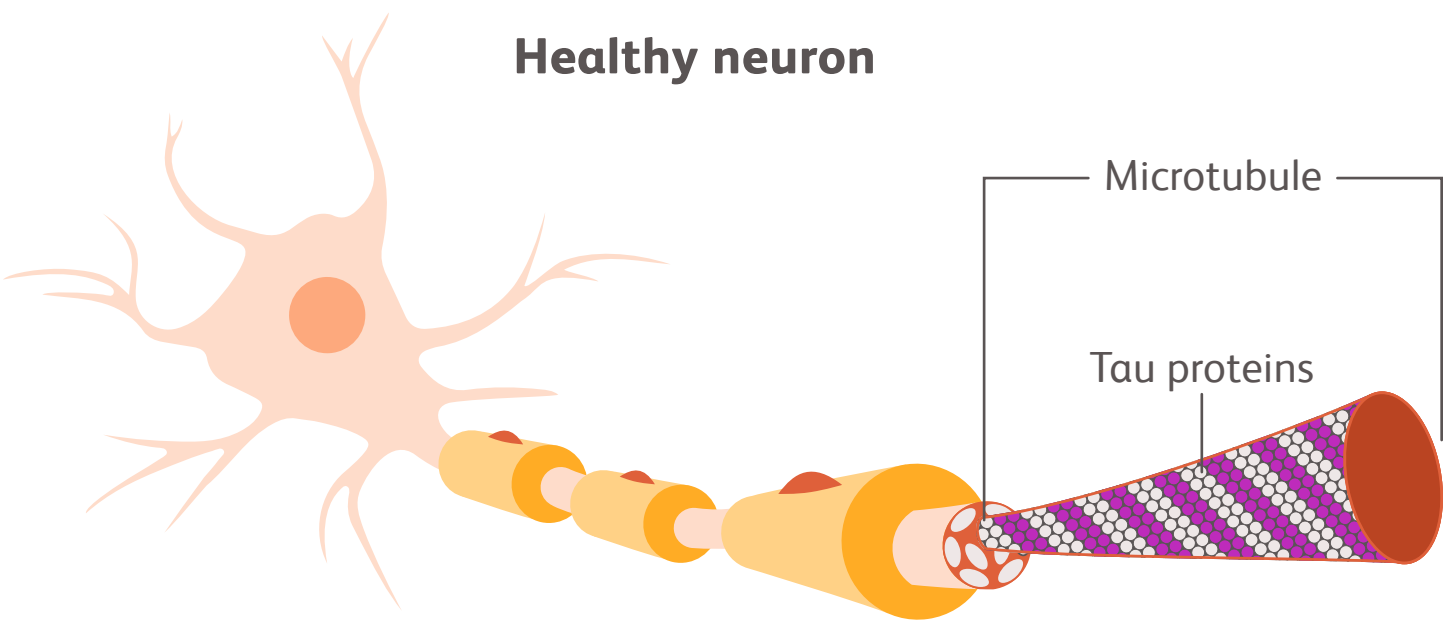
Bristol Myers Squibb®

Tau in Alzheimer's disease

What is tau?

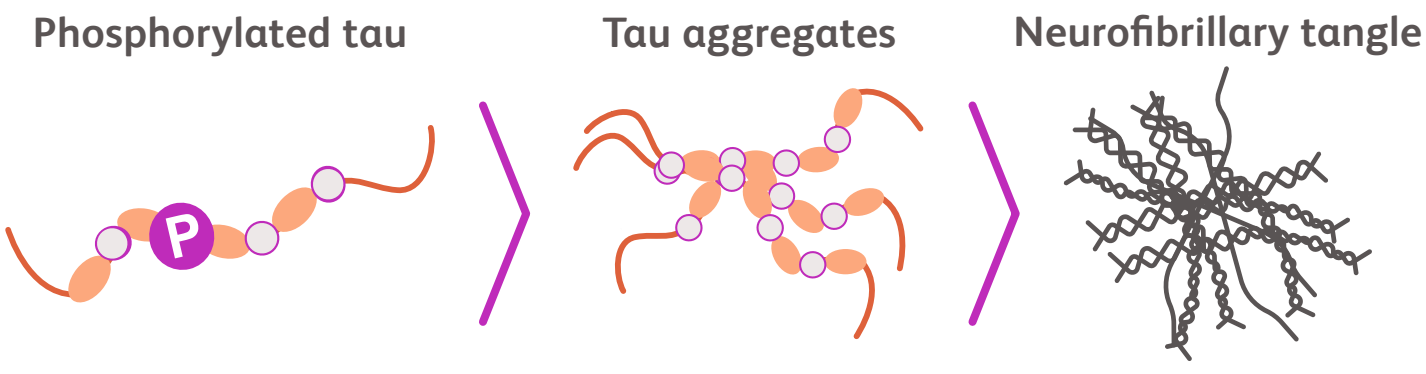
Tau is a protein found predominantly in neurons in the brain. Neurons have an internal skeleton made up of microtubules. Tau proteins help to stabilize these microtubules, allowing the neurons to maintain their shape.[1,2]



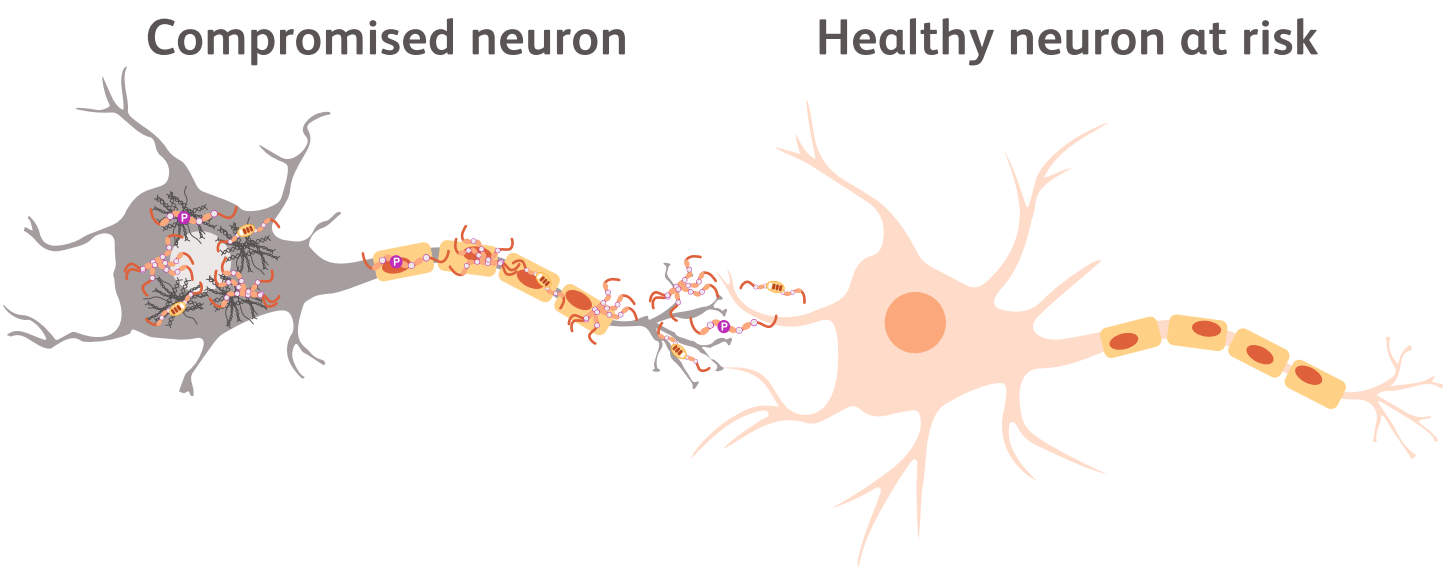
The role of tau in Alzheimer's disease

Pathological forms of tau caused by chemical changes in the protein contribute to disease processes in Alzheimer's disease.

Pathological tau proteins can detach from the microtubules, aggregate and form **neurofibrillary tangles**, a key marker of the disease along with amyloid-B plaques. Neurofibrillary tangles are associated with **loss of synapses and neurons, correlating with cognitive decline**.[1,3]



A main driver for disease progression is the **spread of tau throughout the brain**.[4] When a neuron dies, pathological tau proteins are released from the cell and can spread to neighboring healthy cells, 'infecting' them.



Tau deposition in Alzheimer's disease correlates with[4-7]:

- Symptom onset at a younger age and faster disease progression
- Disease duration: Tau protein undergoes changes over the course of the disease
- Neurodegeneration which contributes to cognitive impairment, one of the defining symptoms of the disease

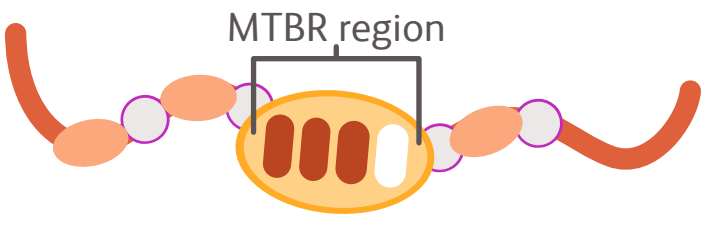
These correlations provide strong evidence for the development of therapeutic strategies targeting tau.

Targeting tau protein for disease modification

Scientific rationale suggests that stopping the spread of tau proteins from neuron to neuron may help halt the development and/or progression of the disease.[2]

Researchers are exploring ways to more precisely target and remove tau from the brain, in particular tau proteins that are found outside of neurons, which are a major cause of disease progression.

These tau proteins contain a **microtubule binding region (MTBR)** thought to contribute to the cell-to-cell spread of tau. But this MTBR region can also act as a kind of 'handle' for tau's removal from the brain.[3]



Preclinical models have suggested that MTBR may be key to preventing the accumulation and spreading of pathologic tau.[8]

At Bristol Myers Squibb, we are committed to advancing our robust pipeline of potential medicines for neurological disorders with the goal of modifying disease and improving quality of life for patients.

1. Alzheimer's Association. "Tau." Updated October 2021. https://www.alz.org/media/Documents/alzheimers-dementia-tau-ts.pdf.
2. Congdon EE, Sigurdsson EM. Tau-targeting therapies for Alzheimer disease. *Nat Rev Neurol*. 2018 Jul;14(7):399-415.
3. Congdon EE, Ji C, Tetlow AM, et al. Tau-targeting therapies for Alzheimer disease: current status and future directions. *Nat Rev Neurol*. 2023 Dec;19(12):715-736.
4. Horie K, Barthélemy NR, Sato C, et al. CSF tau microtubule binding region identifies tau tangle and clinical stages of Alzheimer's disease. *Brain*. 2021 Mar 3;144(2):515-527.
5. Frontzkowski L, et al. Earlier Alzheimer's disease onset is associated with tau pathology in brain hub regions and facilitated tau spreading. *Nat Commun*. 2022 Aug 20;13(1):4899.
6. Wesseling H, et al. Tau PTM Profiles Identify Patient Heterogeneity and Stages of Alzheimer's Disease. *Cell*. 2020 Dec 10;183(6):1699-1713.e13.
7. Boccalini C, et al. The impact of tau deposition and hypometabolism on cognitive impairment and longitudinal cognitive decline. *Alzheimers Dement*. 2024 Jan;20(1):221-233.
8. Dolan P, et al. Microtubule Binding Region (MTBR)-Specific Antibody PRX005 Prevents Pathological Tau Progression via Blockade of Neuronal Internalization. Oral presentation at AD/PD 2021; March 9-14, 2021; Virtual. Partnership with BMS.