



Seeding of Tau Protein Aggregation

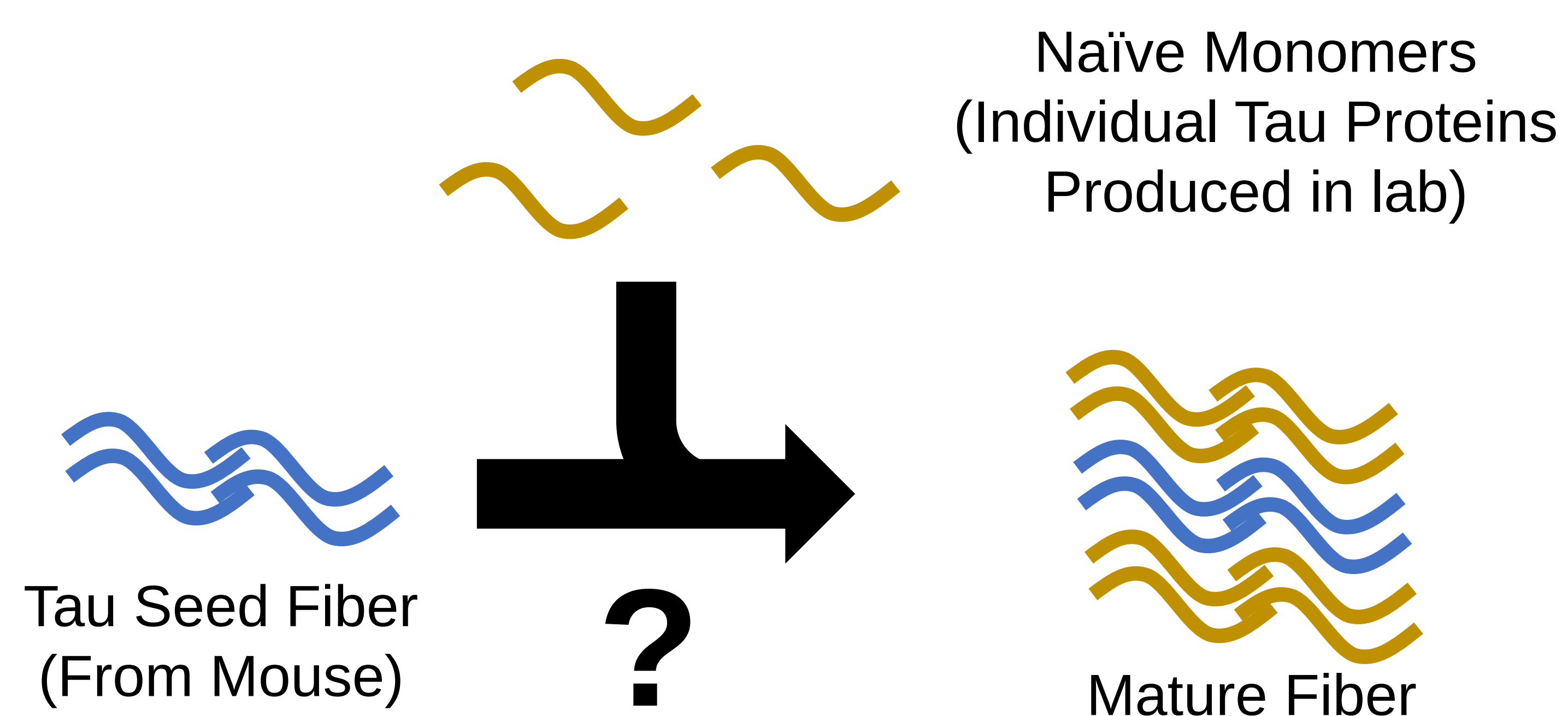
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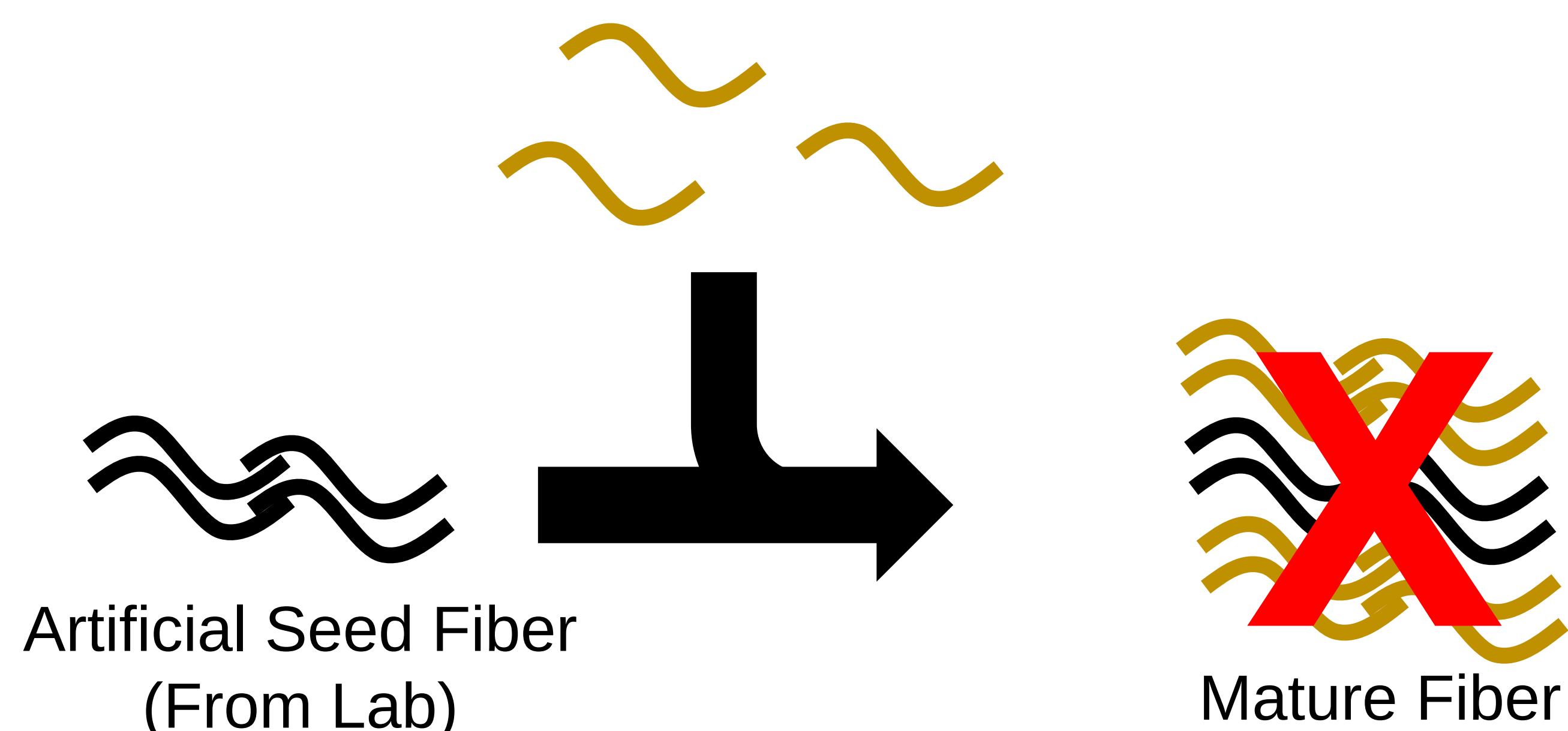
Summary

No one knows how the tau fibers that cause Alzheimer's disease spread throughout the brain. The current hypothesis is called seeding, in which large fibers grow from a small seed fiber. However, nobody knows the mechanism of seeding, or why fibers extracted from the brain are seeding active but fibers made in lab are not. We aim to figure out these unknowns. We investigated them by studying the effect of seeding conditions on fiber formation (aggregation). We quantified aggregation through Th T fluorescence, and we tested the effect of tau mutations on fiber formation.

Tau Fibers from Mice are Active Seeds, but not Artificial Tau Fibers

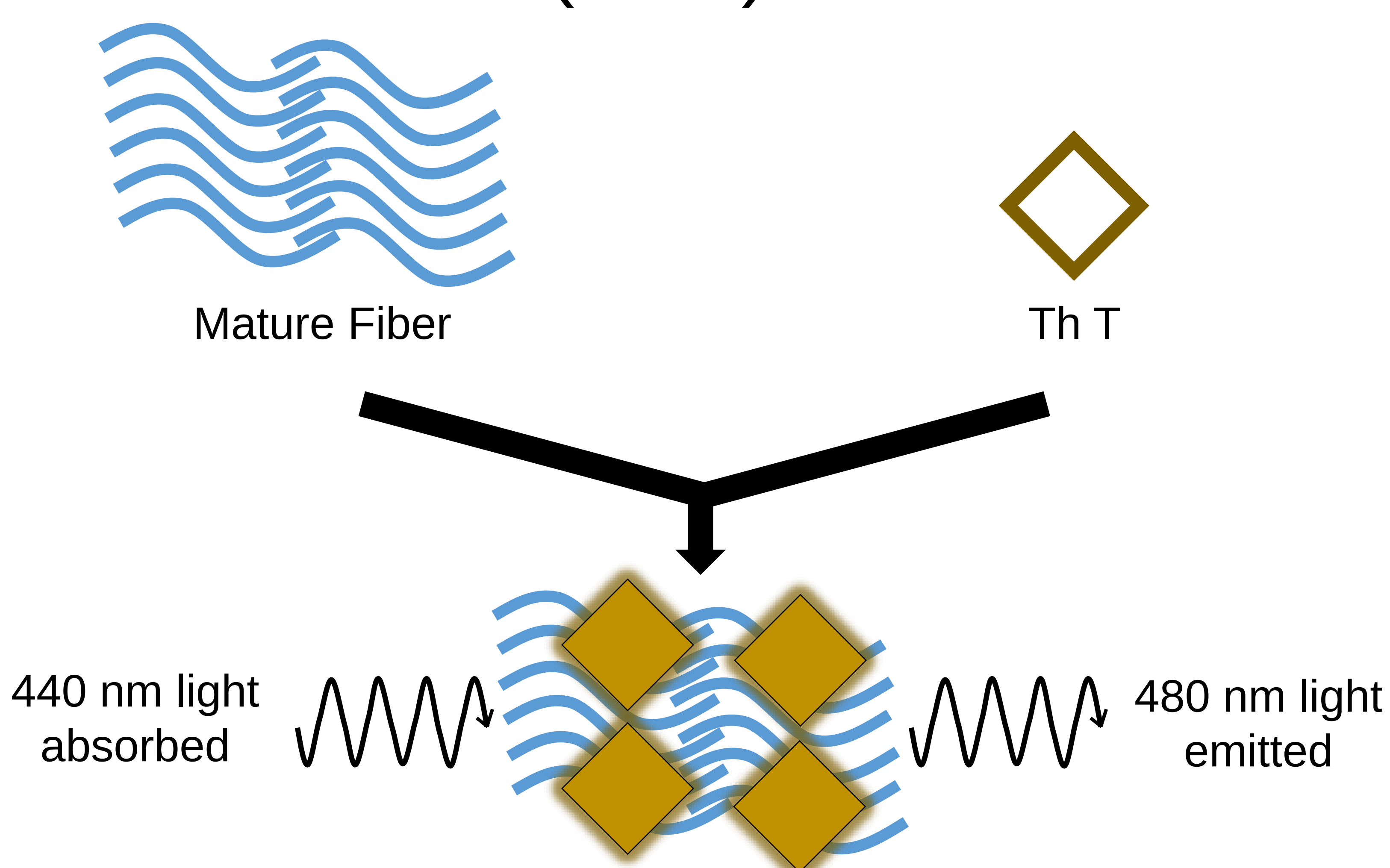


The mechanism in which the seed fiber induces aggregation is unclear.

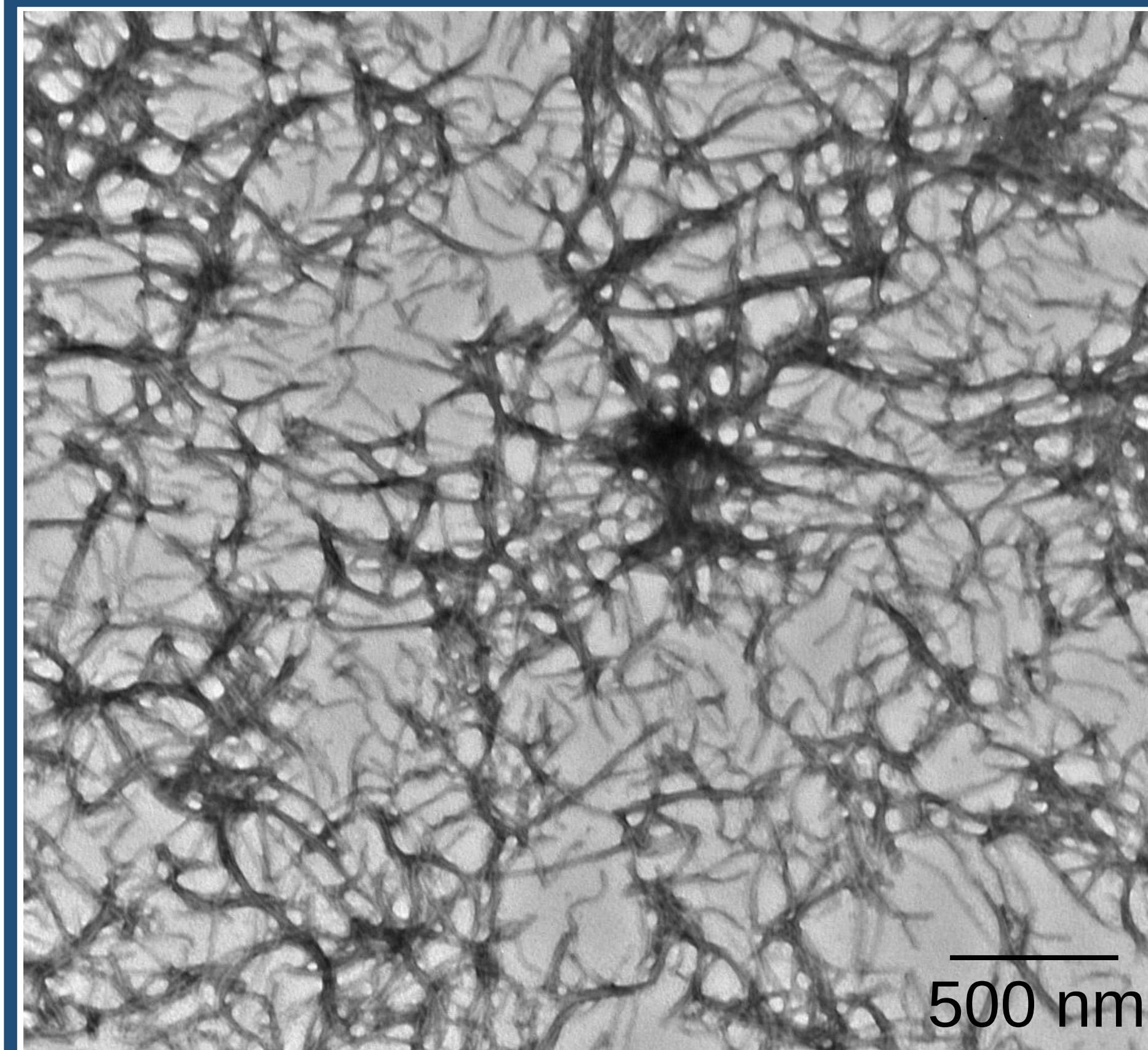


There is something special about diseased brain fibers that allow them to be active seeds, whereas fibers made in lab cannot.

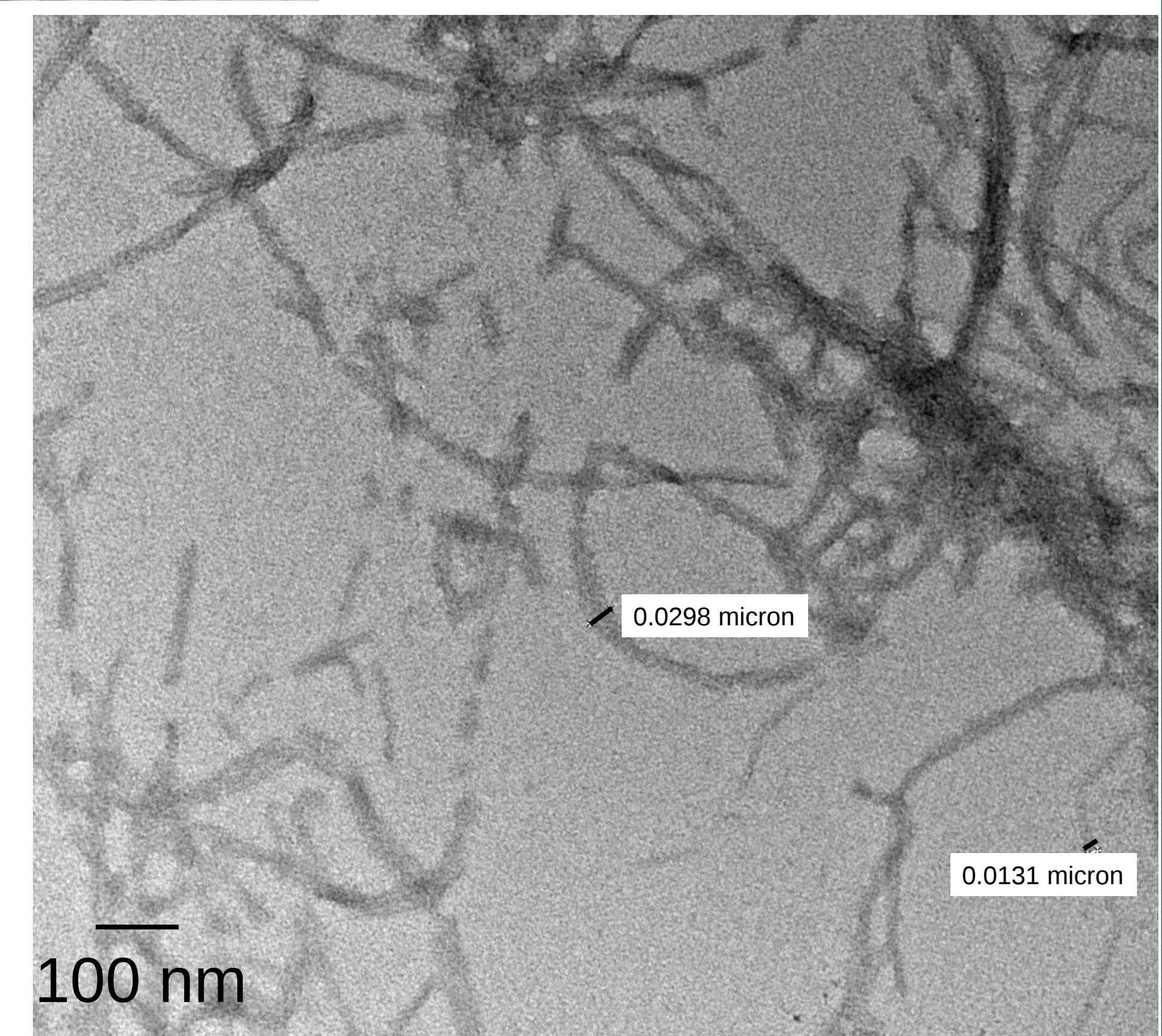
Fiber Formation Is Quantified Through Thioflavin T (Th T) Fluorescence



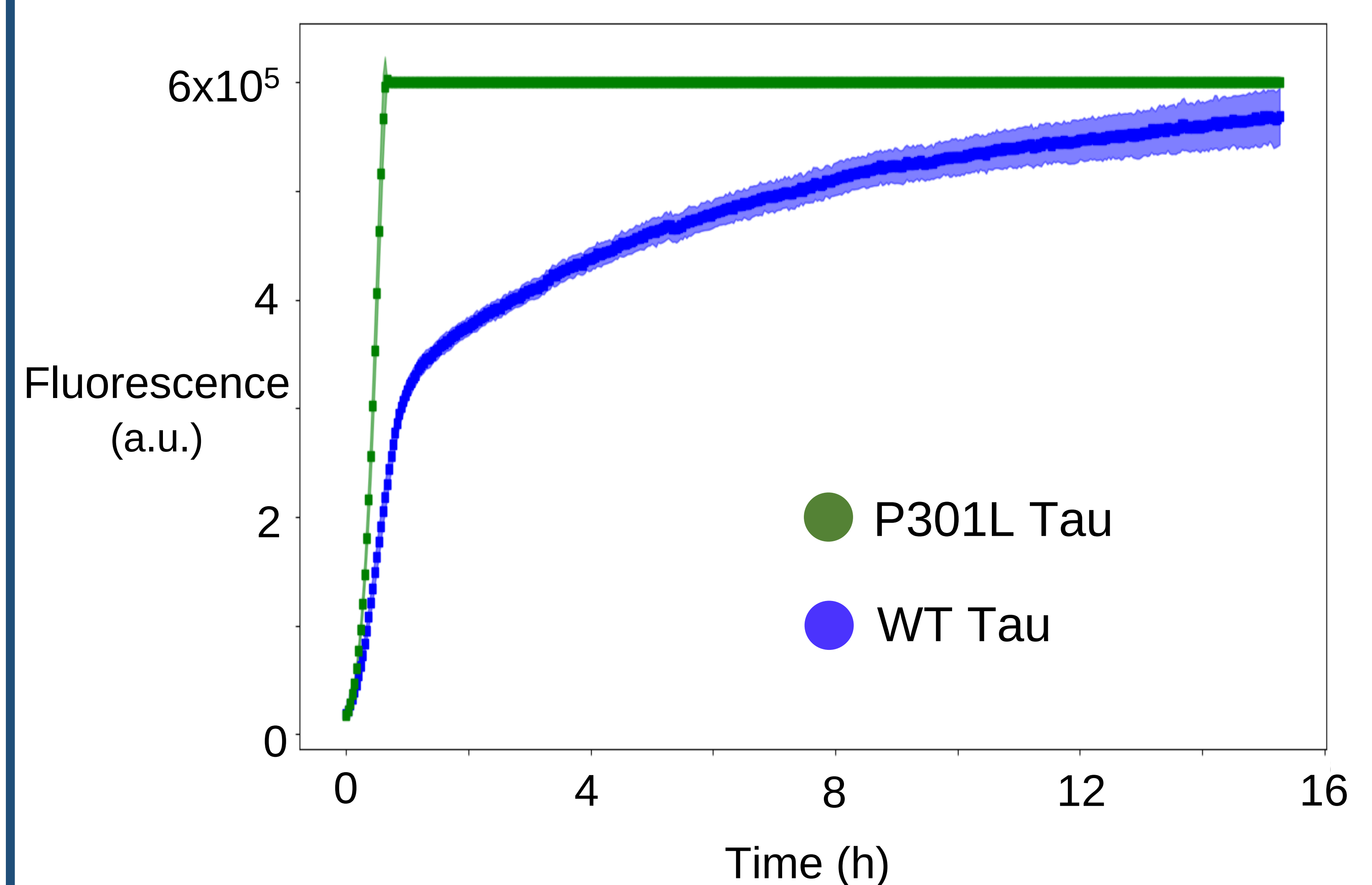
Th T binds to fibers and fluoresces, indicating their presence



Tau fibers imaged through transmission electron microscopy.



P301L Tau Is More Aggregation Prone Than Wild Type (WT) Tau



Conclusion

From the data, we see that the P301L mutation caused tau to both aggregate faster and in greater quantity than WT tau. Therefore, we can conclude that the P301L mutation causes tau protein to become more aggregation prone than WT tau. For future experiments, we will study the effects of pH, salt concentration, and sonication on seeding. We hope that this will shed light on the seeding mechanism and the missing link between diseased brain fibers and artificial lab fibers.

Acknowledgments



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