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Validation and characterization of 3xTg (APP/Bin1/COPS5) mice as a new neuropathological model of Alzheimer's disease

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In this study, we characterize the neuropathological profile and genetic expression pattern specific for this improved triple transgenic mice (APP/Bin1/COPS5) model of Alzheimer's disease (AD) during the first year of life. This novel triple transgenic mouse model over-expresses the Swedish mutation of APP (human amyloid precursor protein) together with Bin1 (bridging integrator 1, AMPH2) and COPS-5 (COP9 constitutive photomorphogenic homolog subunit 5, Jab1), which closely mimics AD human brain pathology. By using histopathological biomarkers and comparative AD gene-expression analysis, we identified an improved neuropathological profile that constitutes a more suitable AD mouse model for neurodegenerative research studies. Results from mice brain histopathological characterization at 3 and 6 months of age show that combined APP, Bin1 and COPS5 expressing genes promote the severity of AD hallmarks in a progressive manner along brain maturation. When compared with simple (APP) or double (APP/PS1) transgenic mice, this triple transgenic mice (APP/Bin1/COPS5), shows significant increase in amyloid-B plaque density at early stages of development (3 months), as well as the associated inflammation hallmarks such as astrogliosis and reactive microglia. These findings support the view that this specific triple gene interaction may generate a powerful degenerative AD mice model, providing new insight into the pathogenesis and molecular/cellular mechanisms driving degenerative neuropathology in AD. This model is a useful tool for assessing the efficacy of therapeutic agents for slowing, preventing or reversing AD progression.

Biography

Ivan Carrera has been focused on the development and degeneration of the central nervous systems of vertebrates. He has more than 30 papers published in peer-reviewed journals, edited books and several invitations to neuroscience meetings.

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