# Tau conditional knockout mice to elucidate the function of tau in the adult brain

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Tau conditional knockout mice to elucidate the function of tau in the adult brain

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**Research Abstract**
Abstract Tau is a protein involved in several neurodegenerative disorders, including Alzheimer's disease (AD), frontotemporal dementia, Pick's disease, and corticobasal degeneration. Growing evidence points to tau as a valid therapeutic target for mitigating some of these disorders. However, the role of tau in the adult brain remains elusive. We used homologous recombination to flox exon 4 of the mouse tau gene. By combining these tau floxed mice with an inducible, neuronal-specific, CRE line, we are uniquely positioned to selectively knockout Mapt in adult

neurons. In this application, we will test the hypothesis that tau is necessary for learning and memory in the adult brain. Specifically, we will leverage these newly developed tau conditional knockout mice by removing tau from the brains of 6-month-old mice. This will be accomplished by crossing the tau floxed mice with a tamoxifen-inducible Cre recombinase, whose expression is controlled by a neuronal specific promoter. We will assess the acute and chronic effect of knocking out tau by testing mice in a battery of cognitive and non-cognitive behavioral tests, one week and two months after the Cre-mediated removal of Mapt. We will also perform rescue experiments using the three major murine tau isoforms. These experiments will determine whether removing tau in the brain of adult mice has an effect on cognitive and motor function. This is a critical step towards the development of anti-tau therapies for AD and other tauopathies. In summary, we have generated the much needed tau conditional knockout mice, which will allow us to selectively and inducibly ablate Mapt in the adult brain. These mice may have a long-lasting impact on the field and may represent an invaluable tool to evaluate the role of tau and study potential anti-tau therapies in AD and other tauopathies.

**Further information available at:**

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