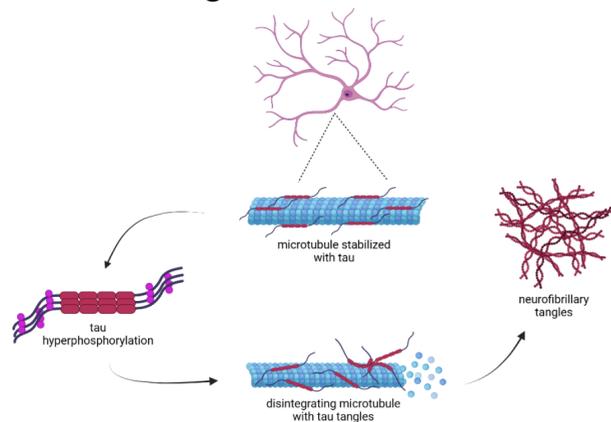


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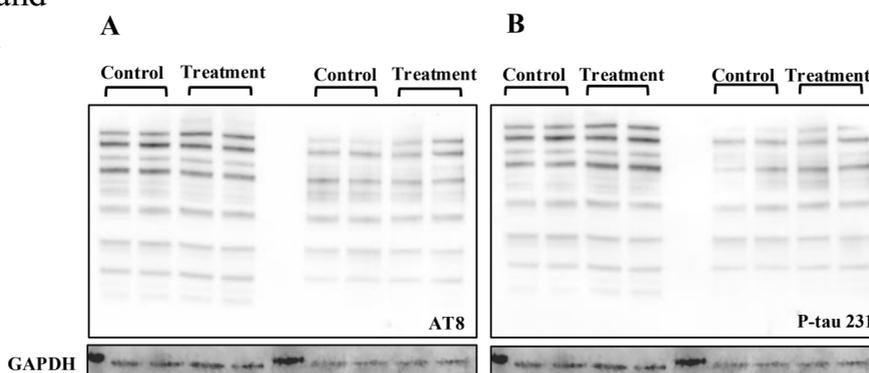
## Background

- Atherosclerosis leads to narrowed or blocked blood vessels that can cause vascular cognitive impairment and dementia.
- Atherosclerosis is also associated with CSVD, known to cause microvascular endothelial dysfunction and cerebral microbleeds.
- Endothelial damage is considered a key contributor to cognitive impairment and dementia, but the underlying mechanism remains unclear.
- Hyperphosphorylated tau is the primary pathological driver of Alzheimer's disease and vascular dementia and is often present with CSVD.<sup>1</sup>
- This study aims to test whether phosphorylated tau can be directly induced under atherogenic conditions.



## Results

- The molecular density, or concentration, of phosphorylated tau was higher in the treatment groups when compared to the control.
- There were multiple bands on the western blots, leading to an increase in molecular weight compared to the control.
- For primary antibody AT8, the P value measured by an unpaired T test was 0.7621.
- For primary antibody P-tau 231, the P value measured by an unpaired T test was 0.4746.
- There is a trend of increase in tau phosphorylation under atherogenic factors.



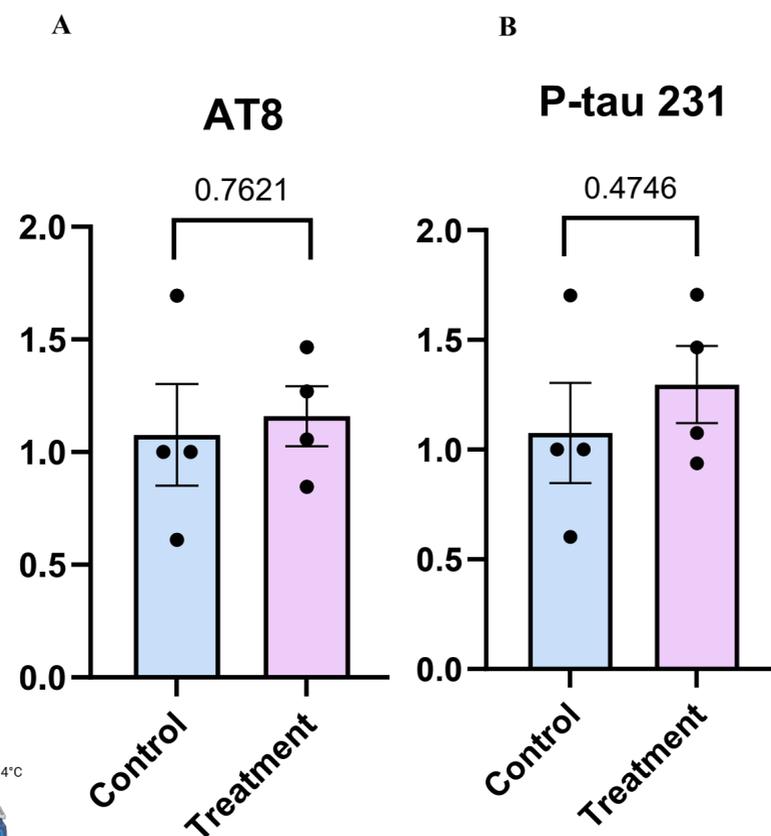
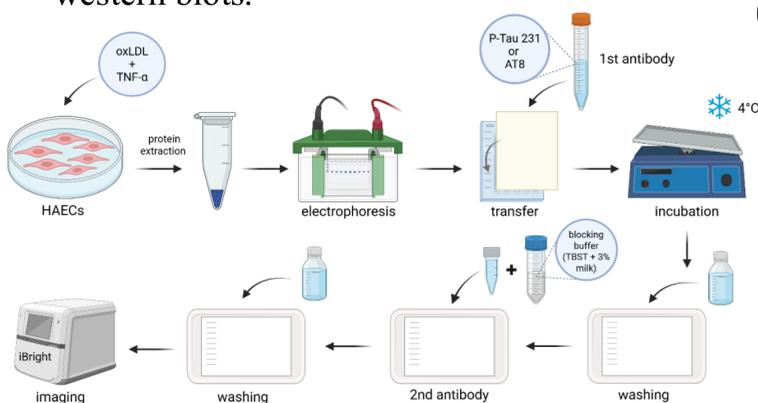
**Figure 1.** (A) Western blot using the AT8 primary antibody, which detects phosphorylated tau at serine 202/threonine 205, compared to GAPDH. (B) Western blot using the P-tau 231 primary antibody, which detects phosphorylated tau at threonine 231, compared to GAPDH.

## Conclusion

- The multiple bands on the western bands are suspected to be phosphorylated tau aggregates, abnormal clumps of tau protein, that increase molecular weight and concentration.
- This finding suggests that atherogenic conditions may directly stimulate tau pathology in cerebrovascular endothelial cells, thereby contributing to vascular-initiated tau pathology and dementia.
- More replicate experimentation is needed to gather more robust data and determine whether the trend of increase in tau phosphorylation under atherogenic factors continues.
- Future research will then focus on human brain microvascular endothelial cell to better understand the effects of atherogenic factors on cerebral blood vessels, directly looking at how phosphorylated tau affects the brain and is involved in cognitive dysfunction and dementia. Shifting focus from HAECs to human brain endothelial cells allows for research on the cerebral vascular system and on the tau pathology in this area.

## Methods

- A combined treatment of oxLDL and TNF- $\alpha$  was exposed to HAEC.
- Proteins from the treated cells were extracted through cell lysis.
- The proteins were then used in western blots to determine the concentration of tau protein.
- The phosphorylated tau at threonine 231 and serine 202/threonine 205 was detected by antibodies P-tau 231 and AT8, respectively.
- Image J was used to determine the protein density of the bands acquired from the western blots.



**Figure 2.** (A) The molecular density of phosphorylated tau of the treatment group compared to the control group at serine 202/threonine 205. (B) The molecular density of phosphorylated tau of the treatment group compared to the control group at threonine 231.

## References

- <sup>1</sup>Faraco, G.; Hochrainer, K.; Segarra, S. G.; Schaeffer, S.; Santisteban, M. M.; Menon, A.; Jiang, H.; Holtzman, D. M.; Anrather, J.; Iadecola, C. Dietary Salt Promotes Cognitive Impairment through Tau Phosphorylation. *Nature* **2019**, *574* (7780), 686–690. DOI:10.1038/s41586-019-1688-z. Figures created with BioRender

## Acknowledgements

I would like to thank my mentor, Dr. Han, for the opportunity to learn and work in the Han Lab, as well as her patience and dedication throughout this project. Thank you to the members of the Vascular Biology Section at the Boston University Chobanian and Avedisian School of Medicine for their support and expertise.