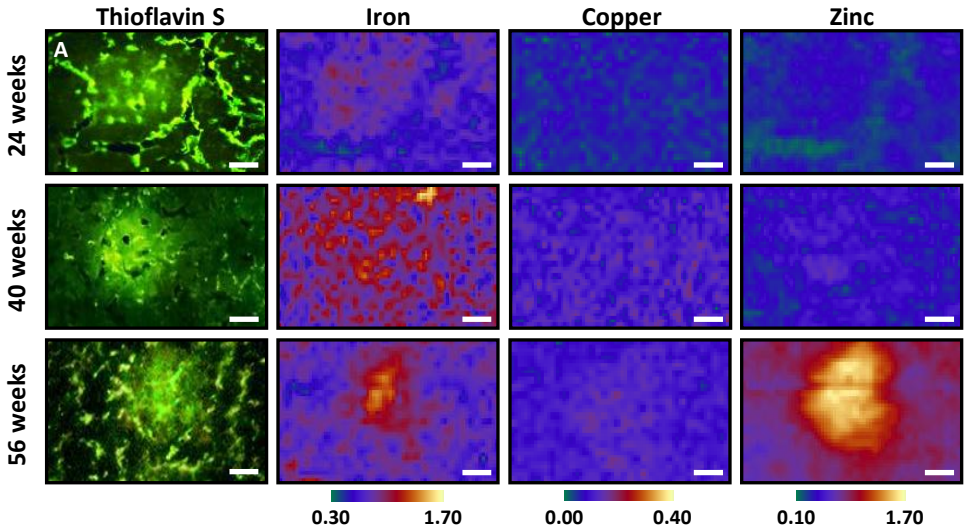
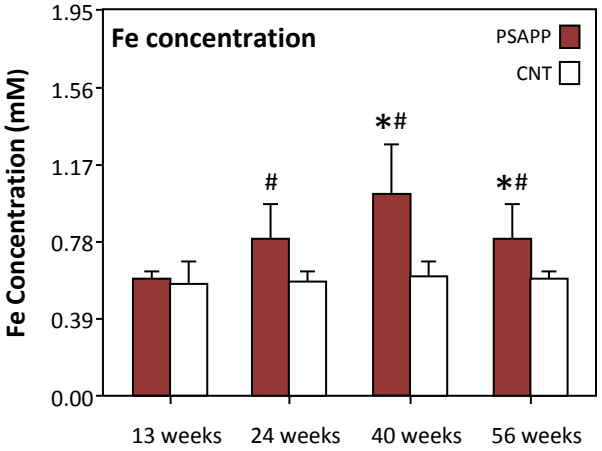
Time-Dependent Metal Accumulation in the Brain of a Mouse Model of Alzheimer's Disease

- End-stage human Alzheimer's disease (AD) is characterized by accumulations of Fe, Cu, and Zn in amyloid plaques.
- Metal accumulation the AD brain may represent a mechanism for plaque toxicity and is a potential target for early diagnosis. However, the time course for metal accumulation is currently unclear.
- Using the PSAPP mouse model of AD, we conducted a time course study of Fe, Cu, and Zn content and distribution in the cortex and hippocampus using X-ray fluorescence microscopy.
- Results showed that mouse plaques do not accumulate Fe or Cu and very little Zn – in contrast to human plaques – which may be correlated with the lack of neurodegeneration in the PSAPP mouse model.
- Also, Fe in the the cortex was 39% higher than age-matched controls animals at an early stage, corresponding to initial plaque formation.
- Since plaque formation in human Alzheimer's disease is presumed to occur years before the first cognitive symptoms appear, quantification of iron in the cortex could be useful for early diagnosis of AD.





(Top) Thioflavin S epi-fluorescence and XFM images of Fe, Cu, and Zn over the course of time in a PSAPP mouse plaque. Scale bar is 10 microns.

(Left) Fe concentration in the cortex of PSAPP and control mice over the course of time.

A.L. Leskovjan, A. Lanzirotti, L.M. Miller (2009). Amyloid plaques in PSAPP mice accumulate less metal than plaques in human Alzheimer's disease. *NeuroImage* **47(4)**: 1215-20.

A.L. Leskovjan, A. Kretlow, A. Lanzirotti, R. Barrea, S. Vogt, L.M. Miller. Increased brain iron coincides with early plaque formation in a Mouse Model of Alzheimer's Disease. Submitted to *Science*, May 2010.

funded by NIH R01-GM66873