



Plenary Lecture-PhD

PL03

Marmoset as Research Models of Alzheimer's Disease

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Our limited understanding of the mechanisms that trigger the emergence of Alzheimer's disease (AD) has contributed to the lack of interventions that stop, prevent, or fully treat this disease. We believe that developing a nonhuman primate model of AD will be an essential step toward overcoming the limitations of other model systems and is crucial for investigating primate-specific mechanisms underlying the cellular and molecular root causes of the pathogenesis and progression of AD.

The common marmoset (*Callithrix jacchus*), a small nonhuman primate species native to Brazil, has quickly become a promising animal model for biomedical and neuroscience research. We formed a new consortium with funding from the National Institute on Aging to create, characterize, and validate MArmosets as Research MOdels of AD (MARMO-AD). This consortium develops and studies gene-edited marmoset models with genetic risk factors for AD, comparing them to wild-type aging marmosets from birth throughout their lifespan using non-invasive, long-term assessments. These include analyzing the genetic, molecular, functional, behavioral, cognitive, and pathological features of aging and AD.

The consortium successfully generated viable founders carrying PSEN1 C410Y and A426P mutations using CRISPR/Cas9 techniques, demonstrating germline transmission in the C410Y line. Longitudinal characterization of these models, their germline offspring, and normal aging outbred marmosets is ongoing. Notably, our neuroimaging pipeline enables visualization of the marmoset brain anatomy with remarkable cytoarchitectonic detail, playing a vital role in elucidating the pathophysiological mechanisms behind neurodevelopmental and neurological disorders.

By establishing marmoset models of AD, we will be able to examine primate-specific cellular and molecular root causes that underlie the development and progression of AD, overcome limitations of other model organisms, and support future translational research to speed up the process of delivering therapies to patients.