

Scientists uncover the structure of tau filaments from Alzheimer's disease

July 6 2017



PET scan of a human brain with Alzheimer's disease. Credit: public domain

Researchers at the MRC Laboratory of Molecular Biology (LMB) have, for the first time, revealed the atomic structures of one of the two types of the abnormal filaments which lead to Alzheimer's disease.



Understanding the structures of these filaments will be key in developing drugs to prevent their formation.

The researchers, whose study is published today in *Nature*, believe the structures they have uncovered could also suggest how tau protein may form different filaments in other neurodegenerative diseases.

Alzheimer's, the most common neurodegenerative disease, is characterised by the existence of two types of abnormal 'amyloid' forms of protein which form lesions in the brain. Tau forms filaments inside nerve cells and amyloid-beta forms filaments outside cells. Tau lesions appear to have a stronger correlation to the loss of cognitive ability in patients with the disease.

Almost thirty years ago, scientists at the LMB (including Michel Goedert, one of the senior authors on this paper) identified tau protein as an integral component of the lesions found in Alzheimer's and a range of other neurodegenerative diseases. But, until now, scientists have been unable to identify the atomic structure of the filaments.

The researchers extracted tau filaments from the brain of a patient who had died with Alzheimer's disease. The filaments were then imaged using cryo-electron microscopy (cryo-EM). Senior author Sjors Scheres and colleagues developed new software in order to calculate the structure of the filaments in sufficient detail to deduce the arrangement of the atoms inside them.

Sjors Scheres said: "It's very exciting that we were able to use this new technique to visualise filaments from a diseased brain as previous work depended on artificial samples assembled in the laboratory. Amyloid structures can form in many different ways, so it has been unclear how close these lab versions resembled those in human disease.



"Knowing which parts of tau are important for filament formation is relevant for the development of drugs. For example, many pharmaceutical companies are currently using different parts of tau in tests to measure the effect of different drugs on filament formation; this new knowledge should significantly increase the accuracy of such tests."

Fellow senior author Michel Goedert said: "We have known for almost three decades that the abnormal assembly of tau protein into filaments is a defining characteristic of Alzheimer's disease. In 1998, the dysfunction of tau protein was shown to be sufficient for neurodegeneration and dementia. In 2009, the prion-like properties of assembled tau were identified. These properties allow the abnormal form to convert previously normal forms.

"Until now the high-resolution structures of tau or any other diseasecausing filaments from human brain tissue have remained unknown. This new work will help to develop better compounds for diagnosing and treating Alzheimer's and other diseases which involve defective tau."

Dr Rob Buckle, chief science officer at the MRC, which funded the research, said: "This ground-breaking work is a major contribution to our understanding of Alzheimer's disease. Nearly thirty years ago scientists at the LMB were the first to discover that tau protein plays a key role in the disease. Knowing the basic structure of these filaments in diseased tissue is vital for the development of drugs to combat their formation.

"This research opens up new possibilities to study a range of other diseases where the accumulation of abnormal protein filaments plays a role, including Parkinson's disease, motor neuron disease and prion diseases."

More information: Anthony W. P. Fitzpatrick et al. Cryo-EM



structures of tau filaments from Alzheimer's disease, *Nature* (2017). DOI: 10.1038/nature23002

Provided by Medical Research Council

Citation: Scientists uncover the structure of tau filaments from Alzheimer's disease (2017, July 6) retrieved 2 May 2024 from https://medicalxpress.com/news/2017-07-atomic-protein-tangles-alzheimer-disease.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.