X-Ray Characterization of \textit{Tau}-Induced Microtubule Bundles

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Alzheimer’s is thought to be caused by protein defects in the brain.

Research has usually targeted beta-amyloid plaque.

Studies have shown the resulting treatment to be dangerous in many participants.

Alternative path of study lies in Tau proteins.

beta-amyloid plaque
What are Microtubules and $\text{Tau}$ Proteins?

Axon

Healthy Neuron

Microtubules

Stabilizing Tau Molecules

Diseased Neuron

Disintegrating Microtubules

Axon

Disintegrating Microtubules

Microtubule Subunits Fall Apart

Tangled Clumps of Tau Proteins

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Research indicates Tau protein possibly related to brain diseases (including Alzheimer’s, Parkinson’s, etc).

Use X-ray scattering to discover relationships between Tau protein and neuronal microtubules.
Primary Tau Protein Structure

- Projection Domain
- Proline-rich Region
- Microtubule Binding Repeats (MTBR)
- C-terminal
Primary \textit{Tau} Protein Structure

- Projection Domain
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Making The Samples

One sample made with full \textit{tau} protein, one made with only MTBR segment to discover effects of other three segments

Mixture of \textit{tau} protein, tubulin, GTP, and a buffer

Each sample split into two to be analyzed via X-ray scattering and DIC microscopy
DIC Microscope Examination

Differential Interference Contrast

Observed microtubule formation and bundling

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X-Ray Scattering Examination

Sample placed in quartz capillary and put in centrifuge to create higher concentration point.

Exposed to X-rays, scattered light collected and analyzed.
Observable Differences in Bundling

Full \textit{Tau} vs. MTBR only

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Full Tau X-Ray Scattering

Structure factor
- Represents hexagonal lattice
Full **Tau** X-Ray Scattering

Form factor
  – Corresponds to structure of microtubule
Comparing X-Ray Scattering

Full Tau

MTBR only

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Bundling is Dependent Upon \textit{Ta}u

In the presence of full \textit{Ta}u protein...
- Tubulin forms microtubules
- Microtubules form hexagonal lattice

In the presence of MTBR segment only...
- Bundles lack hexagonal structure
- Microtubules bundle more tightly
What Comes Next?

- Studies will help us understand the functions of the other three segments of *Tau* protein
- Research will improve understanding of *Tau* protein function
- Successful treatment for degenerative brain diseases