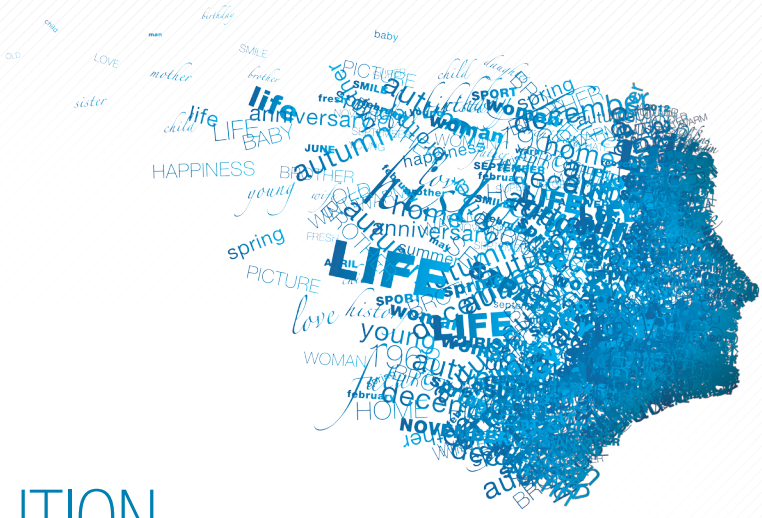

TAU BLUE REVOLUTION

Tau neurofibrillary pathology represents the main hallmark of AD and human neurodegenerative tauopathies. In the last decade, therapeutic strategies targeting misfolded *tau* protein have been gaining momentum. An increasing body of evidence shows that modulation of *tau* cascade has a beneficial effect in the animal models in preclinical studies. *Tau* therapy is becoming the leading therapeutic approach in AD.

10 reasons why Axon Neuroscience believes that tau is the proper target for AD-modifying therapy

1. *Tau* neurofibrillary pathology is the major correlate of clinical symptoms in Alzheimer's disease[1,2,3]
2. Distribution of neurofibrillary pathology defines subtypes of Alzheimer's disease with distinct clinical characteristics[4]
3. Decline in memory that occurs around 12 years before clinically diagnosed Alzheimer's disease may correlate with the presence of neurofibrillary pathology in the temporal areas[5]
4. Neurofibrillary tangles precede amyloid beta pathology[6,7,8]
5. Cortical atrophy measured by MRI is associated with neurofibrillary pathology[9]
6. Neurofibrillary lesions and neuroinflammation display the same regional distribution in Alzheimer's disease and other human tauopathies[10-19]
7. There is strong regional, inversely proportional relationship between the number of neurons and the number of neurofibrillary tangles[20-22]
8. *Tau* pathology in the absence of amyloid pathology strongly correlates with clinical features in human tauopathies such as progressive supranuclear palsy, corticobasal degeneration, tangle-only dementia and argyrophilic grain disease[23-29]
9. *Tau* gene mutations are pathogenic for frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17)[30-32]
10. *Tau* animal models reproduce neuronal and glial tau pathology leading to the progressive cognitive and/or motor impairment[33-35]

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