Identification and Analysis of the Two *Tau* Paralogues in Zebrafish

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Contents

Abstract

The dysfunction of tau protein has been implicated in a number of neurodegenerative diseases, including Alzheimer's disease (AD) and frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17). In these diseases, the tau protein is aberrantly hyperphosphorylated and aggregated to form neuropathological deposits in the cell body of neurons. Evidence from genetics studies has shown a linkage between tau mutations and autosomal dominantly inherited FTD. In Chapter one, our current understanding of the mechanisms of tauopathies is summarized. In addition, multiple animal models for mechanistic studies of tauopathies are reviewed. In this thesis, endogenous tau genes in zebrafish were identified and investigated in an attempt to establish zebrafish as an animal model for study of tauopathies. Paper 1 describes the identification of two genes, *mapta* and *maptb* in zebrafish that represent duplicates of an ancestral tau orthologue. It examines their complex alternative mRNA splicing patterns and their patterns of expression during embryogenesis. Paper 2 (thesis chapter in the form of a manuscript) describes how we might use zebrafish as an animal model to investigate tau function. Two antibodies that detect Mapta and Maptb specifically are described. In addition, we establish that inhibition of Maptb translation causes an impairment of axonogenesis during zebrafish embryogenesis.

Declaration

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List of Publications

Complex splicing and neural expression of duplicated tau genes in zebrafish embryos

Mengqi Chen, Ralph N. Martins and Michael Lardelli

Journal of Alzheimer's Disease, Manuscript accepted 22nd March, 2009

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