



Innovations in Inorganic and Materials Chemistry

Measuring and Imaging Aluminium in Human Brain Tissue

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<https://www.hippocraticpost.com/?s=Exley>

<http://www.keele.ac.uk/aluminium/>



Aluminium in Human Brain Tissue

Our Published Data

Exley C & Esiri M (2006) Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall, UK. *Journal of Neurology Neurosurgery and Psychiatry* 77, 877-879.

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Mirza A, King A, Troakes C and Exley C (2017) Aluminium in brain tissue in familial Alzheimer's disease. *Journal of Trace Elements in Medicine and Biology* 40, 30-36.

<https://www.sciencedirect.com/science/article/pii/S0946672X16303777>

Published Research Continued

Mold M, Umar D, King A, Exley C (2018) Aluminium in brain tissue in autism. *Journal of Trace Elements in Medicine and Biology* 46, 76-82.

<https://www.sciencedirect.com/science/article/pii/S0946672X17308763>

Mold M, Chmielecka A, Rodriguez MRR, Thom F, Linhart C, King A, Exley C (2018) Aluminium in brain tissue in multiple sclerosis. *International Journal of Environmental Research and Public Health* 15, 1777.

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Mold M, Cottle J, Exley C (2019) Aluminium in brain tissue in epilepsy: A case report from Camelford. *International Journal of Environmental Research and Public Health* 16, 2129.

<https://www.mdpi.com/1660-4601/16/12/2129>

Mold M, Cottle J, King A, Exley C (2019) Intracellular aluminium in inflammatory and glial cells in cerebral amyloid angiopathy: A Case Report. *International Journal of Environmental Research and Public Health* 16, 1459.

<https://www.mdpi.com/1660-4601/16/8/1459>

Mold M, Linhart C, Gomez-Ramirez J, Villegas-Lanau A, Exley C (2020) Aluminium and amyloid- β in familial Alzheimer's disease. *Journal of Alzheimer's Disease* 73, 1627-1635.

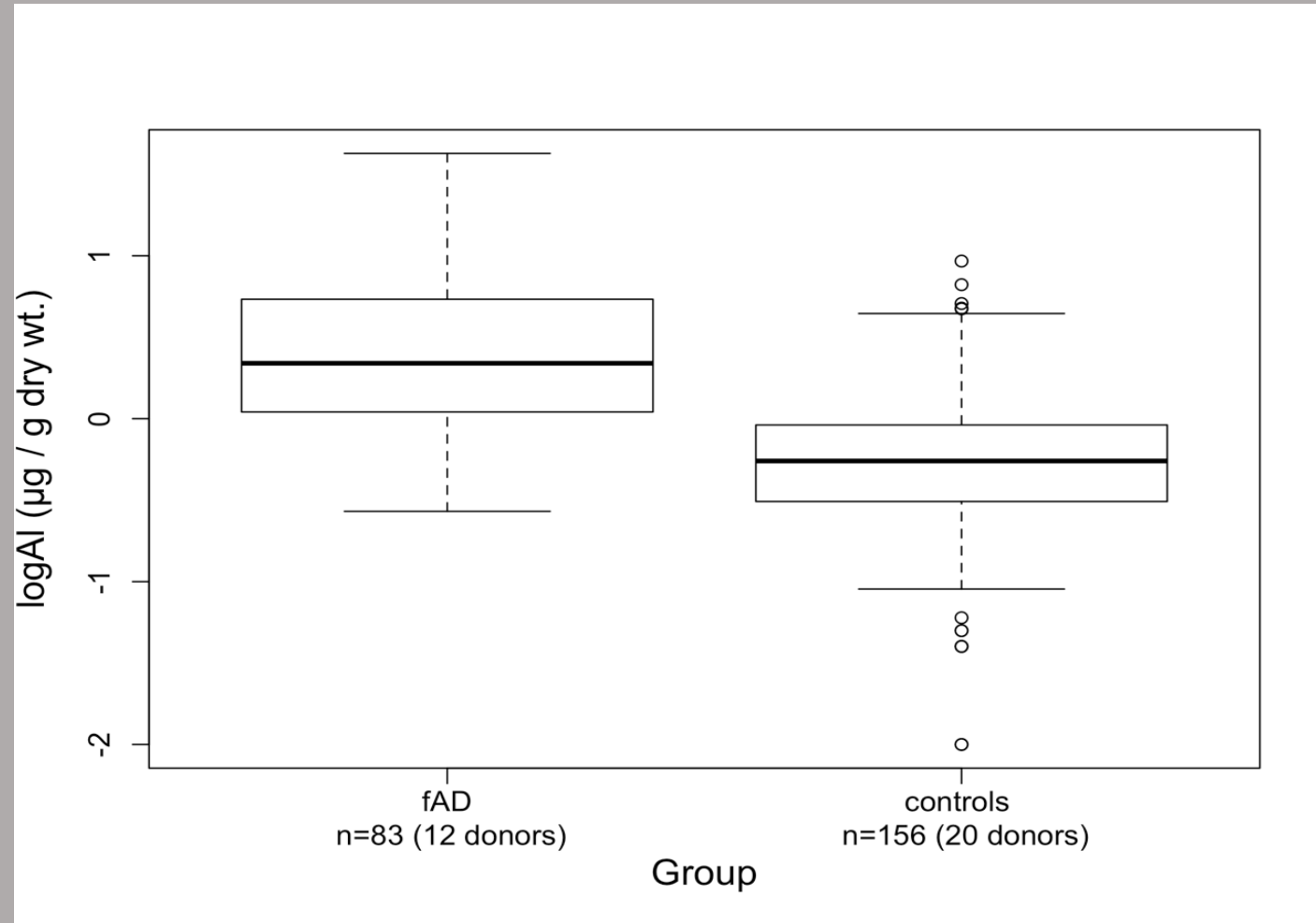
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Aluminium in human brain tissue: how much is too much?

<https://link.springer.com/article/10.1007%2Fs00775-019-01710-0>

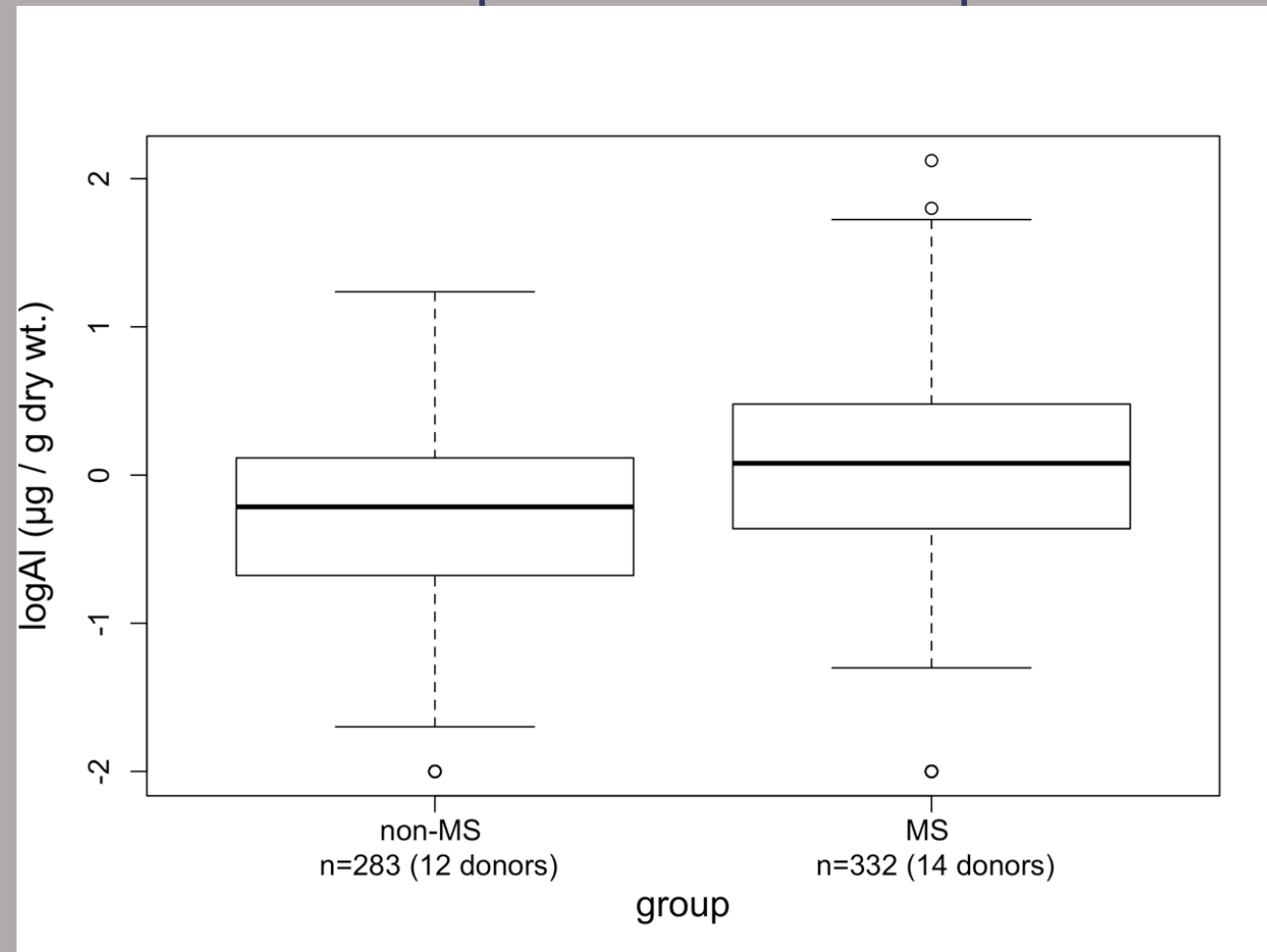
Mold M, Linhart C, Gomez-Ramirez J, Villegas-Lanau A, Exley C (2020) Aluminium and amyloid- β in familial Alzheimer's disease. *Journal of Alzheimer's Disease* 73, 1627-1635.

<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad191140>



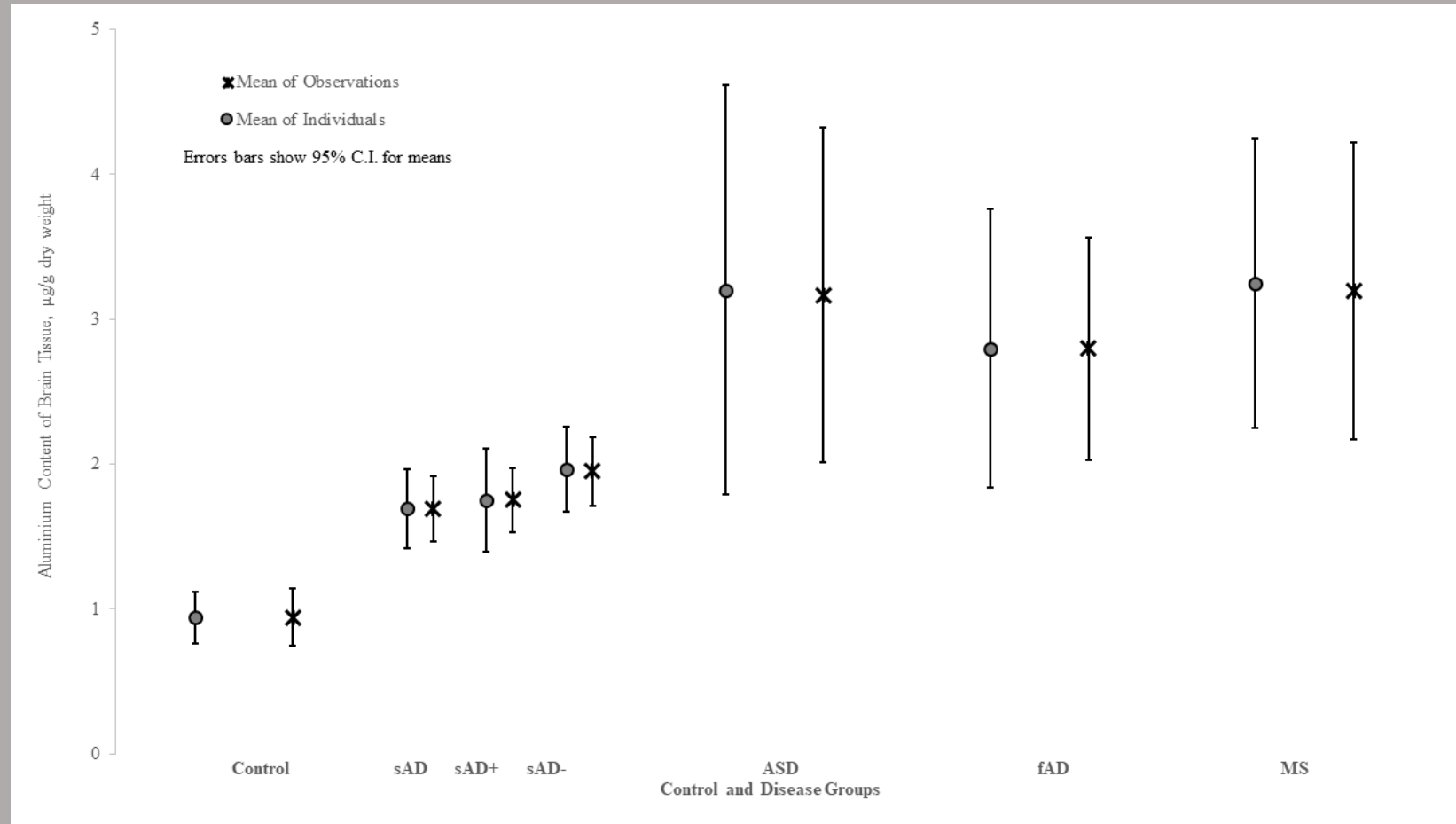
The aluminum content (median and IQR) of fAD brain tissues (2.19; 1.10–5.41) was significantly higher ($p < 0.001$) than control tissues (0.60; 0.35–0.98).

Aluminium in Brain Tissue in Non-neurodegenerative / Non-neurodevelopmental Disease: A Comparison with Multiple Sclerosis



The aluminium content across all lobes were significantly higher in MS donors (mixed effect model, n(samples)= 615 , N(donors) = 26, **p = 0.004**) than non-MS donors.

Aluminium in human brain tissue from donors without neurodegenerative disease: A comparison with Alzheimer's disease, multiple sclerosis and autism.



The aluminium content of brain tissue in the control group was significantly lower than sAD ($P=0.0006$), fAD ($P=0.0020$), ASD ($P=0.0123$) and MS ($P<0.0001$).

So, there is aluminium in your brain
BUT...what does it look like?

The Identification of Aluminum in Human Brain Tissue Using Lumogallion and Fluorescence Microscopy

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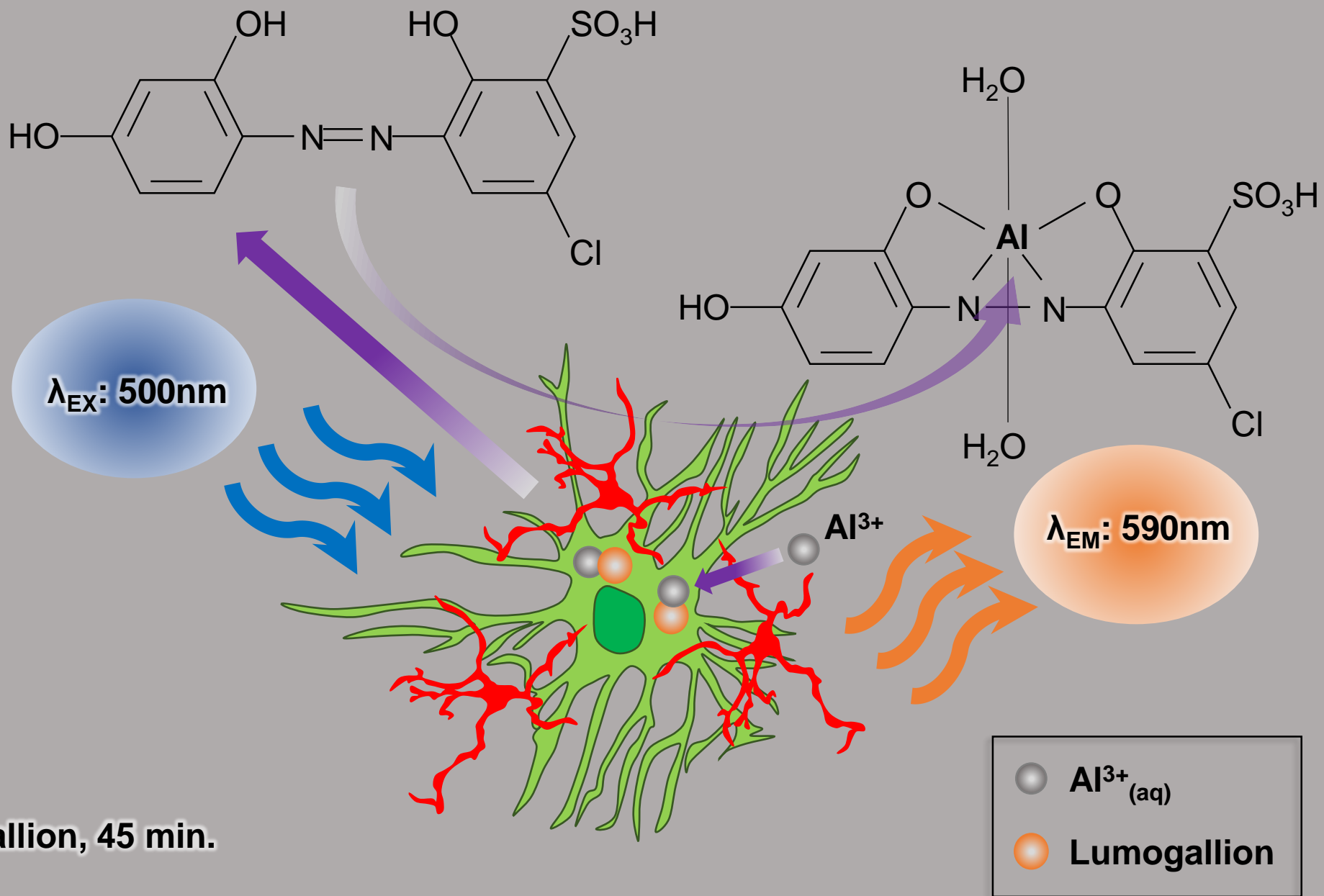
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Accepted 4 July 2016

Abstract. Aluminum in human brain tissue is implicated in the etiologies of neurodegenerative diseases including Alzheimer's disease. While methods for the accurate and precise measurement of aluminum in human brain tissue are widely acknowledged, the same cannot be said for the visualization of aluminum. Herein we have used transversely-heated graphite furnace atomic absorption spectrometry to measure aluminum in the brain of a donor with Alzheimer's disease, and we have developed and validated fluorescence microscopy and the fluor lumogallion to show the presence of aluminum in the same tissue. Aluminum is observed as characteristic orange fluorescence that is neither reproduced by other metals nor explained by autofluorescence. This new and relatively simple method to visualize aluminum in human brain tissue should enable more rigorous testing of the aluminum hypothesis of Alzheimer's disease (and other neurological conditions) in the future.

Keywords: Aluminum, Alzheimer's disease, brain tissue, fluorescence microscopy, lumogallion, transversely heated graphite furnace atomic absorption spectrometry



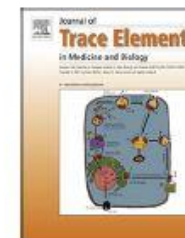
1mM lumogallion, 45 min.



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Aluminium in brain tissue in autism

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ARTICLE INFO

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Human exposure to aluminium

Human brain tissue

Autism spectrum disorder

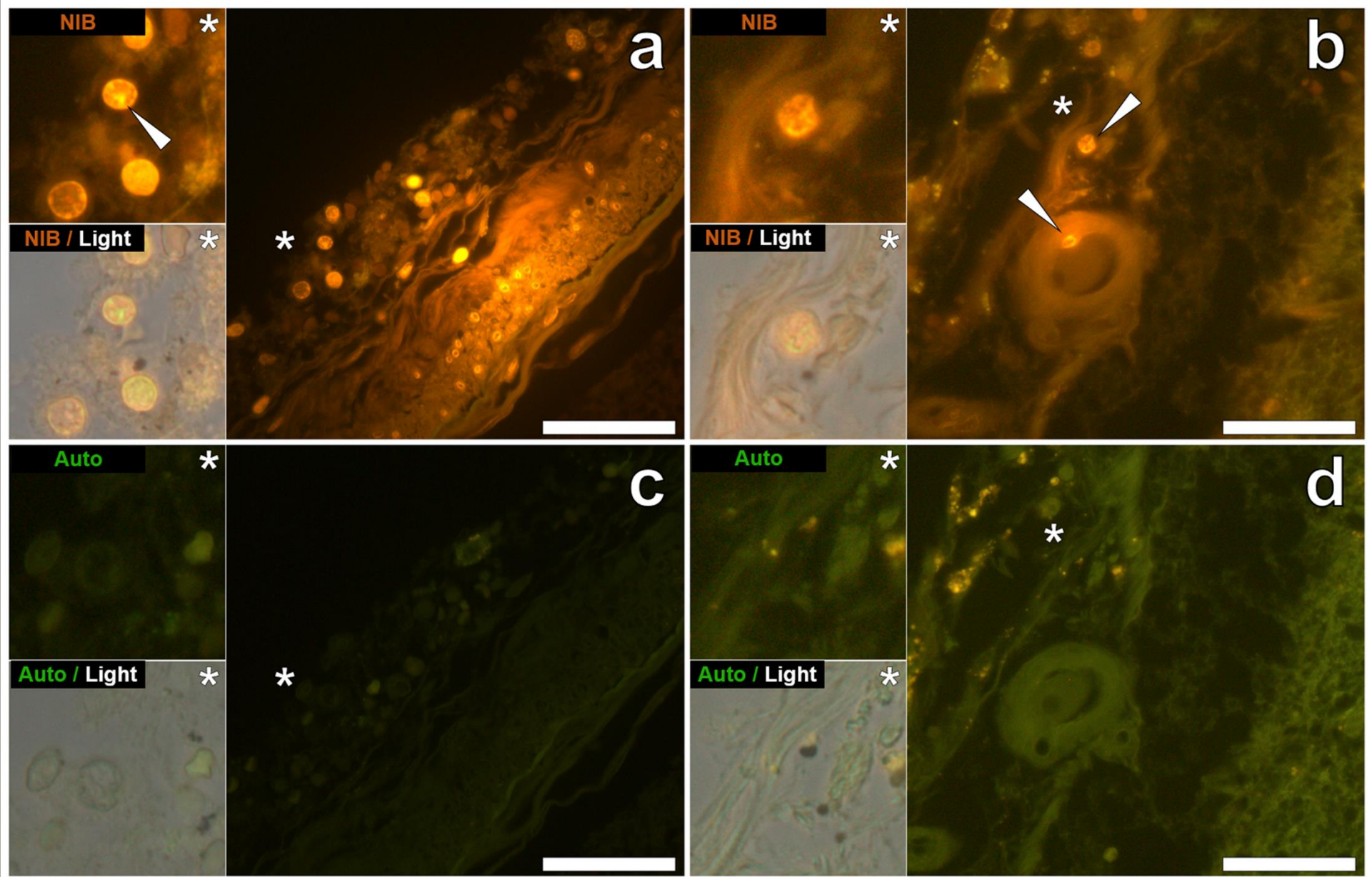
Transversely heated atomic absorption spectrometry

Aluminium-selective fluorescence microscopy

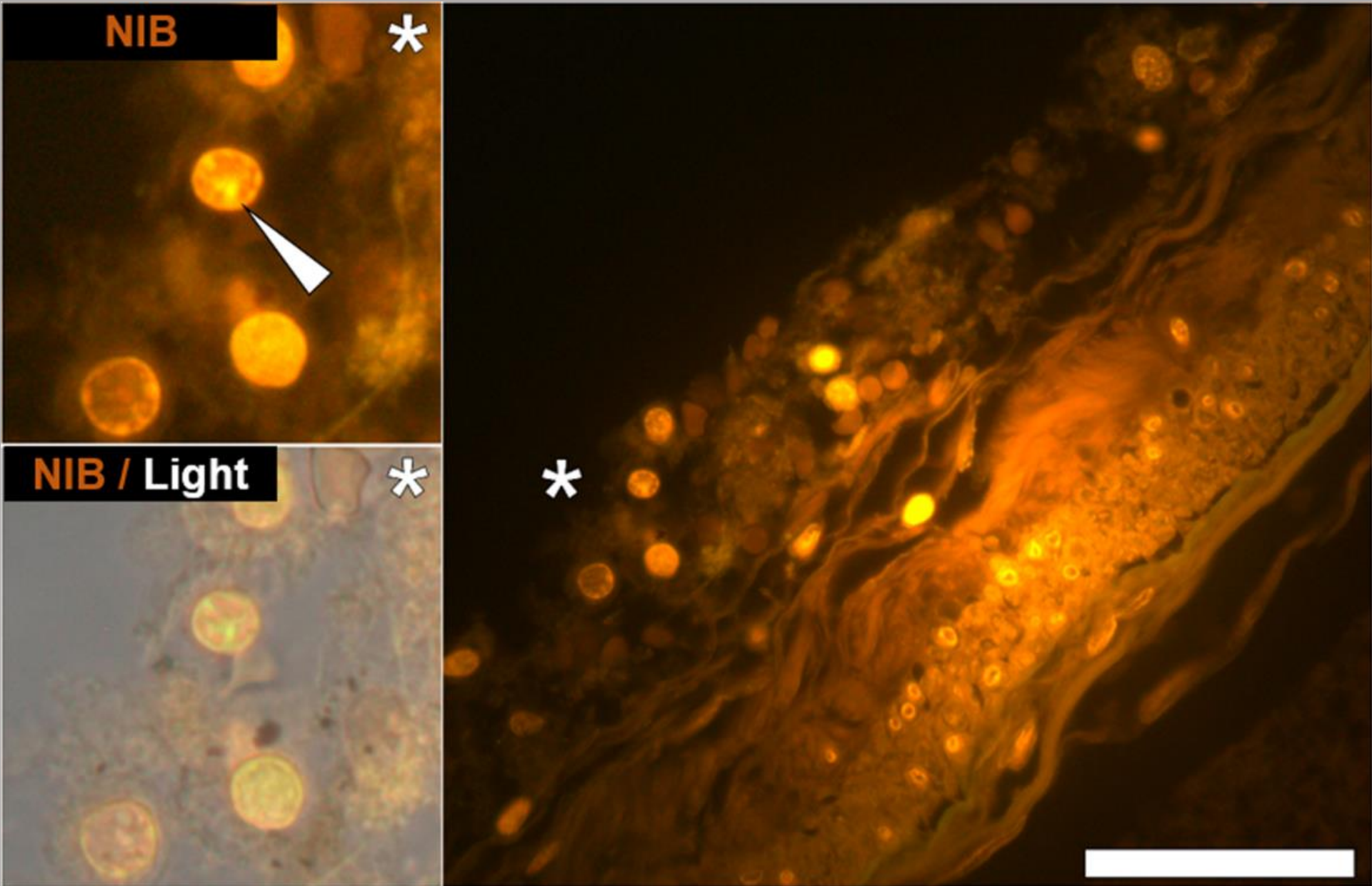
ABSTRACT

Autism spectrum disorder is a neurodevelopmental disorder of unknown aetiology. It is suggested to involve both genetic susceptibility and environmental factors including in the latter environmental toxins. Human exposure to the environmental toxin aluminium has been linked, if tentatively, to autism spectrum disorder. Herein we have used transversely heated graphite furnace atomic absorption spectrometry to measure, for the first time, the aluminium content of brain tissue from donors with a diagnosis of autism. We have also used an aluminium-selective fluor to identify aluminium in brain tissue using fluorescence microscopy. The aluminium content of brain tissue in autism was consistently high. The mean (standard deviation) aluminium content across all 5 individuals for each lobe were 3.82(5.42), 2.30(2.00), 2.79(4.05) and 3.82(5.17) $\mu\text{g/g}$ dry wt. for the occipital, frontal, temporal and parietal lobes respectively. These are some of the highest values for aluminium in human brain tissue yet recorded and one has to question why, for example, the aluminium content of the occipital lobe of a 15 year old boy would be 8.74 (11.59) $\mu\text{g/g}$ dry wt.? Aluminium-selective fluorescence microscopy was used to identify aluminium in brain tissue in 10 donors. While aluminium was imaged associated with neurones it appeared to be present intracellularly in microglia-like cells and other inflammatory non-neuronal cells in the meninges, vasculature, grey and white matter. The pre-eminence of intracellular aluminium associated with non-neuronal cells was a standout observation in autism brain tissue and may offer clues as to both the origin of the brain aluminium as well as a putative role in autism spectrum disorder.

• **A2: Hippocampus & frontal lobe, 50-year-old Male**

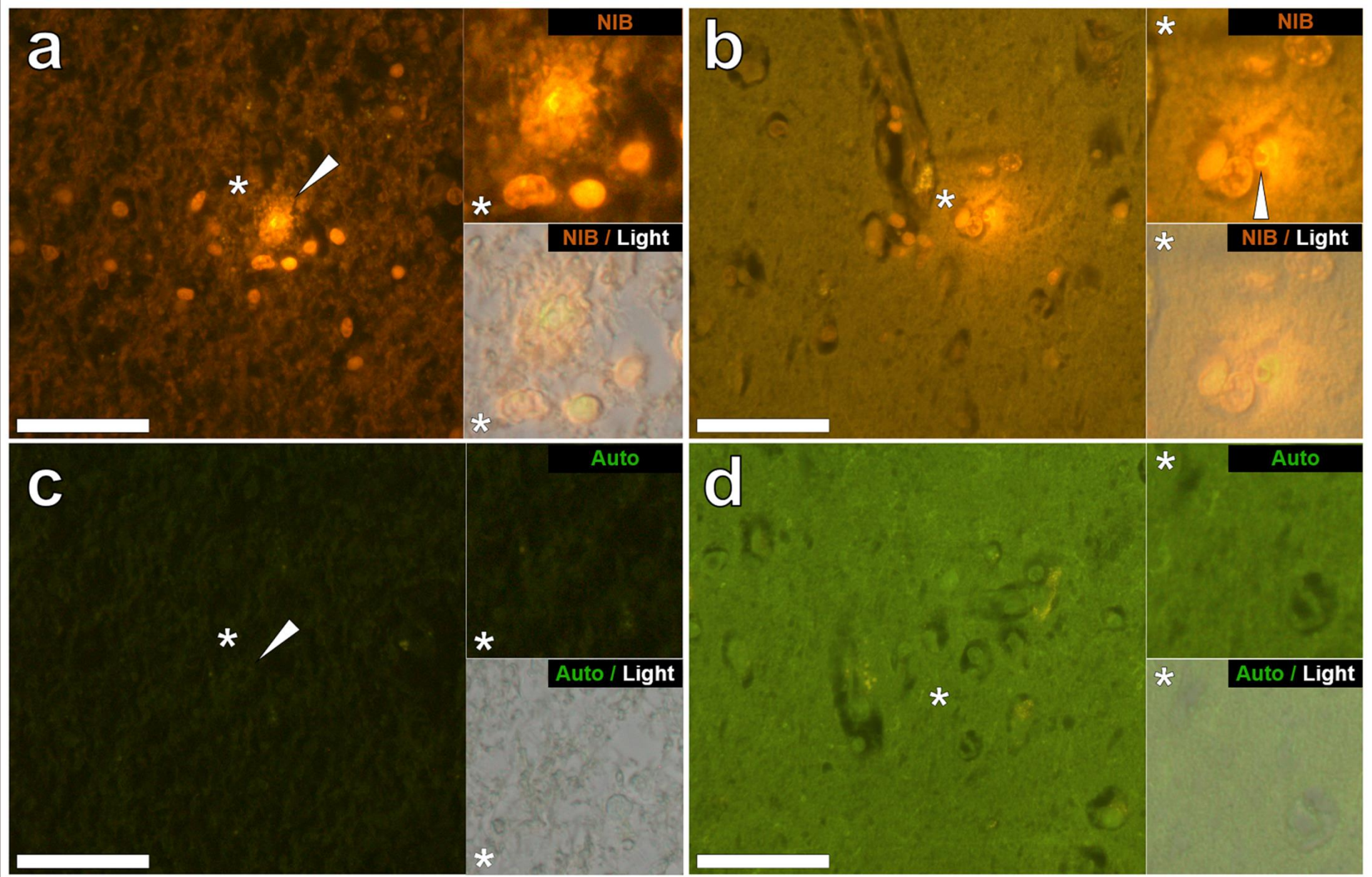


Mononuclear inflammatory cells (lymphocytes) in **leptomeningeal** membranes in the hippocampus (**a & c**) and frontal lobe (**b & d**) of a 50-year-old male donor with autism.



Aluminium in leptomeningeal membranes (50, M)

• **A4: Hippocampus & parietal lobe, 15-year-old Male**



Intracellular aluminium in **glia** in the hippocampus (**a & c**) and a **neuronal** cell in the parietal lobe (**b & d**) of a 15-year-old male donor, diagnosed with autism.



Case Report

Aluminium in Brain Tissue in Epilepsy: A Case Report from Camelford

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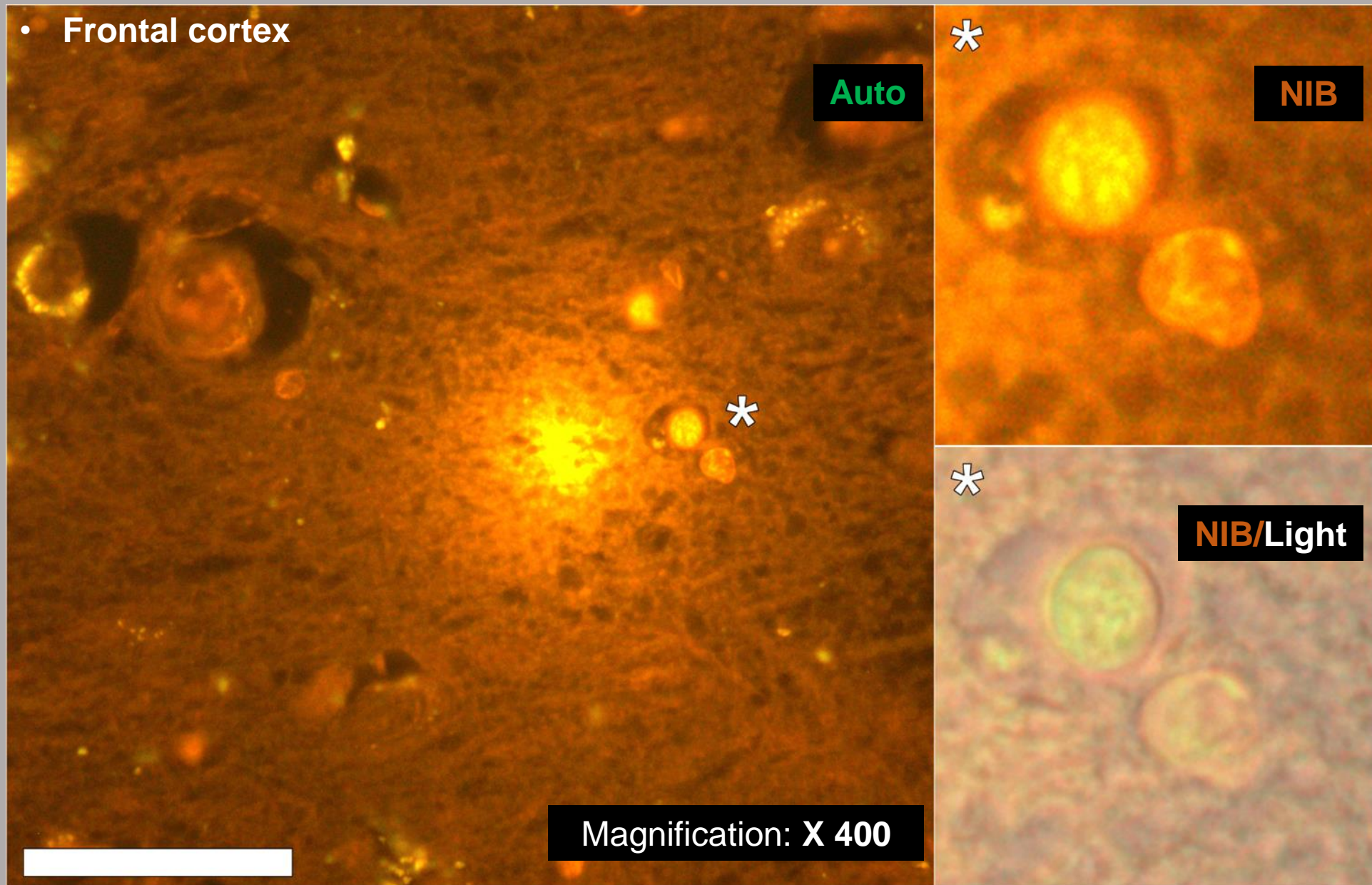
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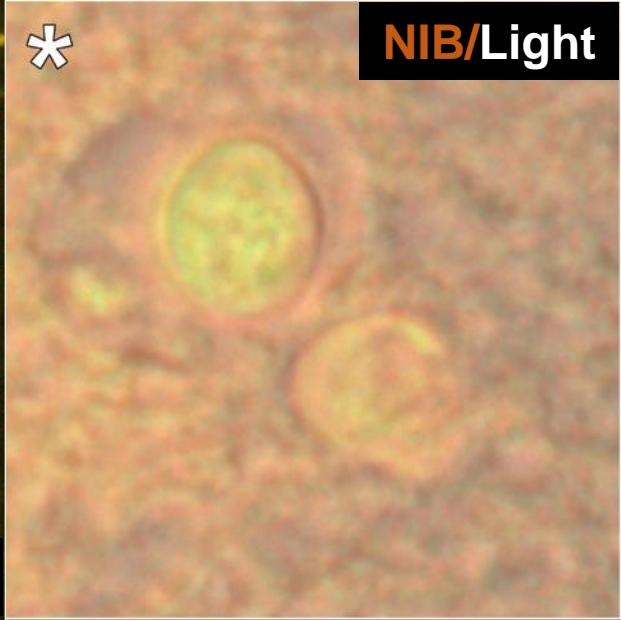
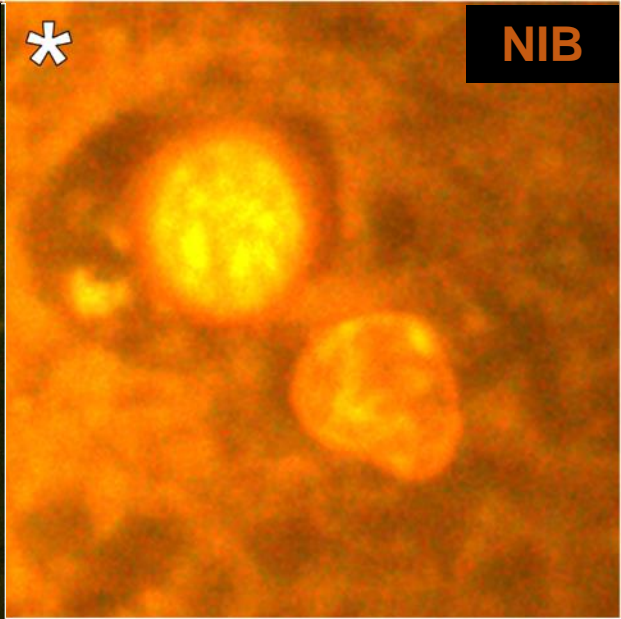
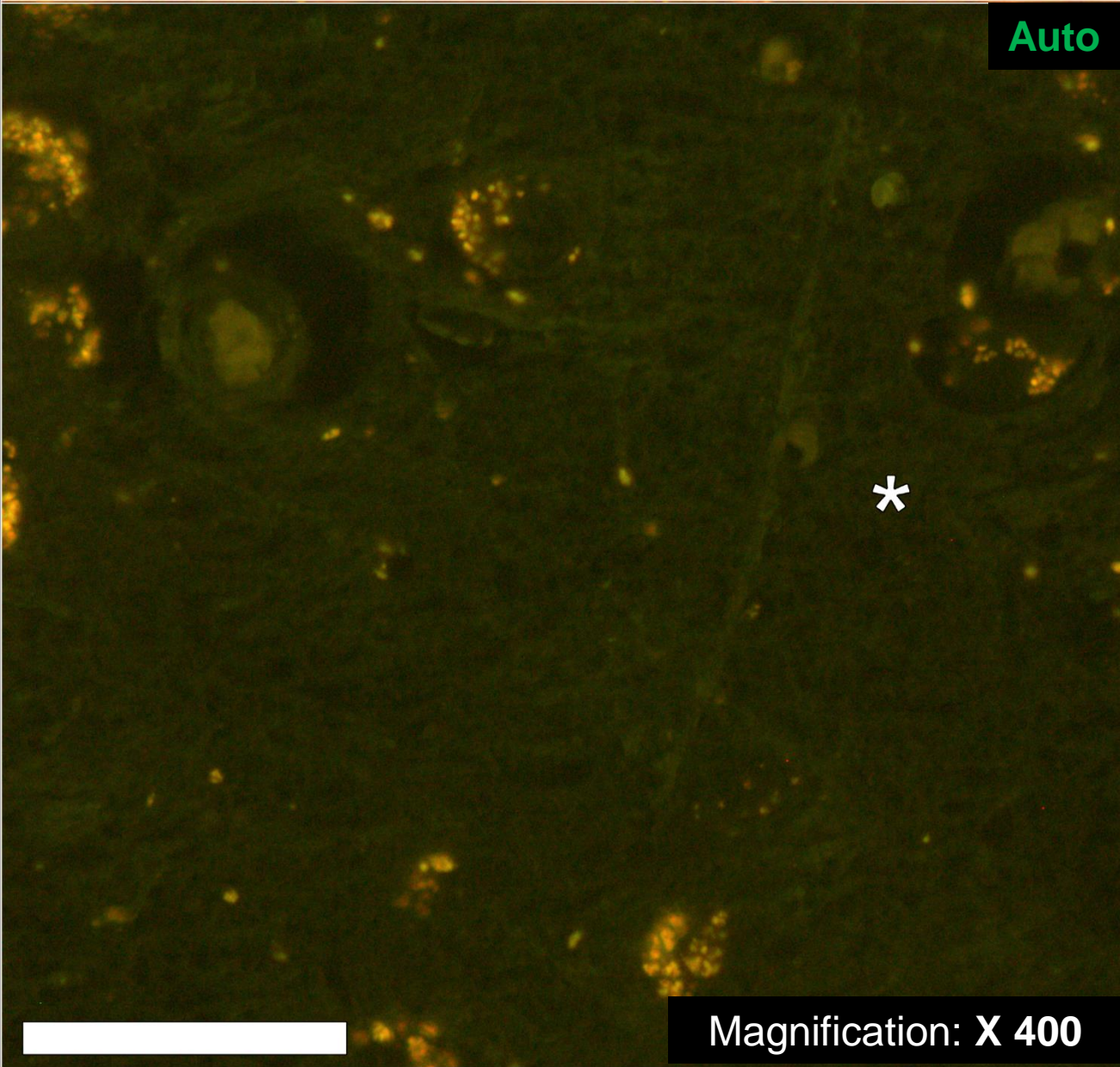
Abstract: (1) Introduction: Human exposure to aluminium is a burgeoning problem. In 1988, the population of the Cornish town of Camelford was exposed to exceedingly high levels of aluminium in their potable water supply. Herein we provide evidence that aluminium played a role in the death of a Camelford resident following development of late-onset epilepsy. (2) Case summary: We have measured the aluminium content of brain tissue in this individual and demonstrated significant accumulations of aluminium in the hippocampus (4.35 (2.80) $\mu\text{g/g}$ dry wt.) and the occipital lobe (2.22 (2.23) $\mu\text{g/g}$ dry wt., mean, SD, $n = 5$), the latter being associated with abnormal calcifications. Aluminium-specific fluorescence microscopy confirmed the presence of aluminium in both of these tissues and made the consistent observation of aluminium-loaded glial cells in close proximity to aluminium-rich cell/neuronal debris. These observations support an inflammatory component in this case of late-onset epilepsy. Congo red failed to identify any amyloid deposits in any tissue while thioflavin S showed extensive extracellular and intracellular tau pathologies. (3) Discussion: We present the first data showing aluminium in brain tissue in epilepsy and suggest, in light of complementary evidence from scientific literature, the first evidence that aluminium played a role in the advent of this case of late-onset adult epilepsy.

Keywords: aluminium in brain tissue; epilepsy; aluminium-specific fluorescence; occipital calcifications; tau pathologies; Camelford in Cornwall

• Frontal cortex



Aluminium-loaded cells in the frontal cortex, morphologically compatible with glia, identified by punctate orange fluorescence, are in close proximity to aluminium-rich extracellular debris



Aluminum and Amyloid- β in Familial Alzheimer's Disease

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and Christopher Exley^{a,*}

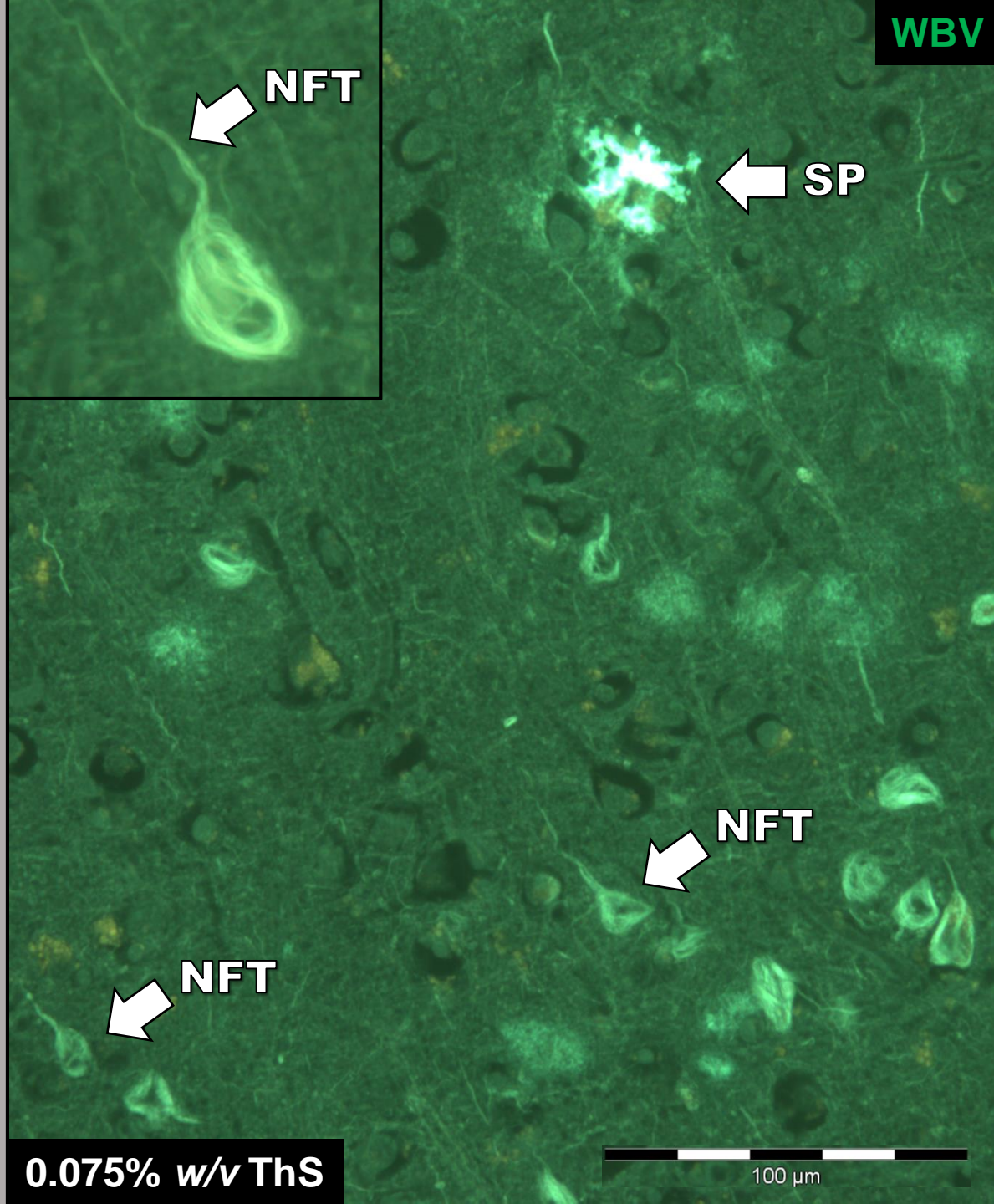
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^b*Institute of Pharmacy/Pharmacognosy, University of Innsbruck, Innsbruck, Austria*

^c*Grupo de Neurociencias de Antioquia, Sede de Investigación Universitaria SIU, Medellín, Colombia*

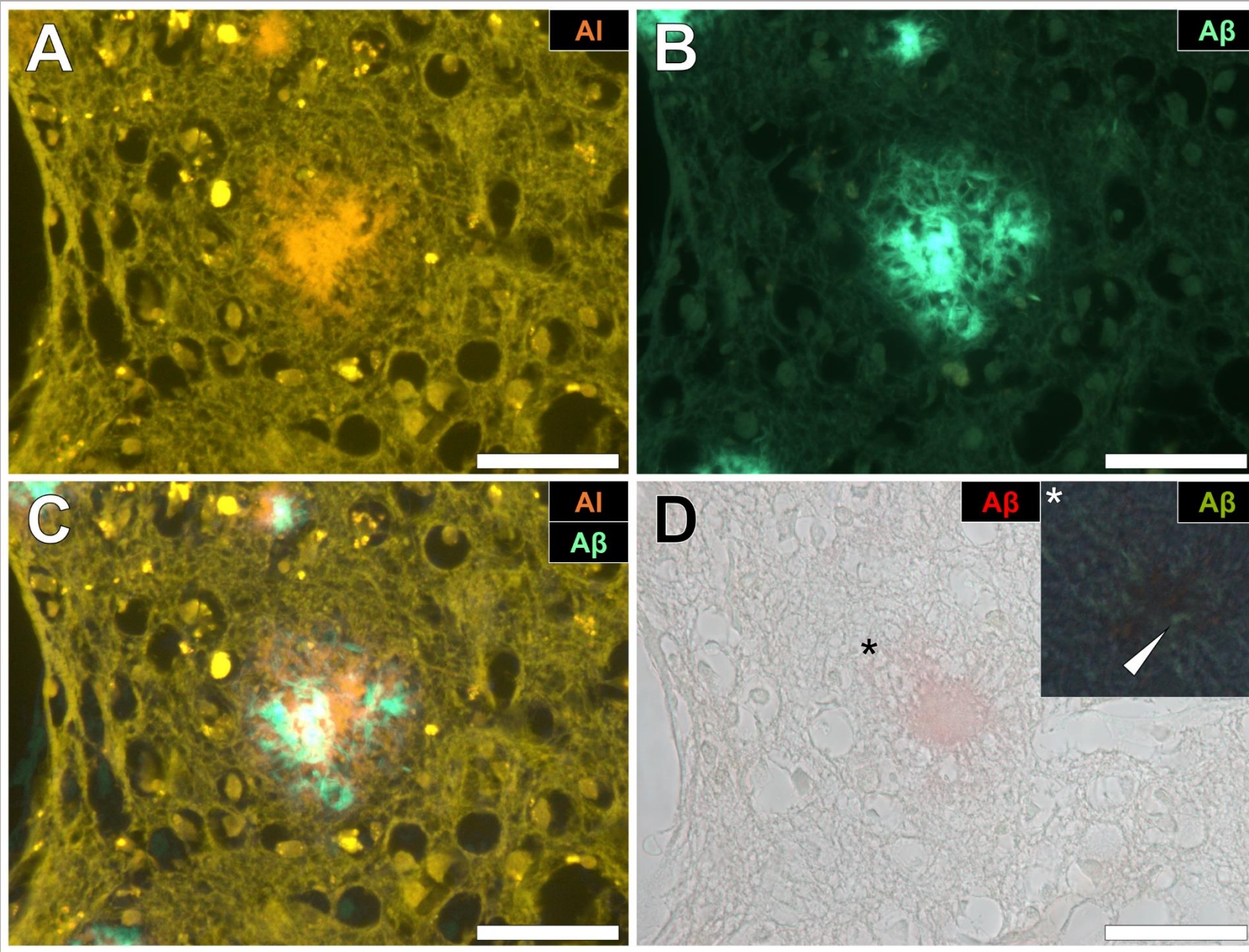
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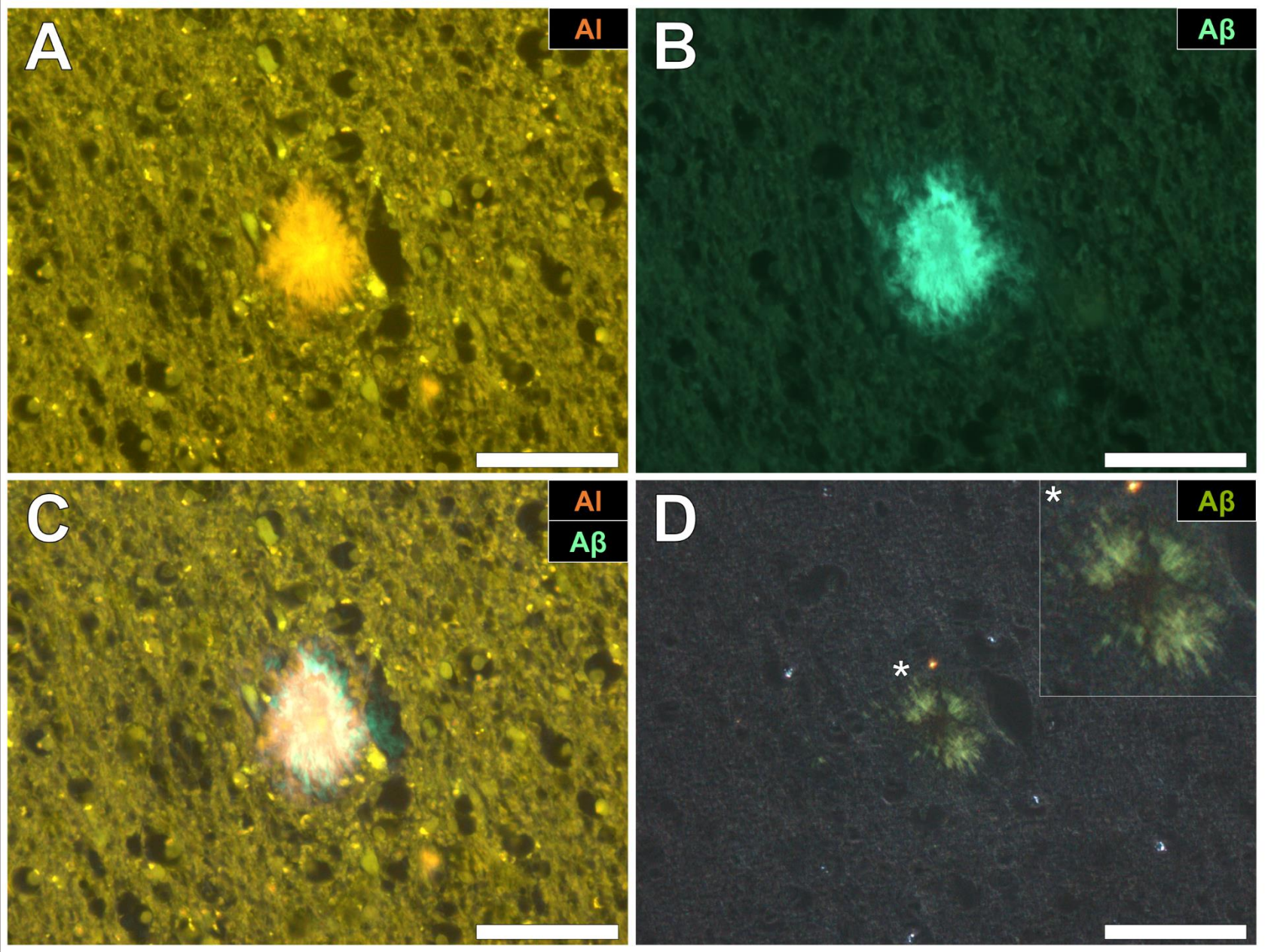
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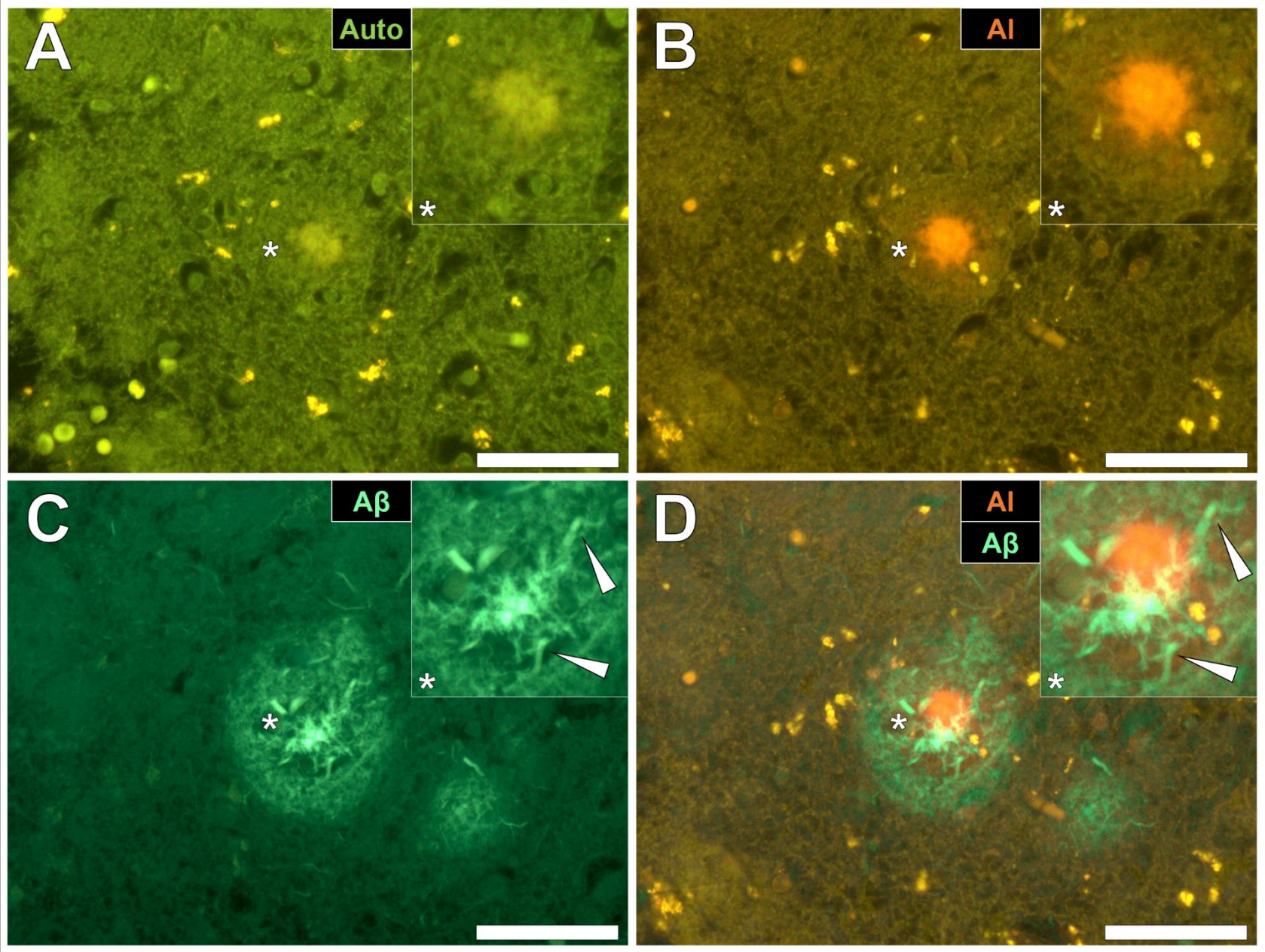


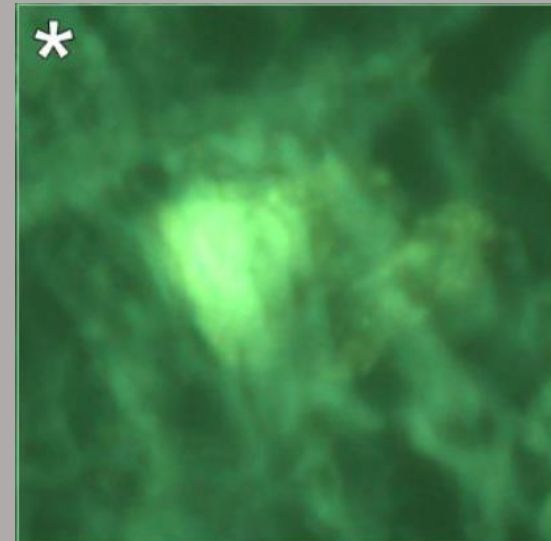
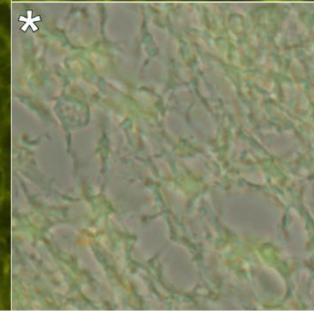
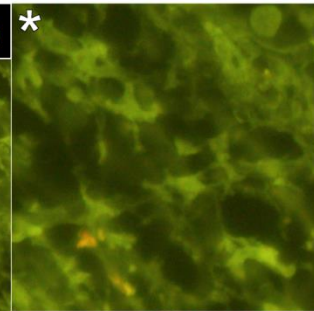
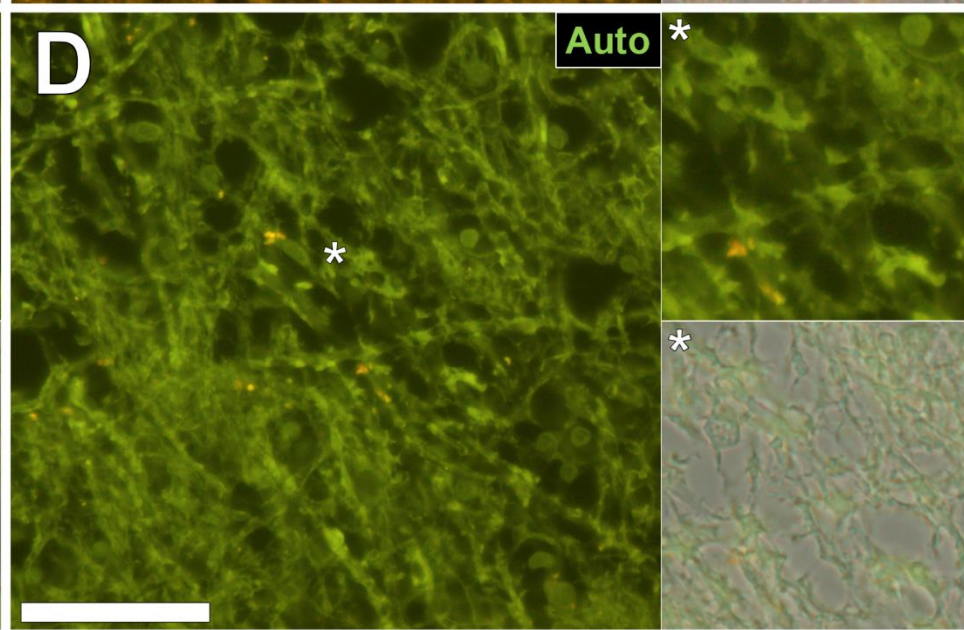
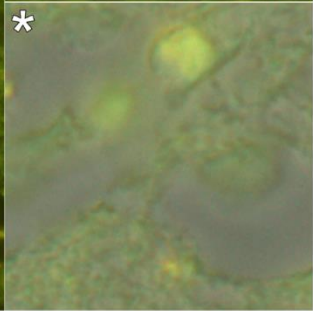
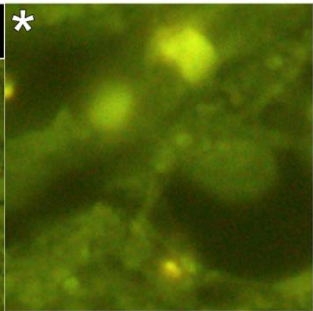
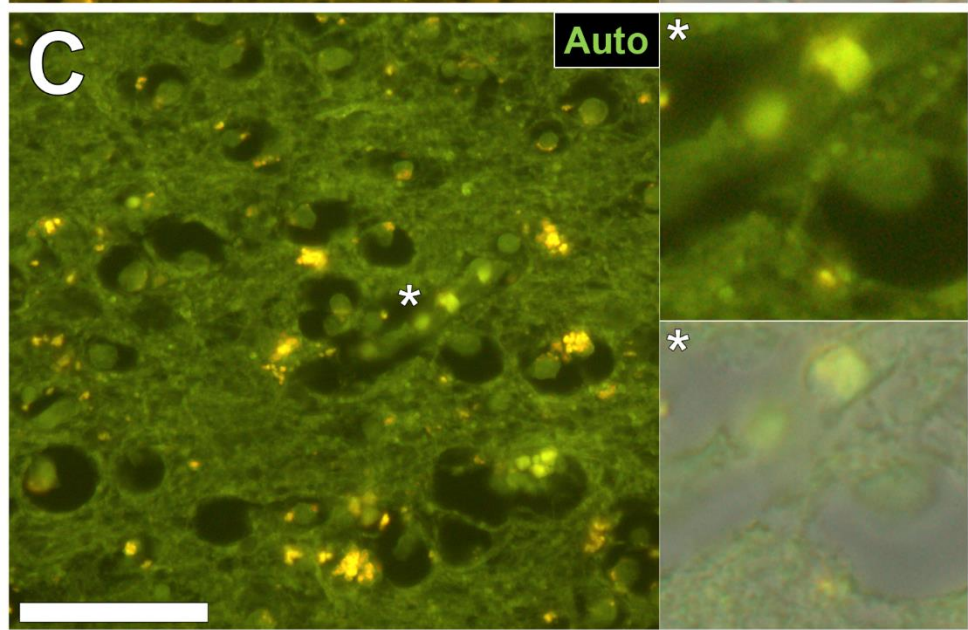
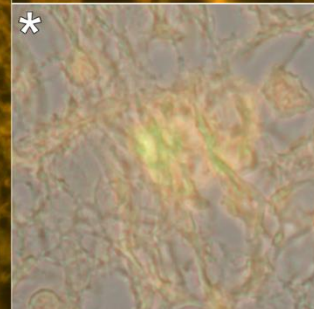
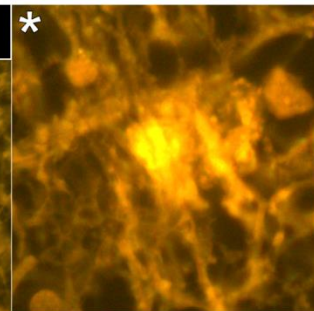
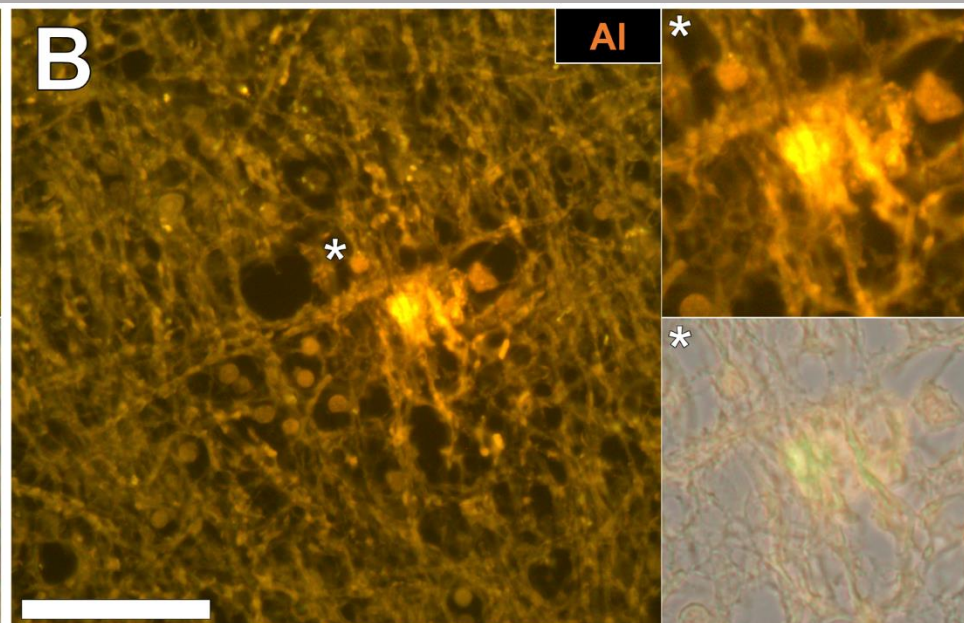
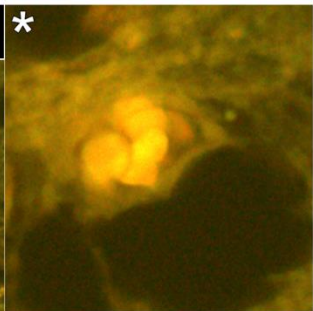
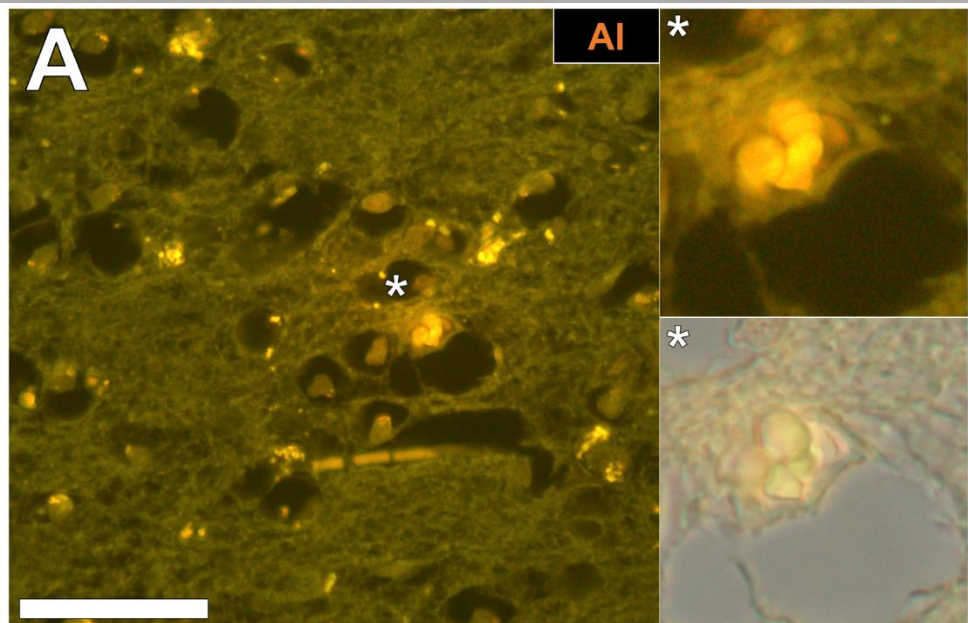
Thioflavin S Staining

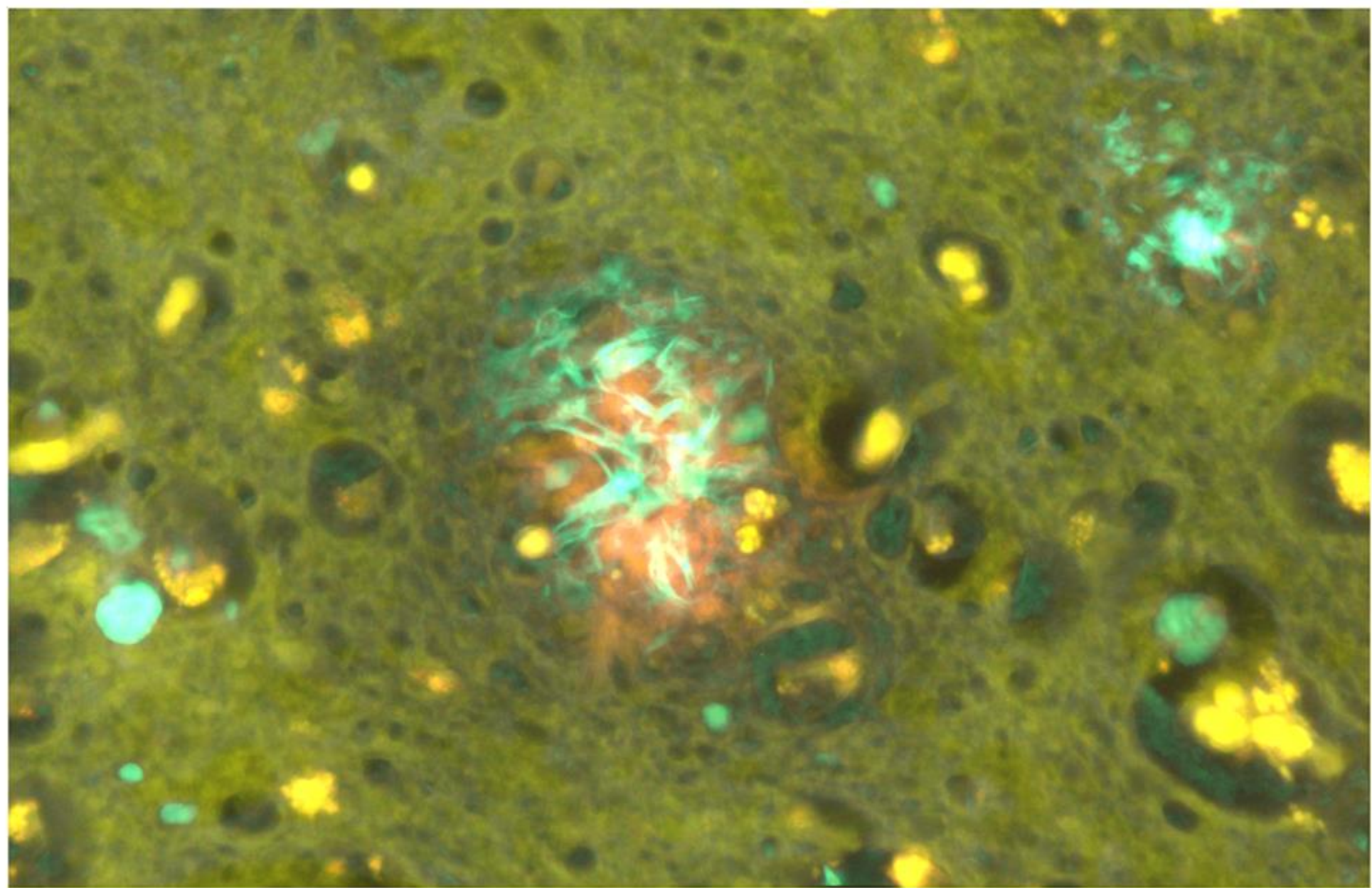
- Colombian donor presenting with *PSEN1 E280A* mutation.
- Early onset / familial Alzheimer's disease (fAD).
- Temporal cortex.
- **Thioflavin S** (ThS) staining reveals senile plaques (**SP**) and neurofibrillary tangles (**NFT**).

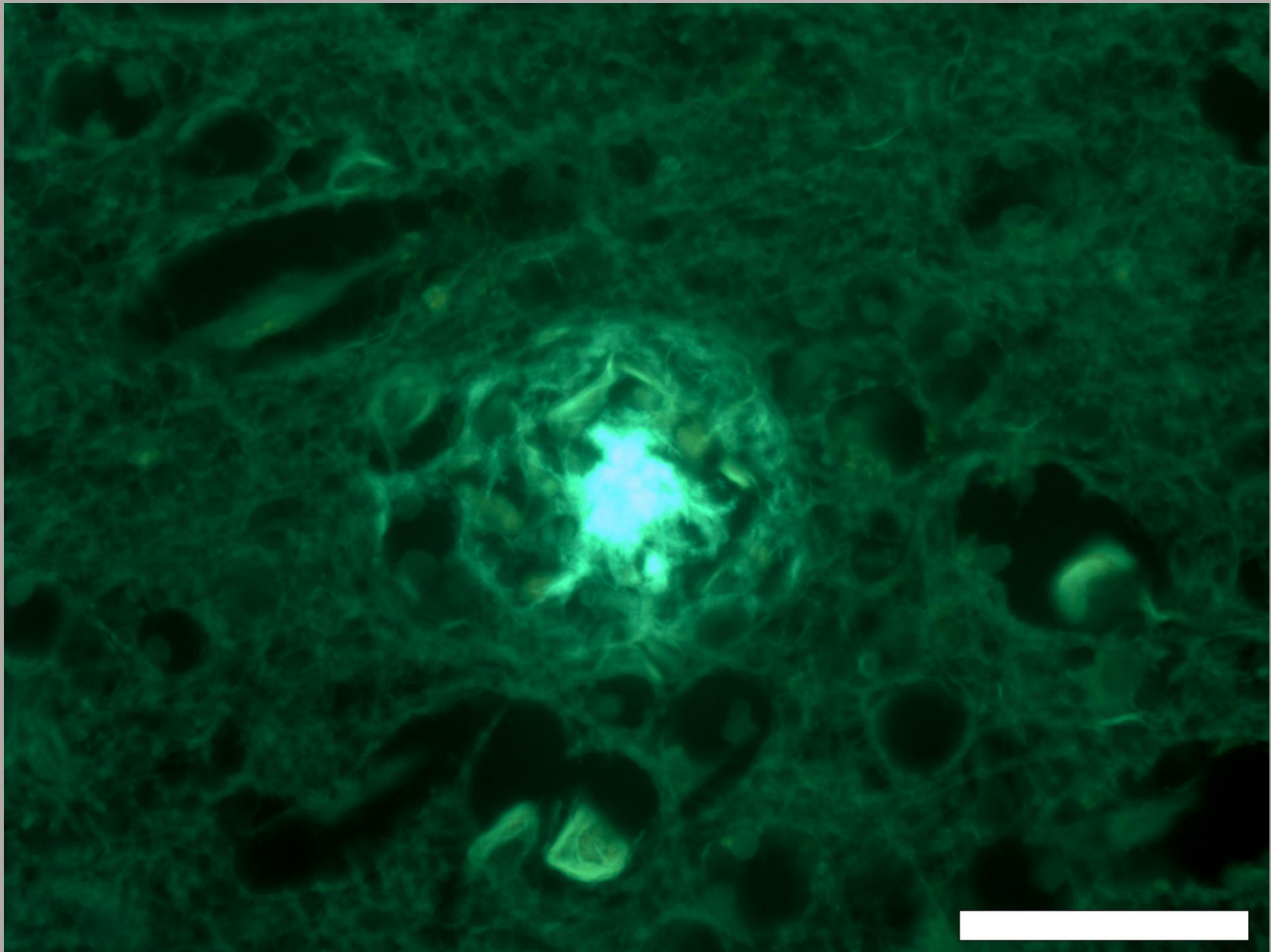


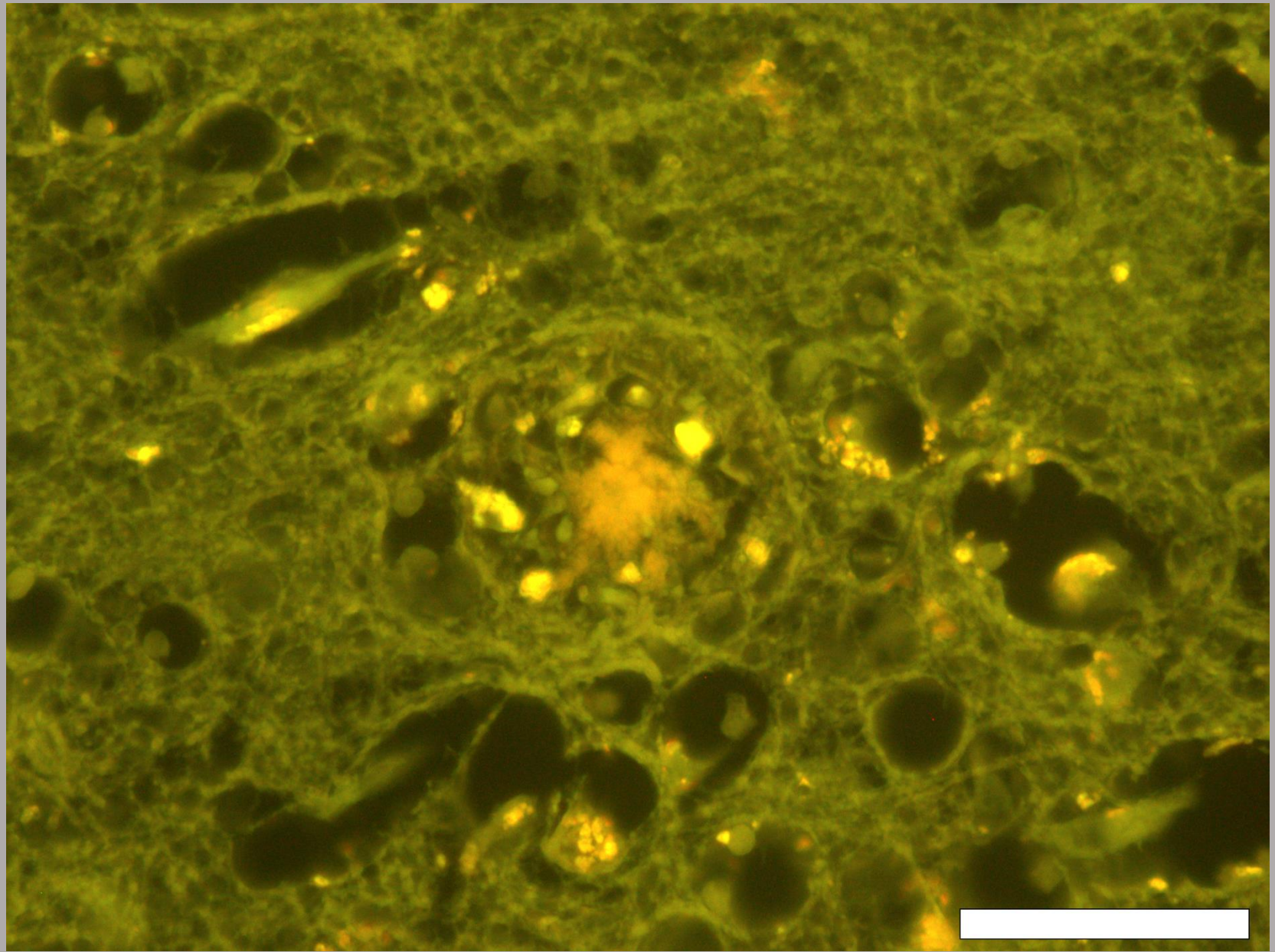


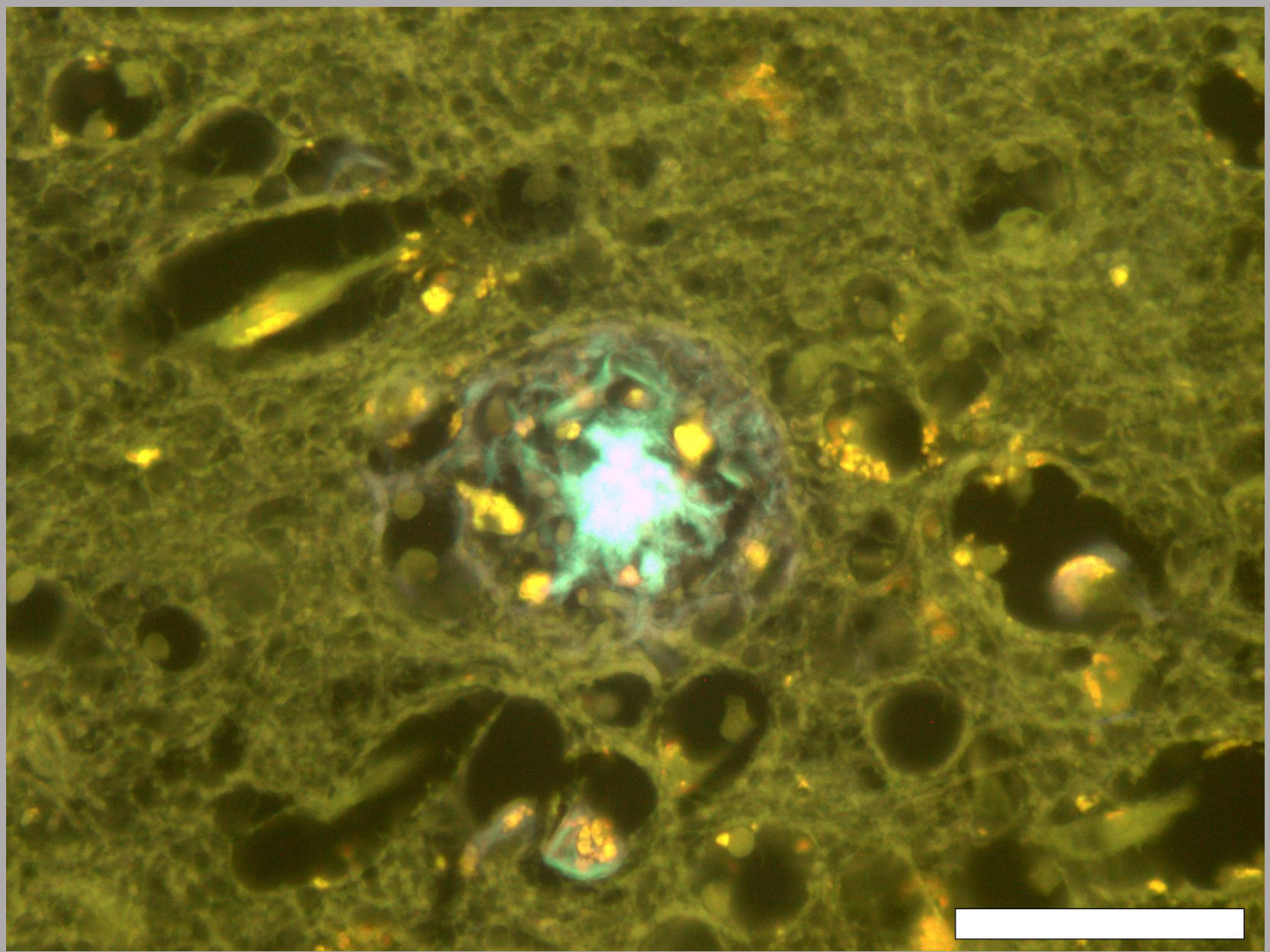












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