

A Humanized Swine Model for Alzheimers Disease

<https://neurodegenerationresearch.eu/survey/a-humanized-swine-model-for-alzheimers-disease/>

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Research Abstract

PROJECT SUMMARY Alzheimer's disease (AD) affects 44 million people worldwide, costing \$605 billion yearly. One in nine Americans over the age of 65 have AD, the 6th leading cause of death in the US. Annually, \$226 billion is spent to care for the 5.3 million Americans with AD. AD

is the only cause of death in the top 10 that cannot be prevented, cured, or slowed, and without the development of treatments for AD, it is expected that by 2050 there will be 16 million Americans with AD, costing \$1.1 trillion yearly. Life expectancy following AD diagnosis is only 3-9 years. AD patients suffer from chronic neurodegeneration, gradual loss of bodily functions, and a poor quality of life. Studying patients with early onset AD has elucidated many genes that play a role in AD including the critical role of the Amyloid Precursor Protein gene (hAPP) and the Microtubule-Associated Protein Tau gene (hMAPT). To date, models of AD have been largely developed in mice, and no therapies developed in these models have proven effective in humans, likely due to the large anatomical and physiological variation between human and rodent brains, coupled with the failure of mice to develop the neurodegenerative processes and brain lesions seen in AD patients. Compared to rodents, swine have much greater genetic, anatomic, and physiological similarity to humans, offering an opportunity to model a complex neuropathological disease in a large animal. The large, gyrencephalic brain of the pig is similar in size and structure to humans, and a model of diffuse brain injury in swine shows AD-like pathology with accumulation of amyloid beta (A β) and Tau. We propose to establish a swine model of AD, allowing researchers to understand the biology of AD, enable doctors to establish methods of early detection, and ultimately lead to the identification of new therapies to prevent, halt the progression of, and reverse AD. We will establish this model using our powerful and proprietary genetic engineering techniques to replace swine APP and MAPT genes with human AD-associated alleles of these genes. This will allow us to precisely model human AD in swine, and develop therapeutics that could be pre-clinically tested for safety and efficacy in our swine and moved directly to human clinical trials. We will assess the resulting animals at 2 months of age by magnetic resonance imaging to determine if they have suffered neurodegeneration by whole brain and hippocampal volume measurement, as well as if amyloid plaques have formed, or they display a pattern of abnormal brain metabolite concentrations, consistent with AD patients.

Further information available at:

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