesions cause disease or are a byproduct of it. As stated earlier, there is no cure for AD and the disease can only be officially confirmed by autopsy after a patient's death.[4] There are currently five FDA-approved Alzheimer's drugs that treat the symptoms of AD, however, they do not treat the underlying causes of the disease.[5]

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The creation of disease models through cellular reprogramming of patient-specific cells has allowed scientists to create human disease models of AD to study the disease in controlled laboratory conditions. Cellular reprogramming is a process when scientists reverse fully differentiated, mature cells into an embryonic state, i.e., creating disease induced pluripotent stem cell lines.

Several ARM members are highly involved in these new efforts. Scientists at The New York Stem Cell Foundation lab have developed a cell-based model of Alzheimer's disease. In this initiative led by Scott Noggle, PhD, the researchers reprogrammed cells of early-onset patients into induced pluripotent stem cells to create cholinergic basal forebrain neurons (the cells affected in Alzheimer's). These cells demonstrate the features of the disease on a cellular level, creating a viable disease model that will be critical for drug discovery and

testing. Preliminary results have demonstrated differences in cellular function in patients. Alzheimer's neurons produced more of the toxic form of beta amyloid, the protein found in amyloid plaques, than healthy neurons.[6]

iPierian has also created disease models from patient-derived pluripotent stem cells to advance their novel drug development programs. After using the disease models to validate the therapeutic targets and mechanisms of disease, they hope to move toward using monoclonal antibodies to treat AD (and other neurodegenerative diseases) by targeting the Tau protein.[7] iPierian i s aiming to start human trials with their potential drugs in 2014.[8]

The California Institute for Regenerative Medicine (CIRM), California's stem cell agency, is supporting the development of technologies to treat AD which includes eleven research grants.[9] CIRM recently awarded StemCells, Inc. a $20 million boost for the company to collaborate with UC-Irvine's Sue & Bill Gross Stem Cell Research Center's neurobiologists and the Institute for Memory Impairments and Neurological Disorders (UCI MIND) to advance the company's human neural stem cell technology in Alzheimer's. Researchers have already reported that StemCells, Inc.'s neural stem cells restored memory and enhanced synaptic function in two animal models similar to AD. It is believed these cells provide growth factors that protect the neurons from degeneration.[10]

Alzheimer's Disease: Economic Impact

$200 Billion
Estimated cost in 2012 to care for people with Alzheimer's disease in the United States.[11]

$18,500–$36,000+
Annual cost to care for an individual Alzheimer's sufferer, depending on the stage of disease.[11]

$200 Billion→$1.1 Trillion
Projected increase in cost to care for Alzheimer's and other dementia sufferers by 2050. (In today's dollars.)[12]

[1] Alzheimer's Foundation of America, "About Alzheimer's: Statistics," 2013, available at www.alzfdn.org/AboutAlzheimers/statistics.html
[2] *World Alzheimer Report 2010: The Global Economic Impact of Dementia,* available at *www*.alz.co.uk/research/files/WorldAlzheimerReport2010.pdf (published by Alzheimer's Disease International, June 2011)
[3] Alzheimer's Association, "What is Alzheimer's?", 2013, available at *www*.alz.org/alzheimers_disease_what_is_alzheimers.asp
[4] Alzheimer's Foundation of America, "About Alzheimer's: Definition of Alzheimer's," 2013, available at *www*.alzfdn.org/AboutAlzheimers/definition.html
[5] Alzheimer's Association, "Science & Progress: Treatment Horizon," 2013, Alzheimer's Association website, www.alz.org/research/science/alzheimers_treatment_horizon.asp
[6] California Institute for Regenerative Medicine (CIRM), "Alzheimer's Disease Fact Sheet," CIRM website, www.cirm.ca.gov/Alzheimers_Disease_Facts
[7] "New York Stem Cell Foundation (NYSCF) Scientists Featured At The Alzheimer's Association International Conference for New Model of Alzheimer's Disease (AD)," NYSCF press release, July 16, 2012, on the NYSCF website, www.nyscf.org/pdfs/NYSCF_PR_Alzheimers2.pdf
[8] "iPierian Advances Monoclonal Antibody Drug Development Programs Targeting Tau Protein and the Complement System for the Treatment of Neurodegenerative Diseases," iPierian press release, May 21, 2012, on the iPierian website, http://www.ipierian.com/drupal/news-events/press-releases/2012/05/ipierian-advances-monoclonal-antibody-drug-development-programs-t
[9] Ron Leuty,"iPierian turns its stem cell technology on Alzheimer's, antibody drugs," *San Francisco Business Times,* May 21, 2012, available at www.bizjournals.com/sanfrancisco/blog/biotech/2012/05/ipieiran-ips-stem-cells-alzheimers-brain.html?page=all
[10] California Institute for Regenerative Medicine (CIRM), "Alzheimer's Disease Fact Sheet," CIRM website, www.cirm.ca.gov/Alzheimers_Disease_Facts
[11] "State stem cell research funding agency awards $37.3 million to aid UC Irvine efforts," University of California, Irvine press release, September 6, 2012, on the *UC Irvine Today* website, http://today.uci.edu/news/2012/09/nr_cirmklassen_120906.php
[12] Alzheimer's Foundation of America, "About Alzheimer's: Cost," *2013,* available at *www*.alzfdn.org/AboutAlzheimers/cost.html
[13] *2013 Alzheimer's Disease Facts and Figures Report* available at *www*.alz.org/alzheimers_disease_facts_and_figures.asp#quickfacts (published by Alzheimer's Association, 2013)