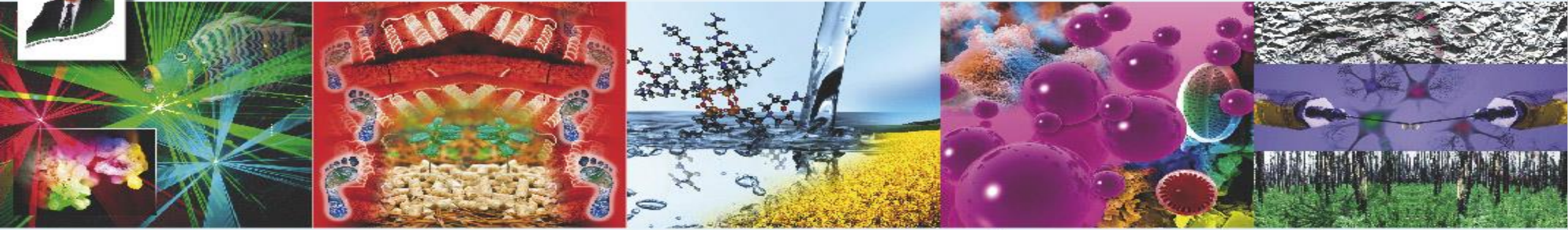




# THE BIRCHALL CENTRE



Innovations in Inorganic and Materials Chemistry

## The Aluminium Age

Christopher Exley PhD FRSB

The Birchall Centre, Lennard-Jones Laboratories, Keele University, Keele,  
Staffordshire, ST5 5BG, UK.

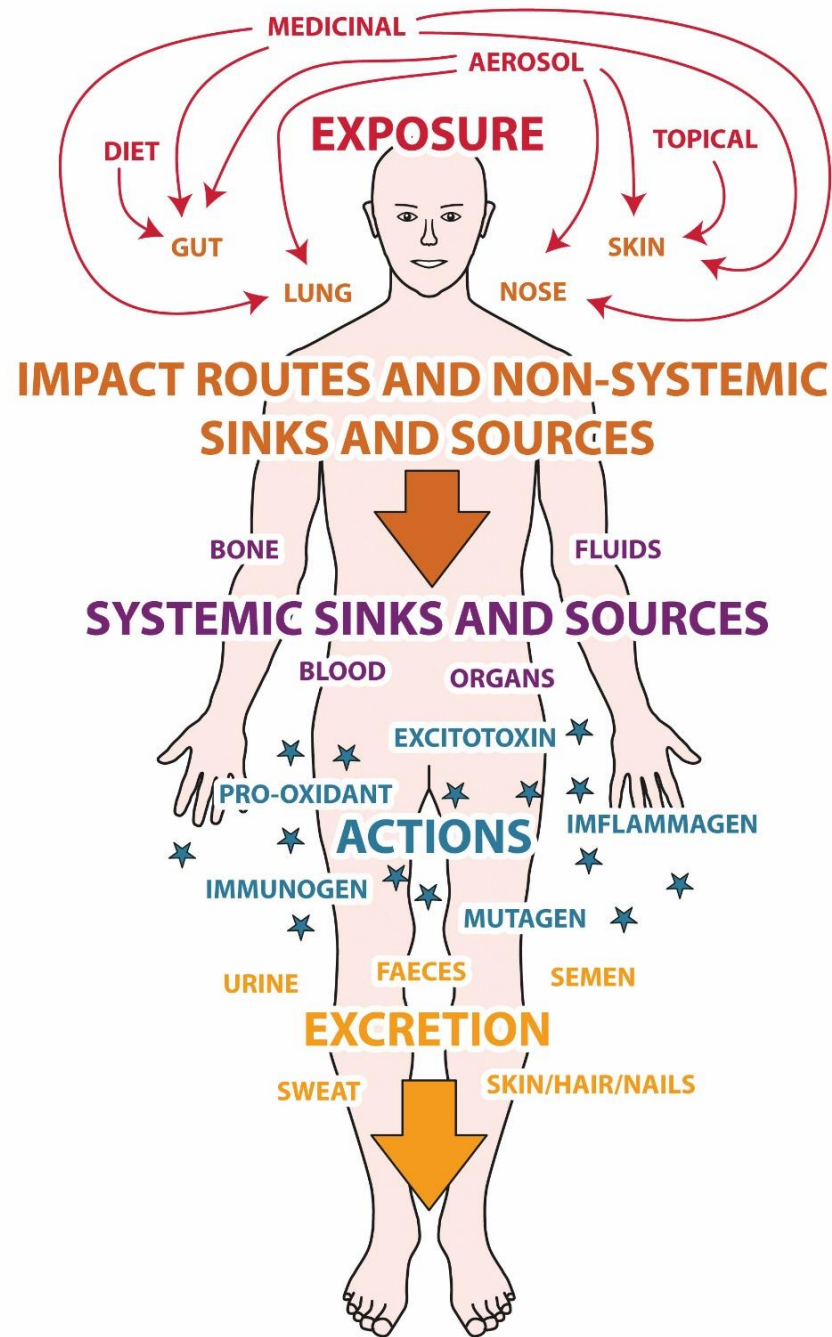
[c.exley@keele.ac.uk](mailto:c.exley@keele.ac.uk)

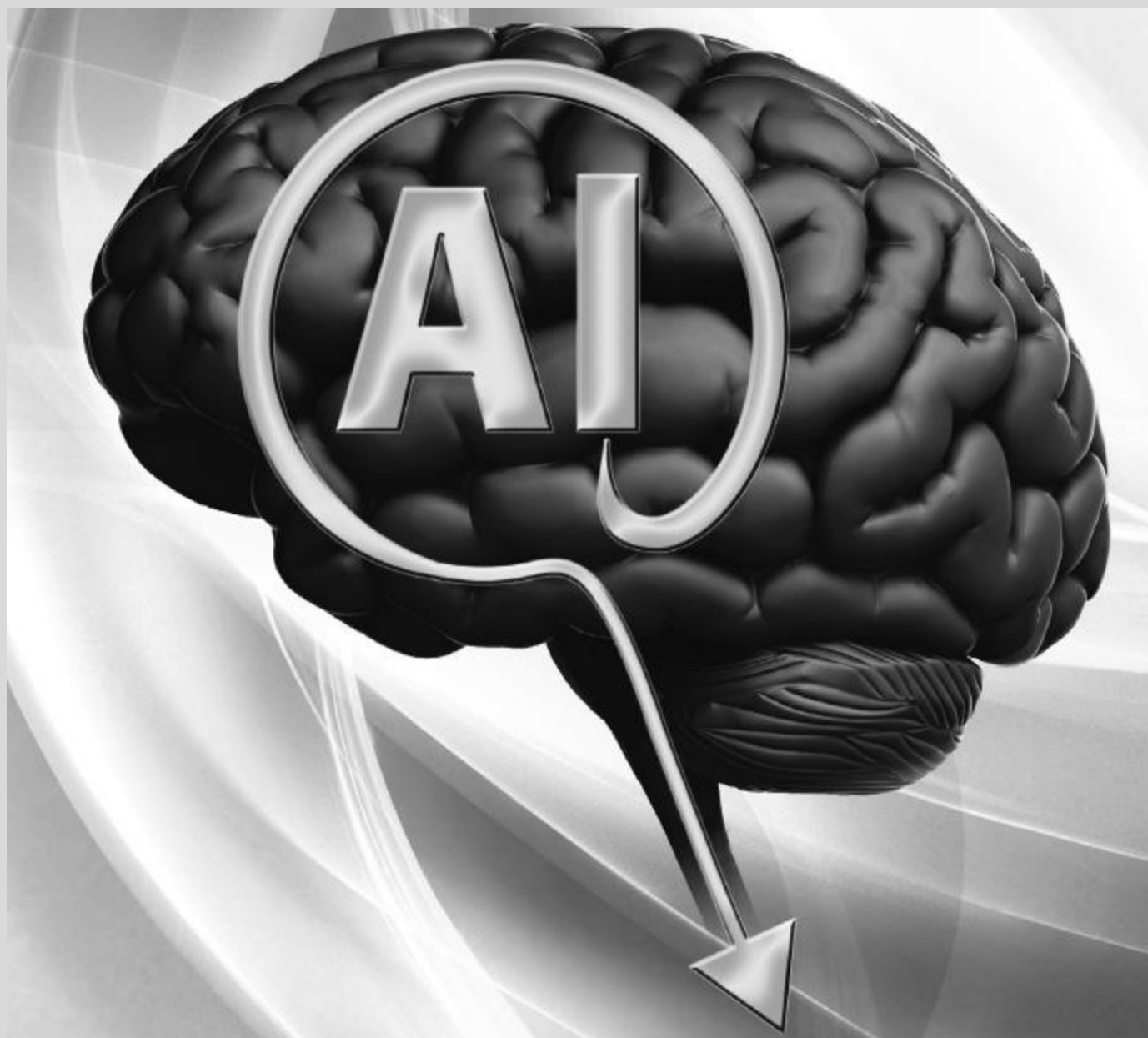
<http://www.keele.ac.uk/aluminium/>

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



<https://pubs.rsc.org/en/content/articlelanding/2013/em/c3em00374d#!divAbstract>





ICNH Dec 9 2018

Cite this: *Metallomics*, 2012, **4**, 56–65

[www.rsc.org/metallomics](http://www.rsc.org/metallomics)

**PAPER**

## **Aluminium, iron and copper in human brain tissues donated to the medical research council's cognitive function and ageing study**

Emily House,<sup>a</sup> Margaret Esiri,<sup>b</sup> Gill Forster,<sup>c</sup> Paul G Ince<sup>c</sup> and Christopher Exley<sup>\*a</sup>

The median Al content of tissues from all **60 brains** (n=713) is 1 µg/g dry wt.

In 52 out of 60 individuals at least one tissue sample exceeded 2 µg Al/g dry wt.

In 41 out of 60 individuals at least one tissue sample exceeded 3.5 µg Al/g dry wt.

Approximately 70% of individuals aged 70 – 103 years had at least one tissue Al content which should be considered as pathological



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

Ambreen Mirza<sup>a</sup>, Andrew King<sup>b,c</sup>, Claire Troakes<sup>c</sup> and Christopher Exley<sup>a,\*</sup>

<sup>a</sup>*The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, UK*

<sup>b</sup>*Department of Clinical Neuropathology, King's College Hospital, London, UK*

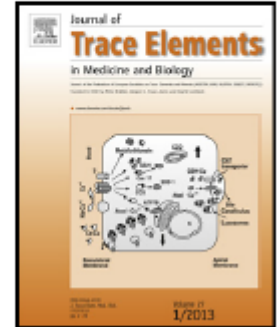
<sup>c</sup>*MRC London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology and Neuroscience, King's College, London, UK*



Contents lists available at ScienceDirect

## Journal of Trace Elements in Medicine and Biology

journal homepage: [www.elsevier.com/locate/jtemb](http://www.elsevier.com/locate/jtemb)



### Toxicology

## Aluminium in brain tissue in familial Alzheimer's disease

Ambreen Mirza<sup>a</sup>, Andrew King<sup>b,c</sup>, Claire Troakes<sup>c</sup>, Christopher Exley<sup>a,\*</sup>

<sup>a</sup> The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom

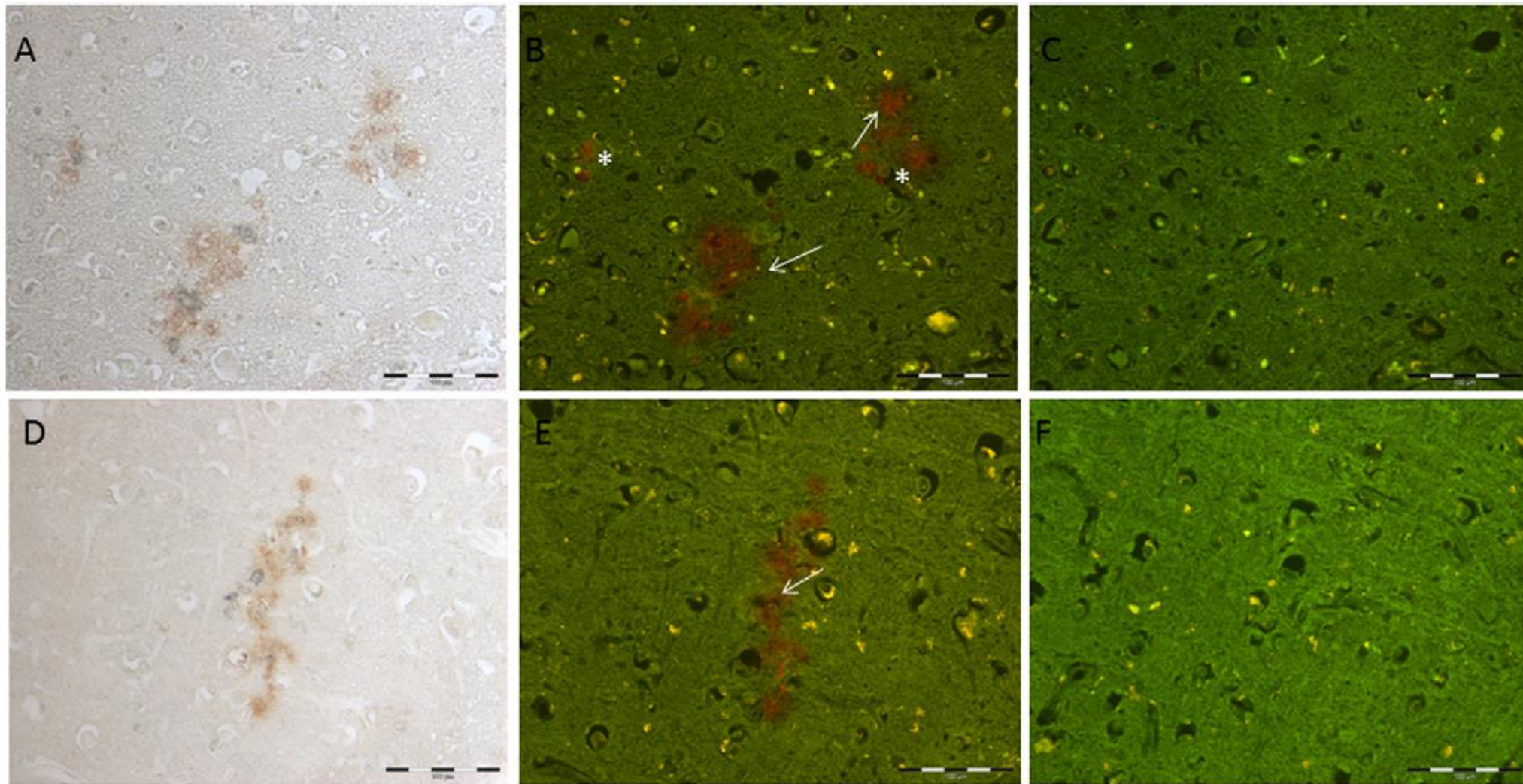
<sup>b</sup> Department Of Clinical Neuropathology, King's College Hospital, London, SE5 9RS, United Kingdom

<sup>c</sup> MRC London Neurodegenerative Diseases Brain Bank, Institute of Psychiatry, Psychology and Neuroscience, King's College, London, SE5 8AF, United Kingdom



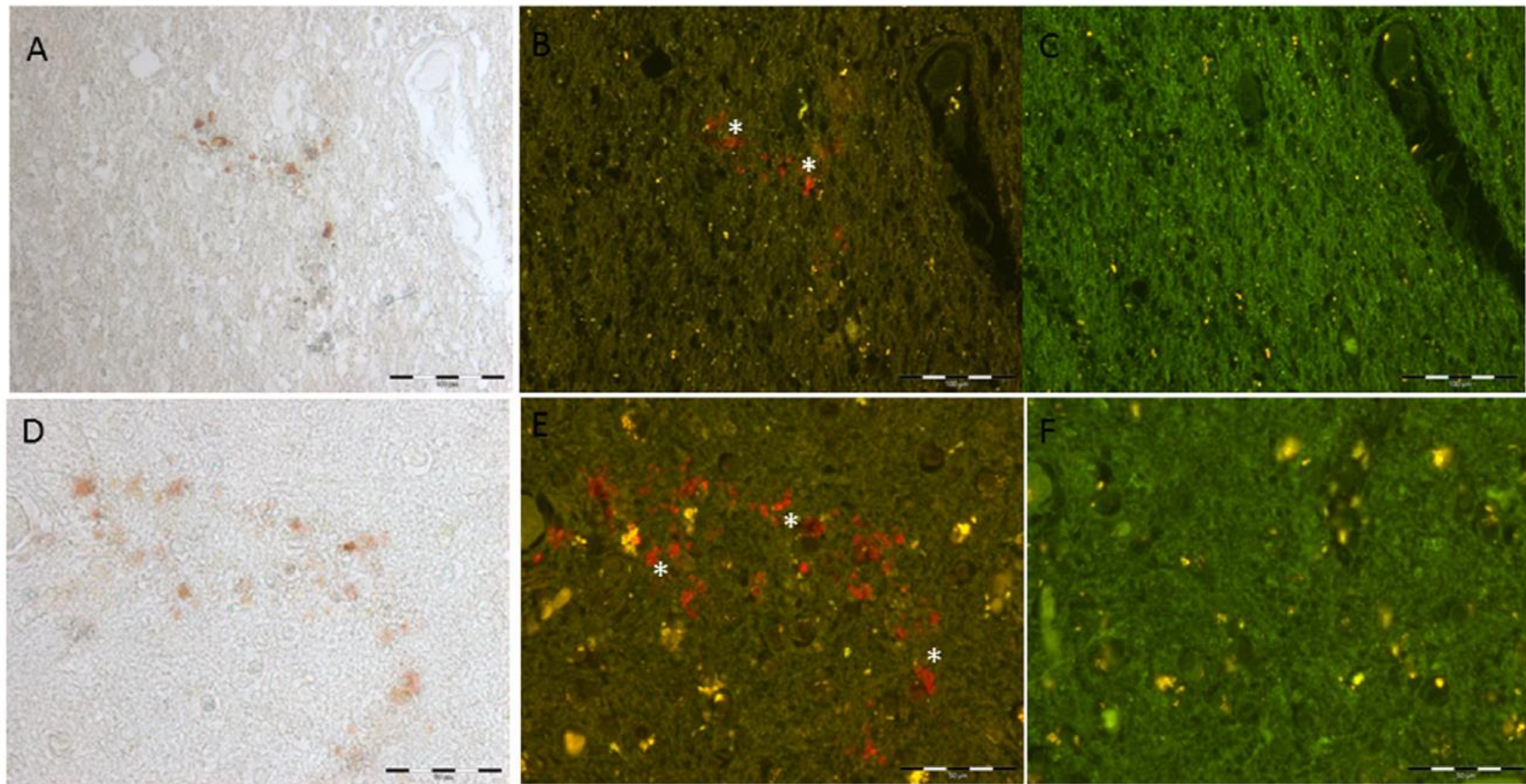
<https://www.sciencedirect.com/science/article/pii/S0946672X16303777?via%3Dihub>





**Fig. 1.** Representative images of aluminium in frontal cortex. Light (A&D) and fluorescence (B&E) microscopy images of lumogallion-stained sections of frontal cortex. Asterisk label suggested intracellular deposits while arrows show diffuse deposits. Fluorescence microscopy of un-stained adjacent tissue sections (C&F) show autofluorescence. Scale bars are all 100  $\mu\text{m}$ .

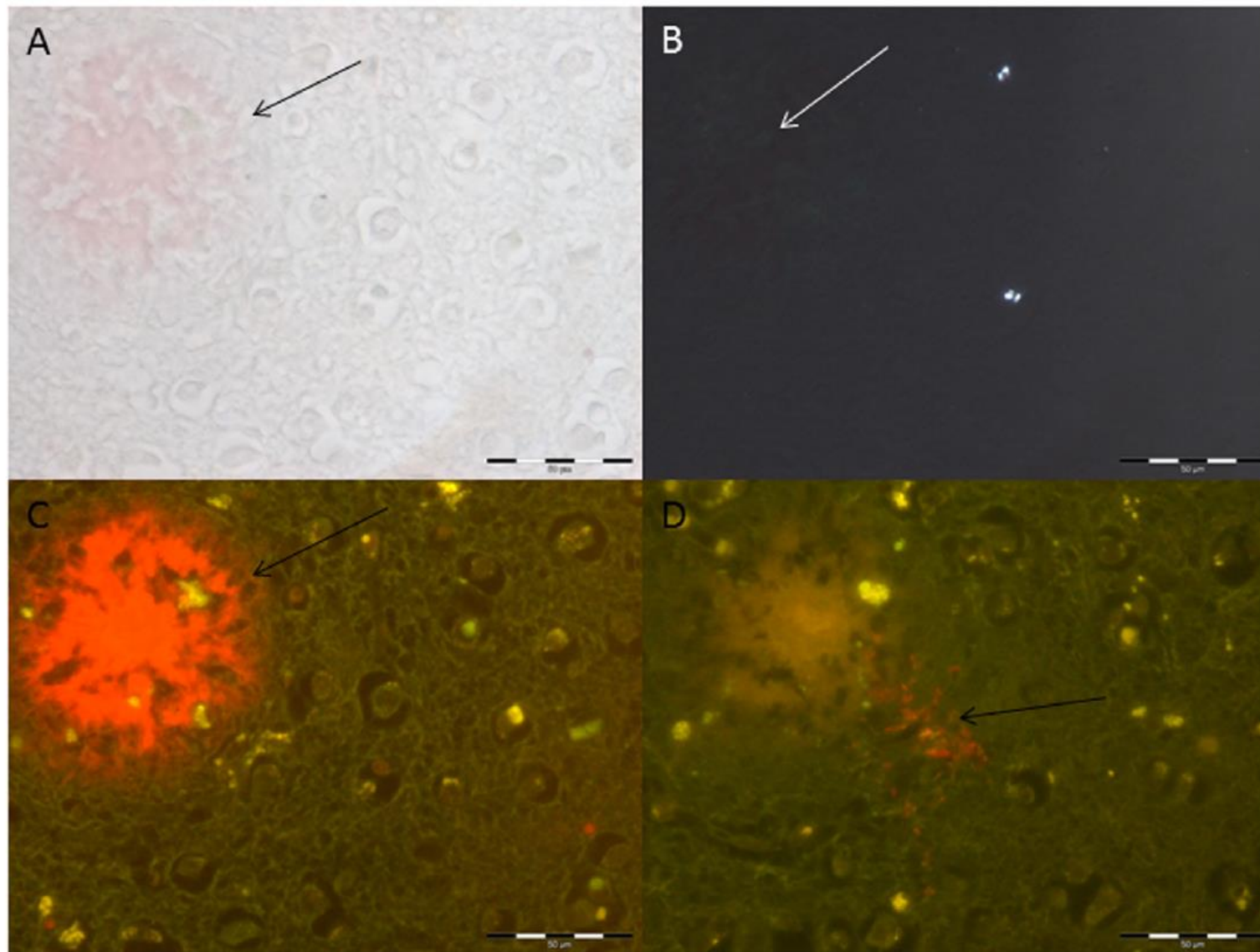




**Fig. 2.** Representative images of aluminium in parietal cortex. Light (A&D) and fluorescence (B&E) microscopy images of lumogallion-stained sections of frontal cortex. Asterisk label suggested intracellular deposits associated with both living and dead cells. Fluorescence microscopy of un-stained adjacent tissue sections (C&F) show autofluorescence. Scale bars are 100  $\mu\text{m}$  (A–C) and 50  $\mu\text{m}$  (D–F).

<https://www.sciencedirect.com/science/article/pii/S0946672X16303777?via%3Dihub>





**Fig. 4.** Co-localisation of amyloid and aluminium in occipital cortex. (A) Light microscopy image of Congo red-stained tissue showing (arrow) senile plaque-like amyloid deposit. (B) Polarising microscopy image of Congo red-stained image showing (arrow) apple-green birefringence characteristic of amyloid in  $\beta$  sheet conformation. (C) Fluorescence microscopy image of Congo red-stained tissue showing (arrow) senile plaque-like amyloid deposit. (D) Fluorescence microscopy image of adjacent section of tissue stained with lumogallion and showing (arrow) significant deposits of aluminium. Scale bars are all 50  $\mu$ m.

<https://www.sciencedirect.com/science/article/pii/S0946672X16303777?via%3Dihub>





International Journal of  
*Environmental Research  
and Public Health*

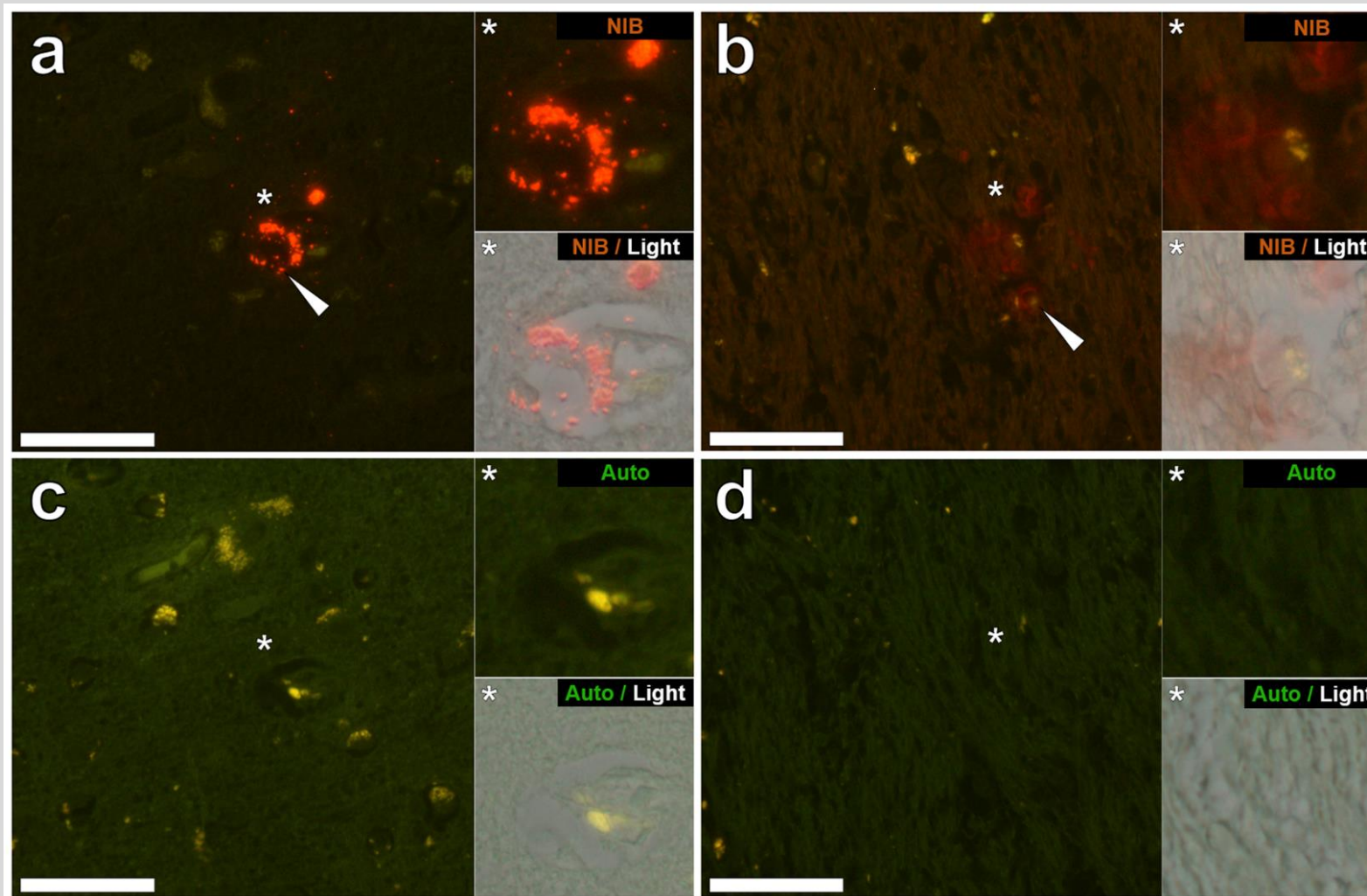


*Article*

# Aluminium in Brain Tissue in Multiple Sclerosis

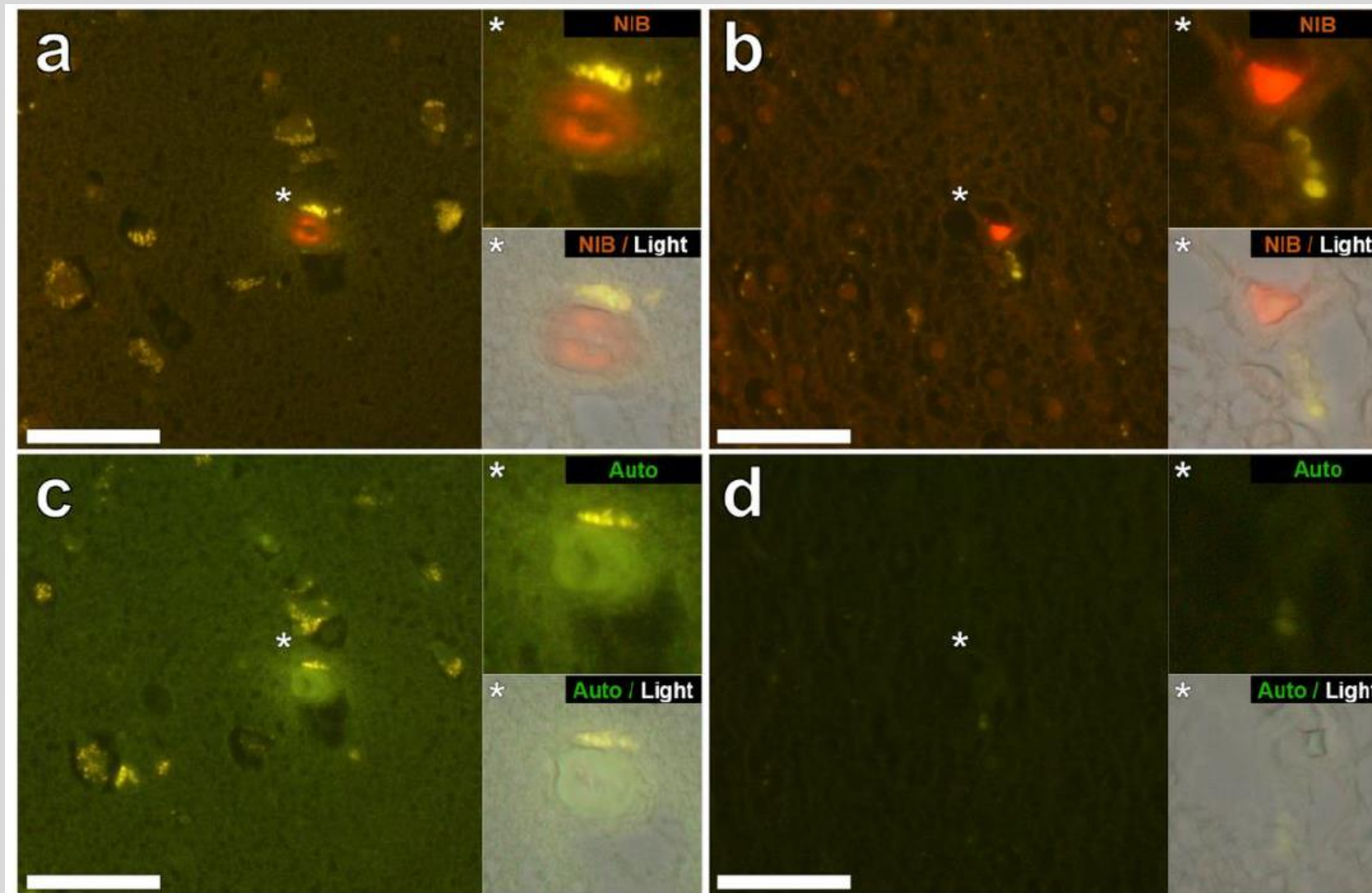
Matthew Mold <sup>1</sup> , Agata Chmielecka <sup>2</sup>, Maria Raquel Ramirez Rodriguez <sup>1</sup>, Femia Thom <sup>2</sup>,  
Caroline Linhart <sup>3</sup>, Andrew King <sup>4</sup> and Christopher Exley <sup>1,\*</sup> 

<https://www.mdpi.com/1660-4601/15/8/1777>



**Figure 1.** Extracellular aluminium in the frontal lobe and hippocampus of a 56-year-old male donor (MS274), diagnosed with RRMS. (a) Intense orange fluorescence (white arrow) indicating punctate deposits of aluminium was observed in the perivascular region of a small blood vessel in the white matter of the frontal lobe, in close proximity to lipofuscin, identified by yellow fluorescence. (b) Extracellular deposits of aluminium, identified as diffuse orange-red fluorescence, appear co-deposited with lipofuscin (white arrow) in white matter adjacent to the parahippocampal gyrus. (c,d) Autofluorescence of serial sections confirms the identity of aluminium in (a,b) respectively. Upper and lower panels depict magnified inserts of the fluorescence channel and bright field overlay. Magnification x400, scale bar 50  $\mu\text{m}$ .

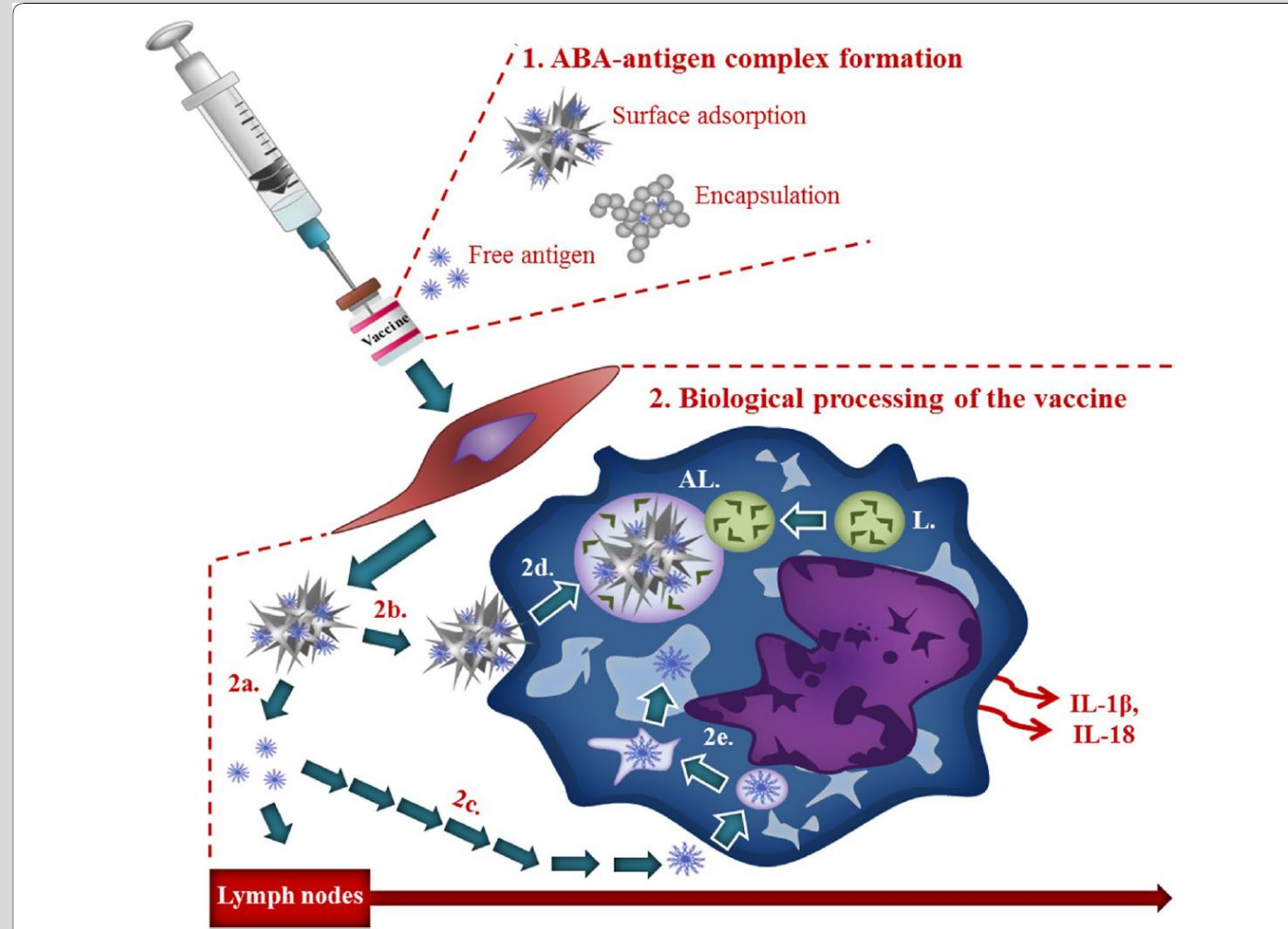




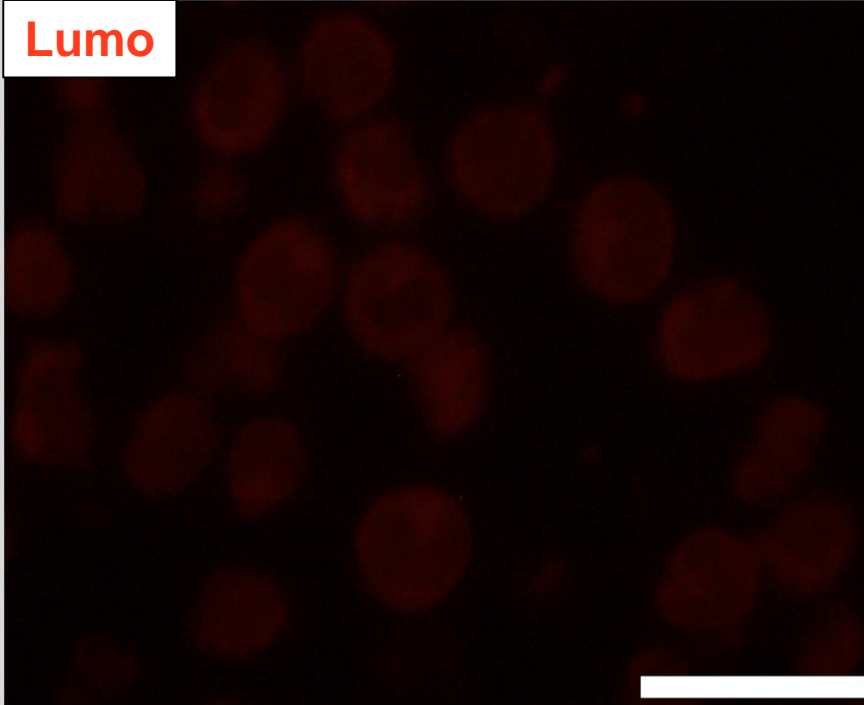
**Figure 3.** Aluminium in the frontal lobe and hippocampus of a 48-year-old female donor (MS317), diagnosed with SPMS. **(a)** Intense orange aluminium fluorescence was identified in refractile corpora amylacea (or mineralised deposits) in the frontal cortex grey matter). **(b)** Intracellular aluminium was also observed in occasional glial-like cells in the parahippocampal gyrus (white matter). Autofluorescence of serial sections **(c,d)** confirms the identity of aluminium in **(a,b)** respectively. Upper and lower panels depict magnified inserts of the fluorescence channel and bright field overlay. Magnification x400, scale bars: 50  $\mu$ m.

# What About the Cellular Response to Aluminium Adjuvants?

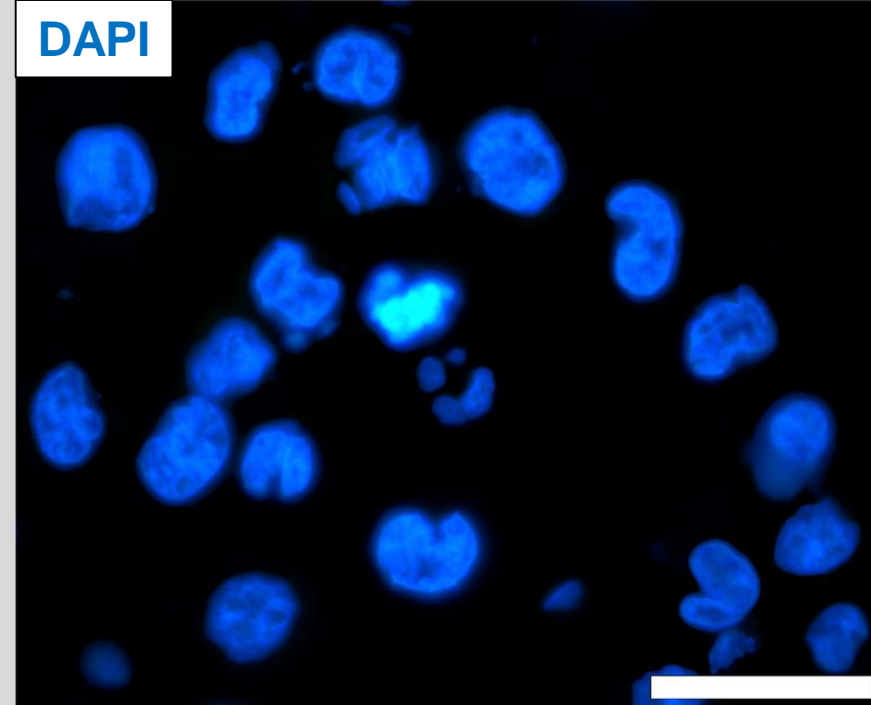
<https://aacijournal.biomedcentral.com/articles/10.1186/s13223-018-0305-2>



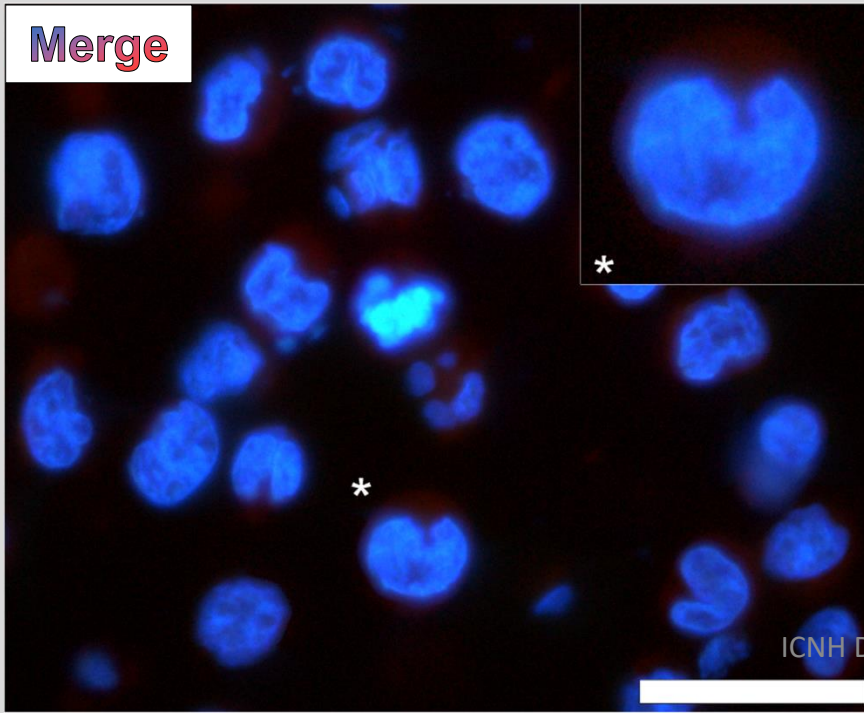
Lumo



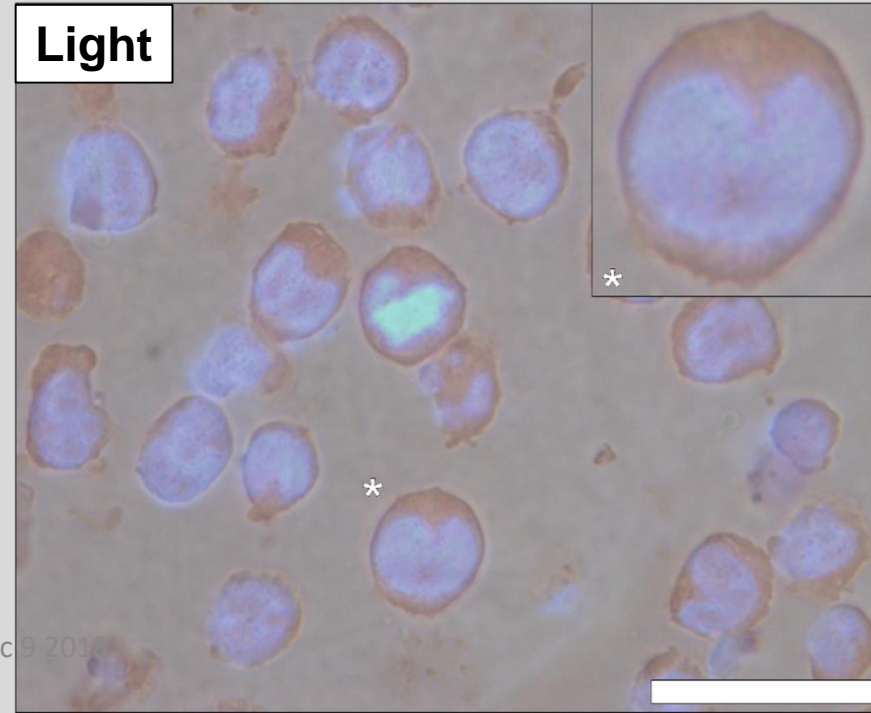
DAPI



Merge

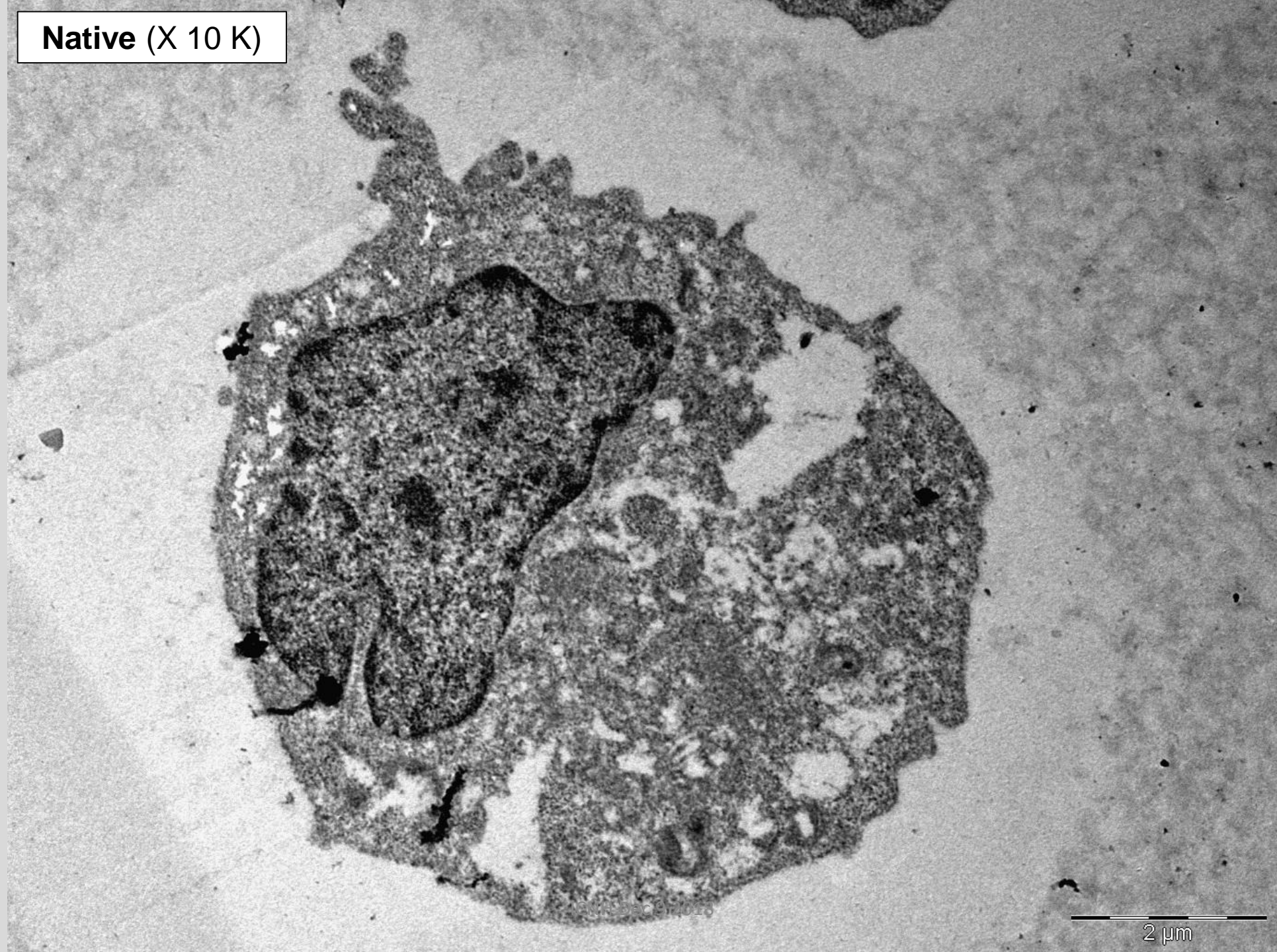


Light





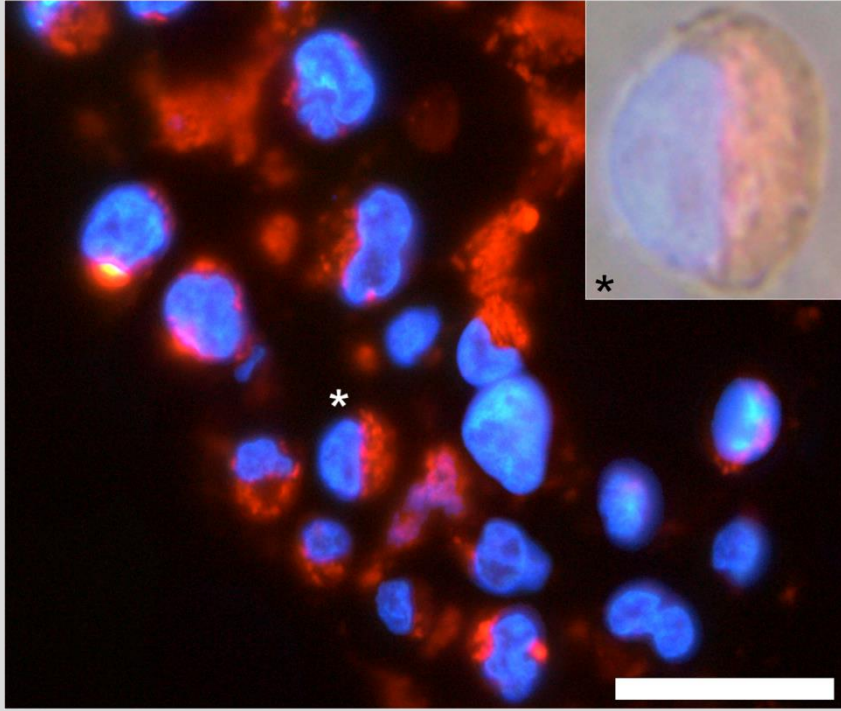
**Native (X 10 K)**



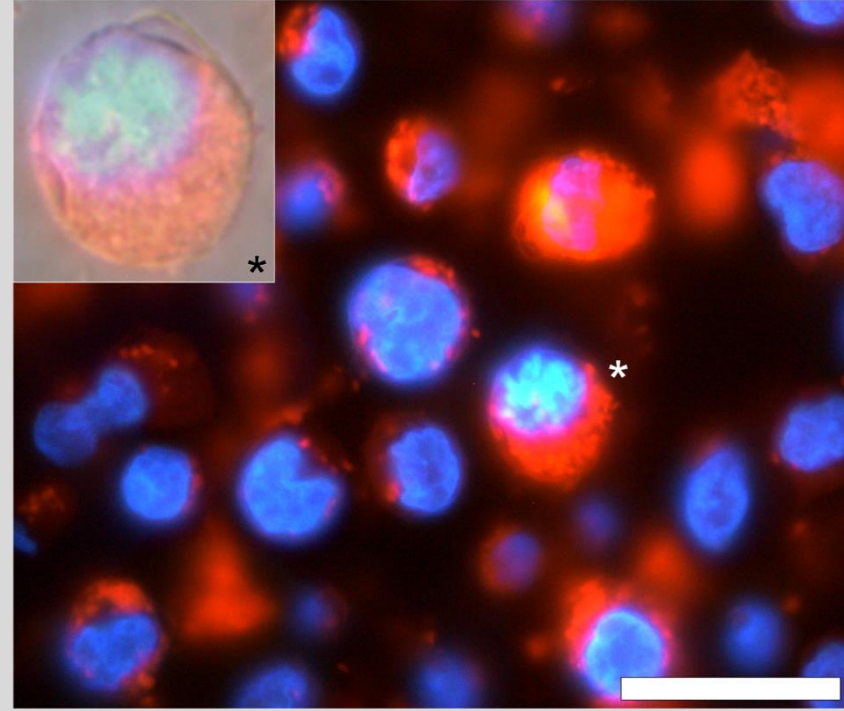
**Alhydrogel®**

***2.5 - 100  $\mu\text{g/mL}$***

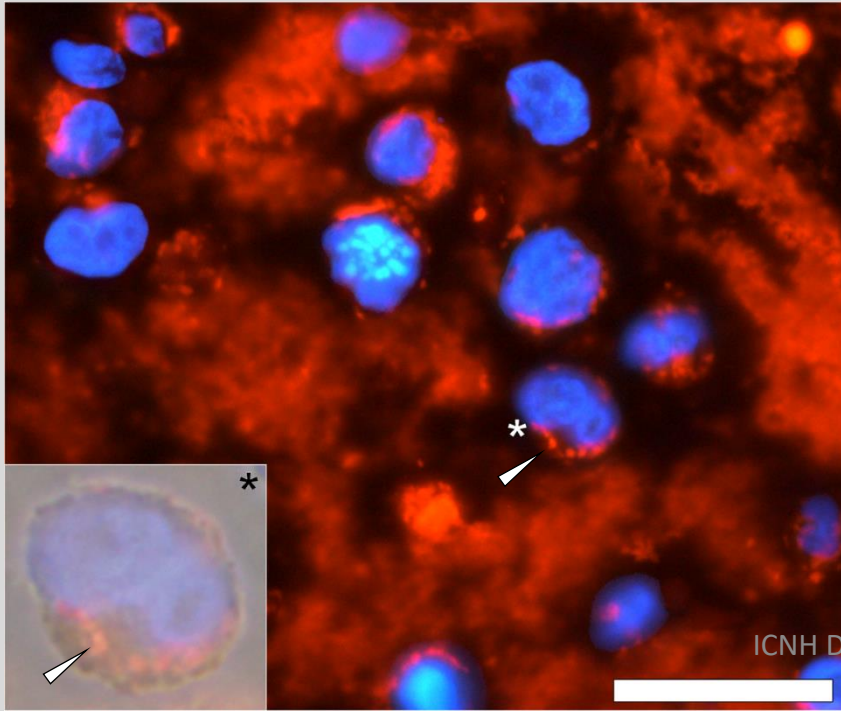
2.5 $\mu$ g/mL



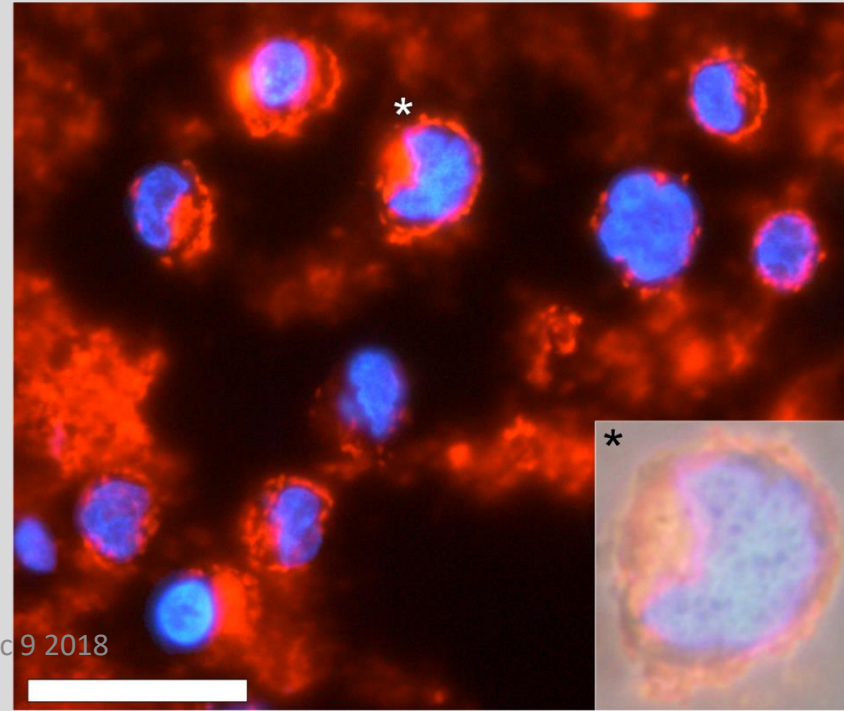
25 $\mu$ g/mL



50 $\mu$ g/mL



100 $\mu$ g/mL





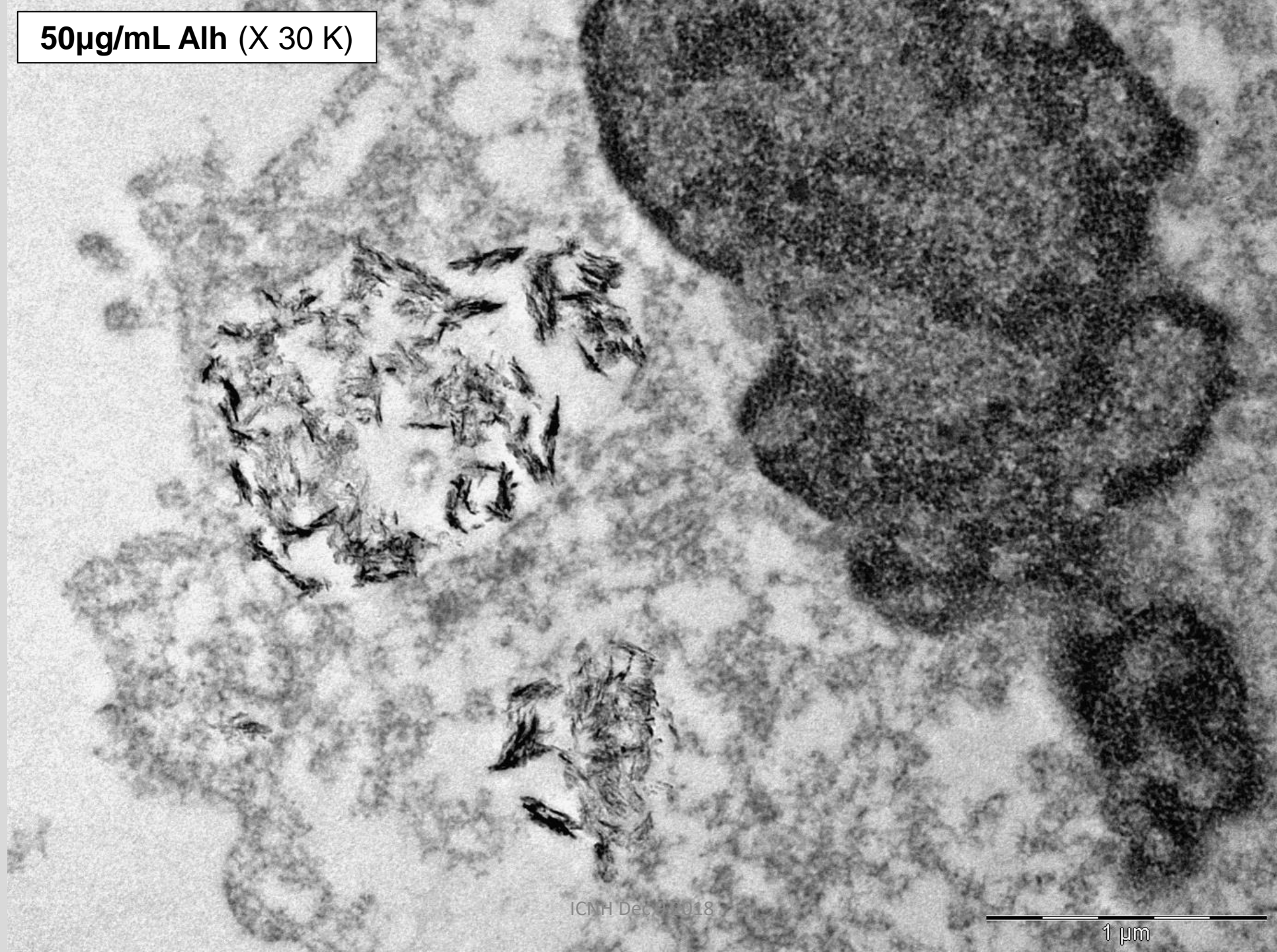
50 $\mu$ g/mL Alh (X 8 K)



ICNH Dec 9 2018

5  $\mu$ m

50 $\mu$ g/mL Alh (X 30 K)



ICMH Dec 4, 2018

1  $\mu$ m

# Serious Adverse Events?

Original Article

## Granulomas Following Subcutaneous Injection With Aluminum Adjuvant-Containing Products in Sheep

Veterinary Pathology

1-11

© The Author(s) 2018



Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/0300985818809142

journals.sagepub.com/home/vet



Javier Asín<sup>1</sup>, Jéssica Molín<sup>1</sup>, Marta Pérez<sup>2</sup>, Pedro Pinczowski<sup>1</sup>,  
Marina Gimeno<sup>1</sup>, Nuria Navascués<sup>3</sup>, Ana Muniesa<sup>1</sup>,  
Ignacio de Blas<sup>1</sup>, Delia Lacasta<sup>1</sup>, Antonio Fernández<sup>1</sup>,  
Lorena de Pablo<sup>4</sup>, Matthew Mold<sup>5</sup> , Christopher Exley<sup>5</sup>,  
Damián de Andrés<sup>4</sup>, Ramsés Reina<sup>4</sup>, and Lluís Luján<sup>1</sup> 

<http://journals.sagepub.com/doi/10.1177/0300985818809142>



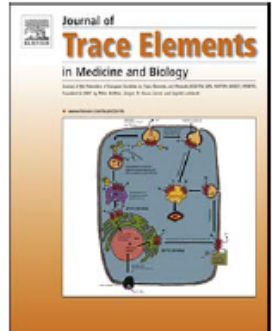
New and important research on sheep and recently published in the journal Veterinary Pathology now provides direct evidence of the fate of aluminium adjuvants following sub-cutaneous injection. The research confirms the **accumulation of aluminium adjuvant in lymph glands**. However, it also shows that while lymph glands are a target destination for aluminium adjuvant for the whole vaccine this is not the case when only the aluminium adjuvant is injected. Essentially the handling of aluminium adjuvant is different between whole vaccine and that which is mainly used as the control or placebo in vaccine safety trials. These seminal data for sheep raise new and important questions about how vaccine safety trials are conducted in humans and offer further insight into the role of aluminium adjuvants in serious adverse events following vaccination.



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Journal of Trace Elements in Medicine and Biology

journal homepage: [www.elsevier.com/locate/jtemb](http://www.elsevier.com/locate/jtemb)



### Aluminium in brain tissue in autism

Matthew Mold<sup>a</sup>, Dorcas Umar<sup>b</sup>, Andrew King<sup>c</sup>, Christopher Exley<sup>a,\*</sup>

<sup>a</sup> *The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom*

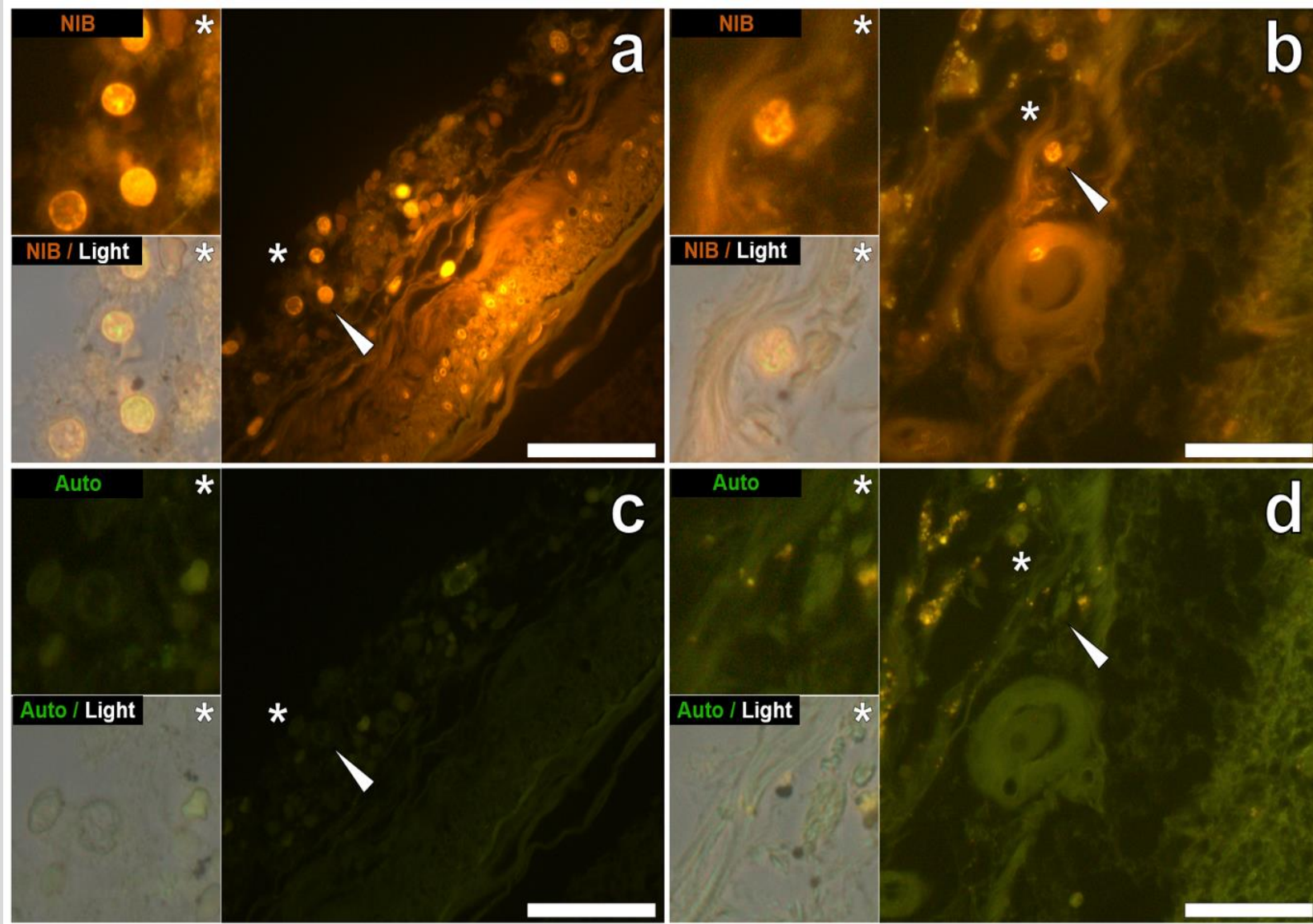
<sup>b</sup> *Life Sciences, Keele University, Staffordshire, ST5 5BG, United Kingdom*

<sup>c</sup> *Department of Clinical Neuropathology, Kings College Hospital, London, SE5 9RS, United Kingdom*



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

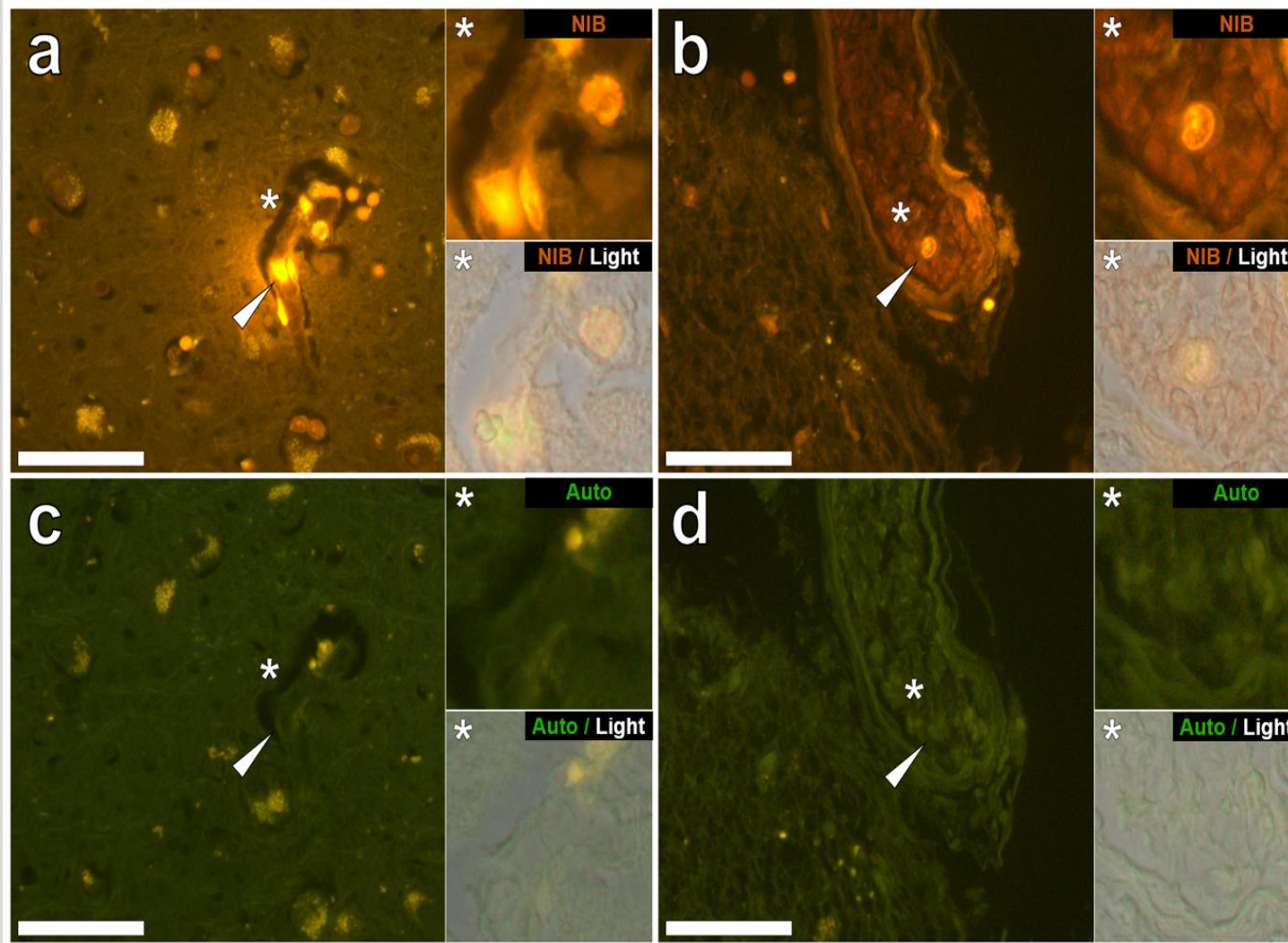
Over 450000 Views on the Publisher's Website



Intrameningeal lumogallion-reactive aluminium identified in the hippocampus (**a & c**) and frontal lobe (**b & d**) of a 50-year-old male donor diagnosed with autism.

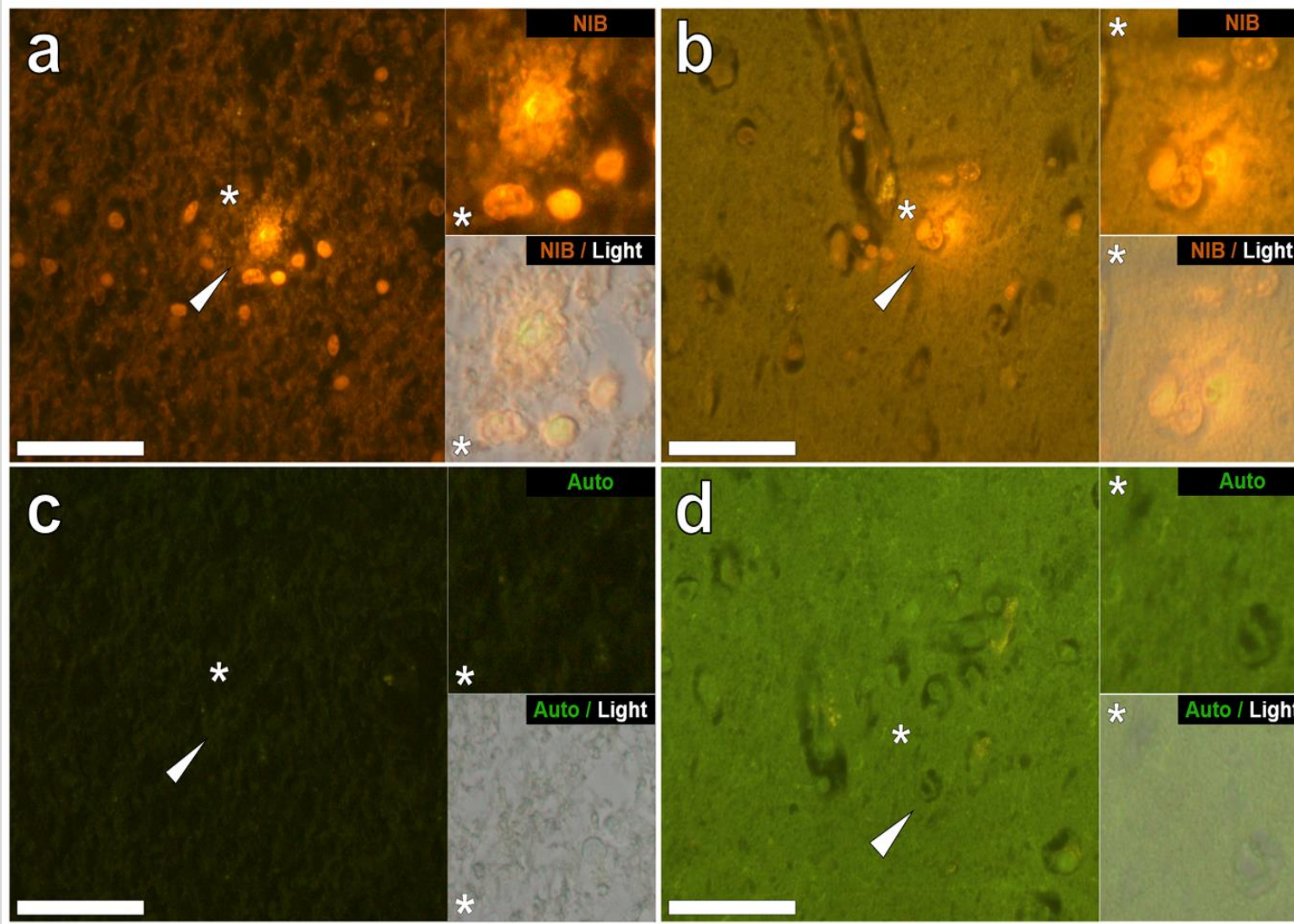
<https://www.sciencedirect.com/science/article/pii/S0946672X17308763>





Intravascular lumogallion-reactive aluminium identified in the hippocampus (**a – d**) of a 50-year-old male donor diagnosed with autism.

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



Lumogallion-reactive aluminium identified in the hippocampus (**a & c**) and parietal (**b & d**) lobe of a 15-year-old male donor diagnosed with autism.

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



The Birchall Centre, Keele University and  
Centro de Investigación Científica de Yucatán



THE THIRTEENTH  
KEELE MEETING ON  
**Aluminium**

**Future Challenges in  
the Aluminium Age**

**23<sup>rd</sup>**  
**27<sup>th</sup>**  
March  
**2019**

Hotel Uxmal Resort Maya  
Yucatán, México



**Keele**  
UNIVERSITY



CONACYT



CICY

[www.keele.ac.uk](http://www.keele.ac.uk) | [c.exley@keele.ac.uk](mailto:c.exley@keele.ac.uk) | [keele2019@cicy.mx](mailto:keele2019@cicy.mx) | [ths@cicy.mx](mailto:ths@cicy.mx)