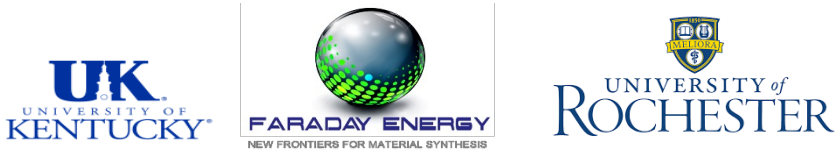
June 21-23, 2022

COMBUSTION GENERATED NANOPARTICLES

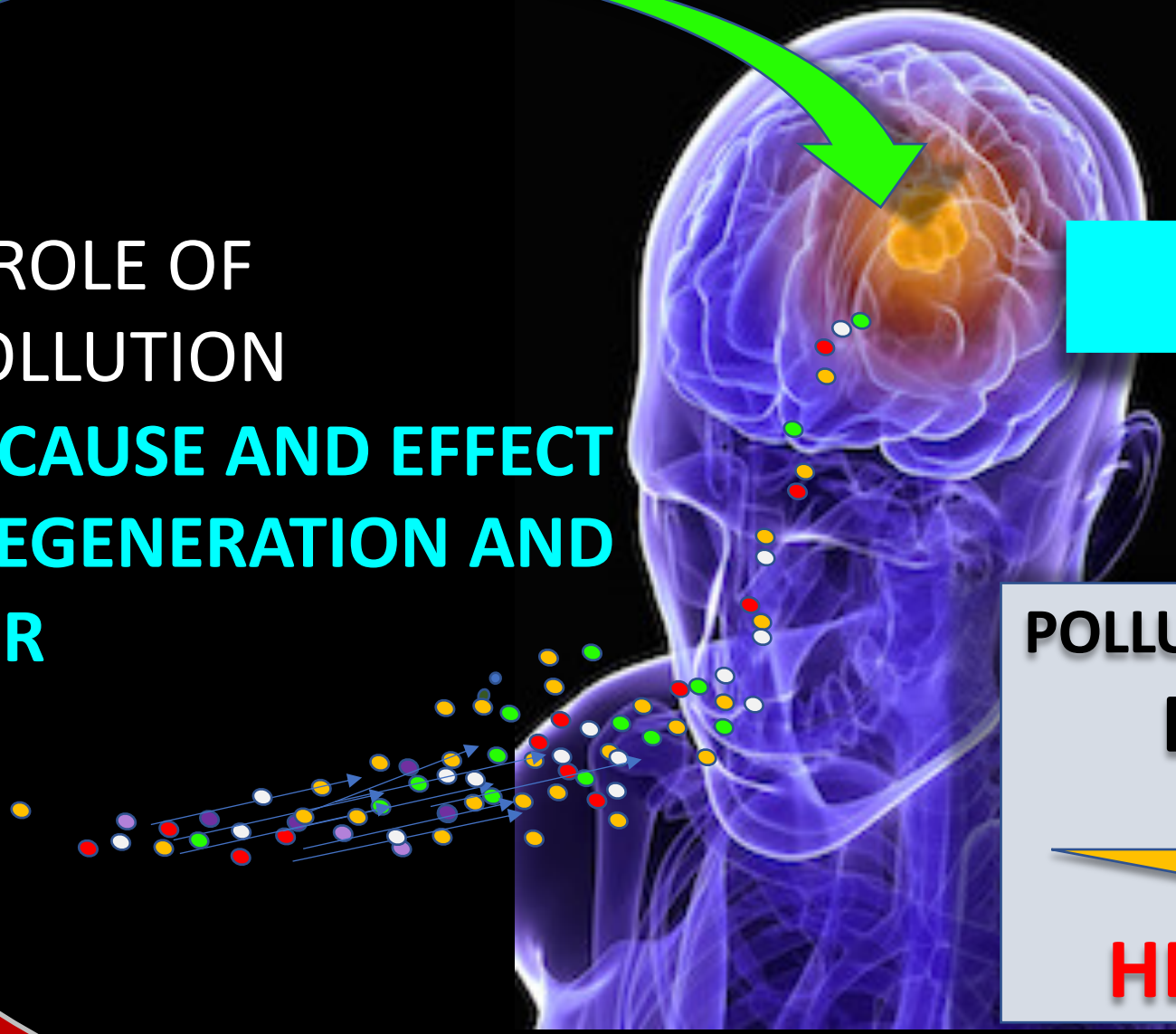
ETH - Conference

Inhalation Exposure to Wildfire and Burn Pit Smoke: A Common Etiology for Neurogenic and Oncogenic Diseases of the Brain Involving Iron?

Uschi M Graham and Günter Oberdörster



WHAT IS THE ROLE OF AIR BORNE POLLUTION PARTICLES → **CAUSE AND EFFECT FOR NEURODEGENERATION AND BRAIN CANCER**



BURN PIT EMISSIONS AND WILDFIRES

POLLUTION PARTICLE Uptake

Bioprocessing

Particle –Tissue Interactions

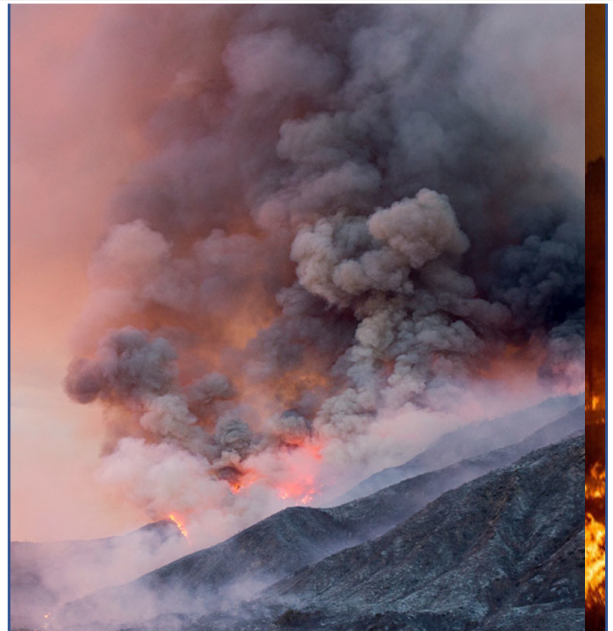
HEALTH EFFECTS ?

Burn Pits

Immediate Risk for:
Military Personnel

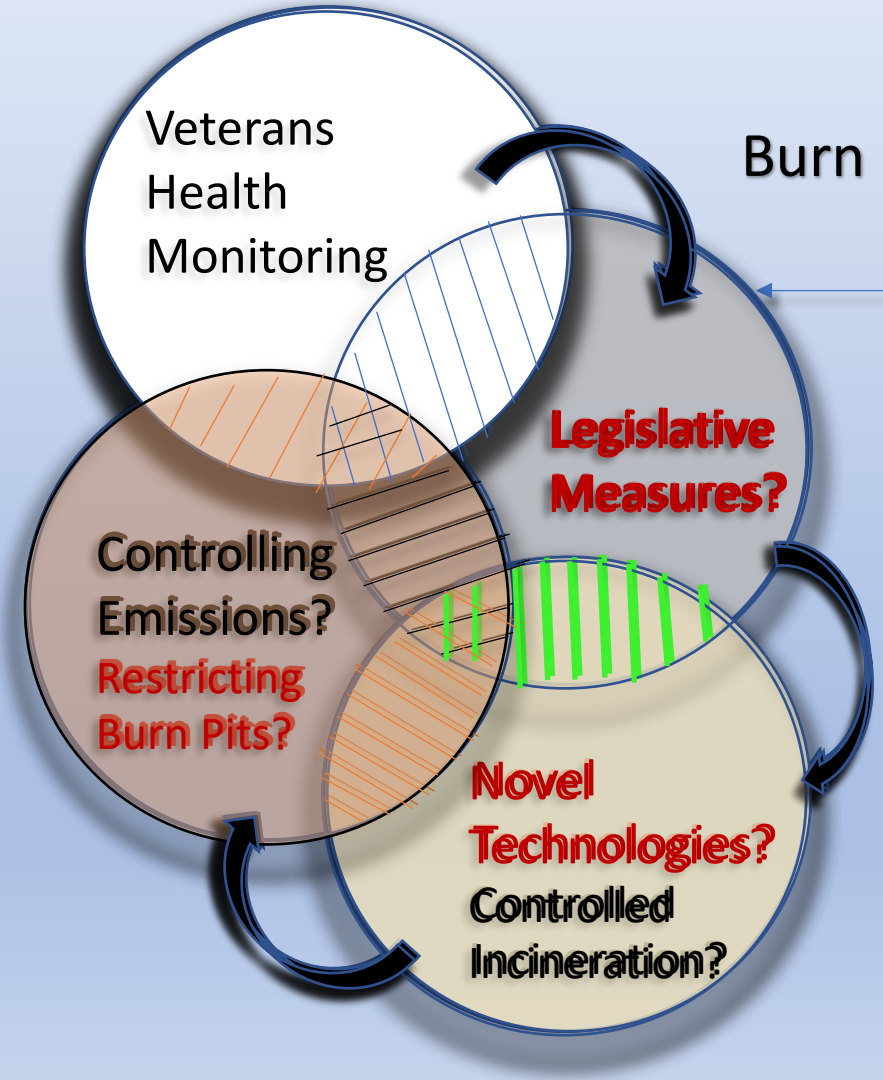
Combustion Particles and Health Effects ?

Wildfires



Immediate Risk for:
Firefighters

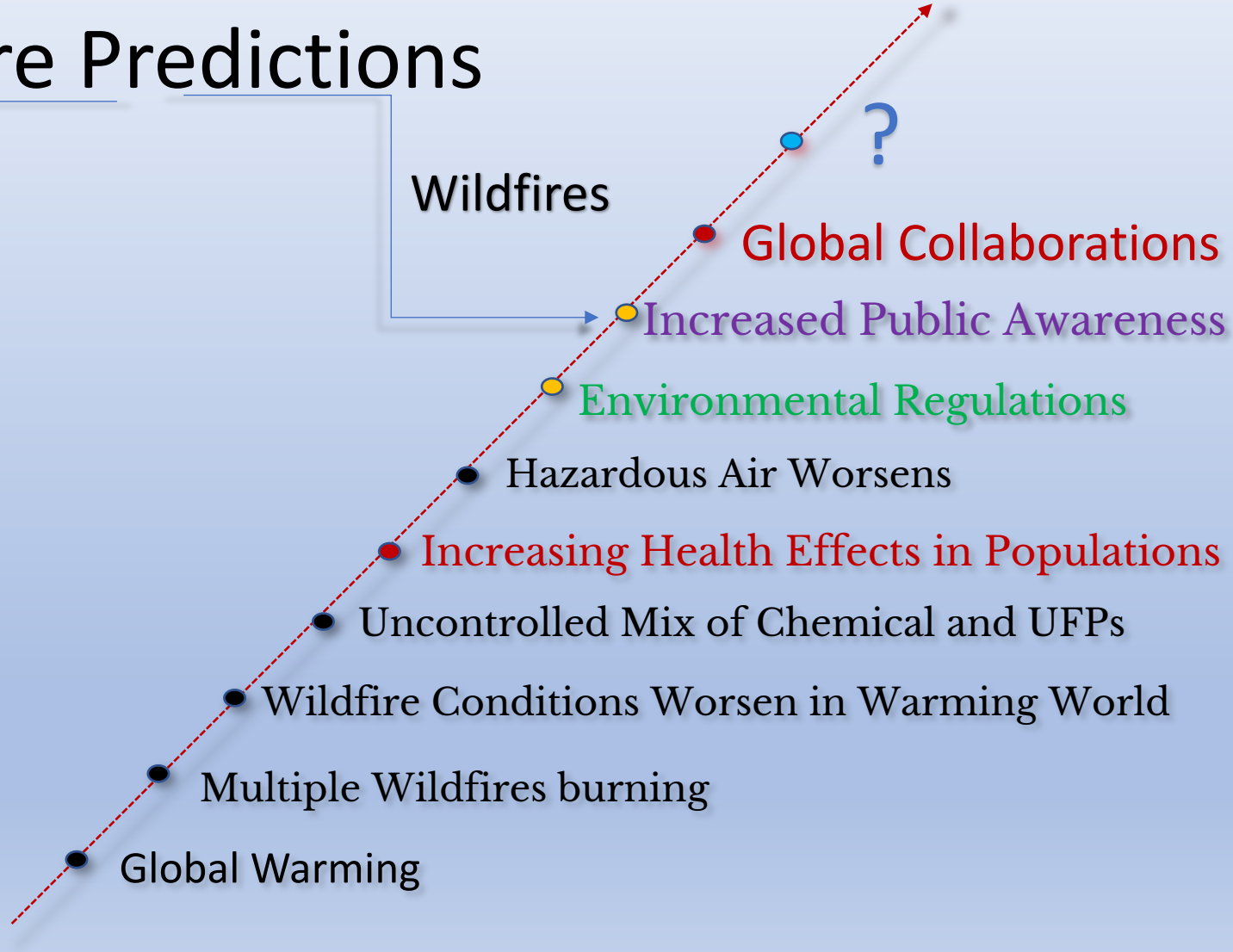
Breathing burn pit and wildfire combustion particles may upset brain and other vital organs



Future Predictions

Burn Pits

Wildfires



THE RELATIVE SIZE OF PARTICLES

From the COVID-19 pandemic to the U.S. West Coast wildfires, some of the biggest threats now are also the most microscopic.

A particle needs to be 10 microns (µm) or less before it can be inhaled into your respiratory tract. But just how small are these specks?

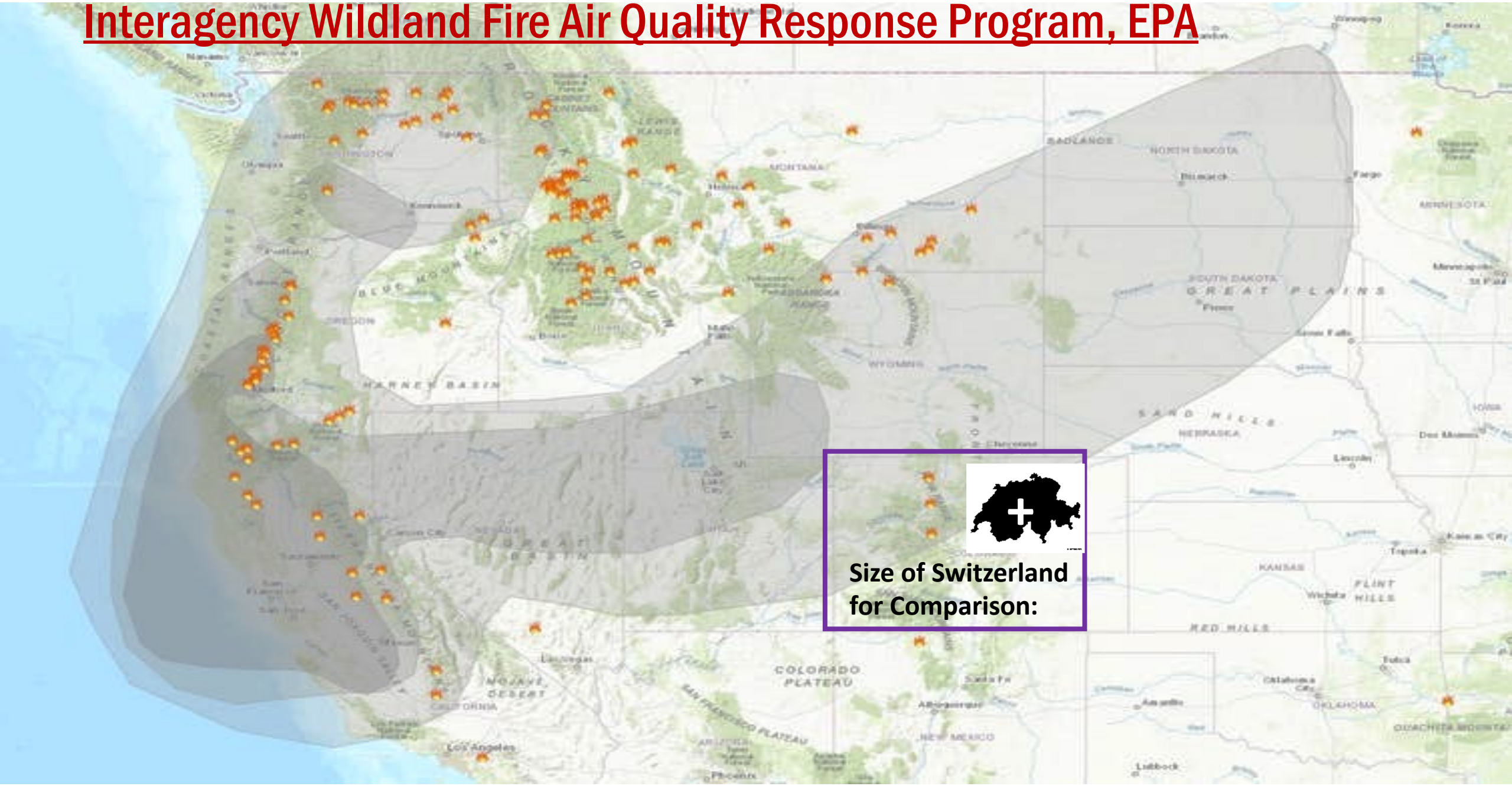
Here's a look at the relative sizes of some familiar particles ↘

Wildfire smoke can persist in air for several days, and even months!

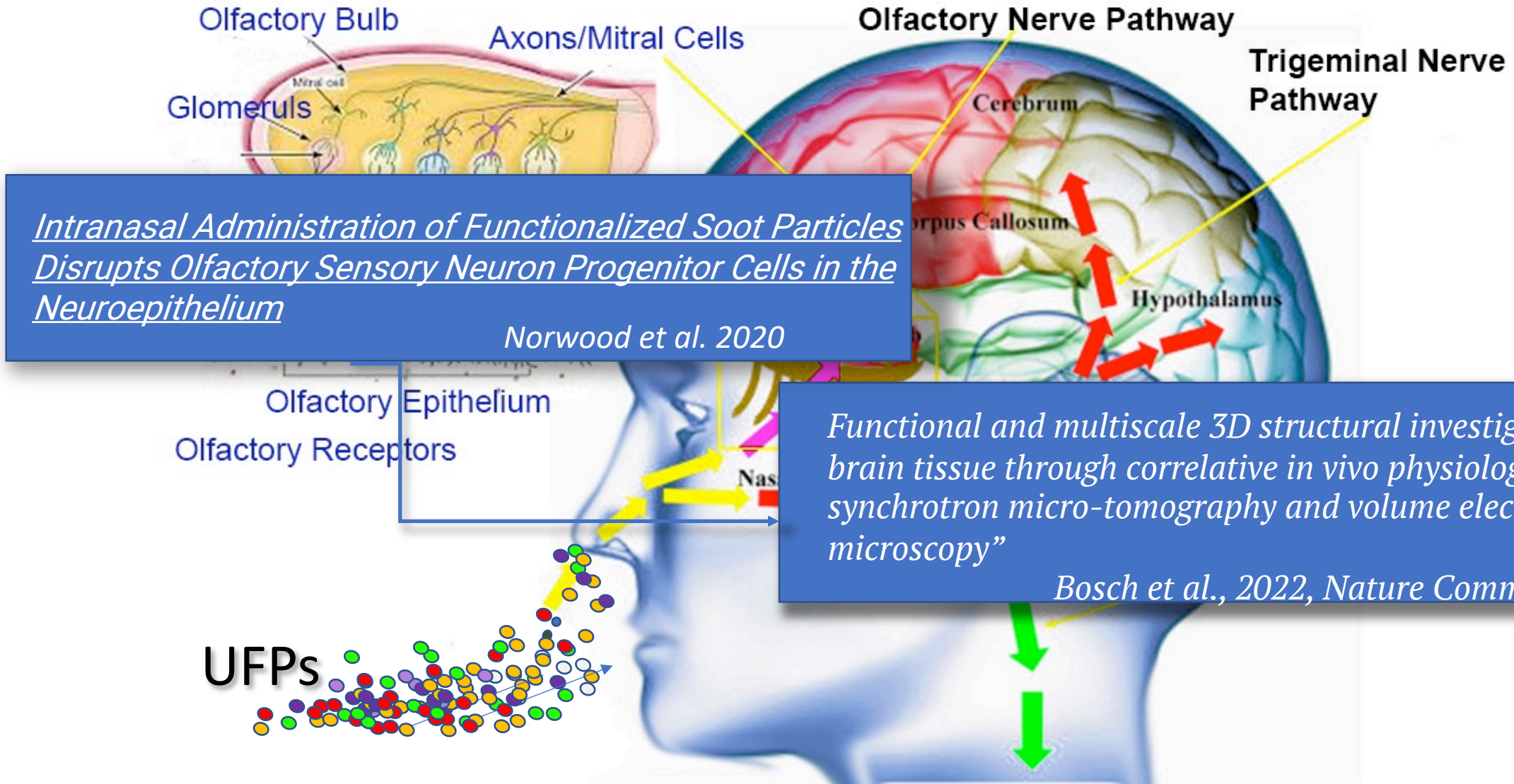
SOURCES Clearstream, Daniel Loverbey, EPA, Financial Times, News Medical, Science Direct, SCMP, Susan Sokolowski, Petroclear, U.S. Dept. of Energy
COLLABORATORS **RESEARCH + WRITING** Carmen Ang, Iman Ghosh | **DESIGN + ART DIRECTION** Harrison Schell

Smoke from large western wildfires was detected as far east as the Dakotas on Aug. 28, 2021.

Interagency Wildland Fire Air Quality Response Program, EPA



Due to minuscule size, NPs have the potential to cross the blood-brain barrier, but also enter via **Olfactory or Trigeminal Nerve Pathways** to potentially cause neurotoxicity, neuroinflammation and neurodegeneration of the central nervous system.



Intranasal Administration of Functionalized Soot Particles Disrupts Olfactory Sensory Neuron Progenitor Cells in the Neuroepithelium

Norwood et al. 2020

Functional and multiscale 3D structural investigation of brain tissue through correlative in vivo physiology, synchrotron micro-tomography and volume electron microscopy"

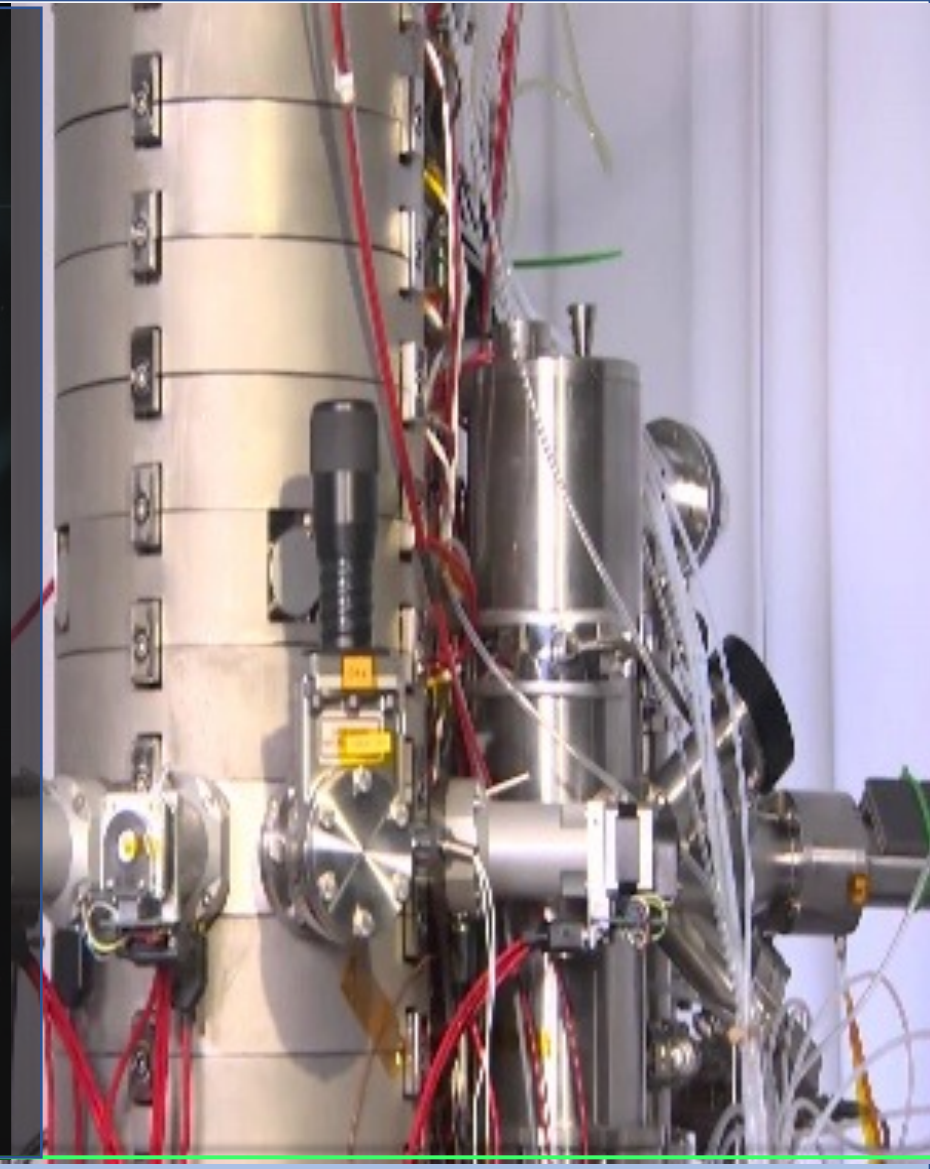
Bosch et al., 2022, Nature Communications.

BASIS FOR BURN PIT AND WILDFIRE EXPOSURE and
Etiology for Neurodegeneration and Brain Cancer ?

Human OB

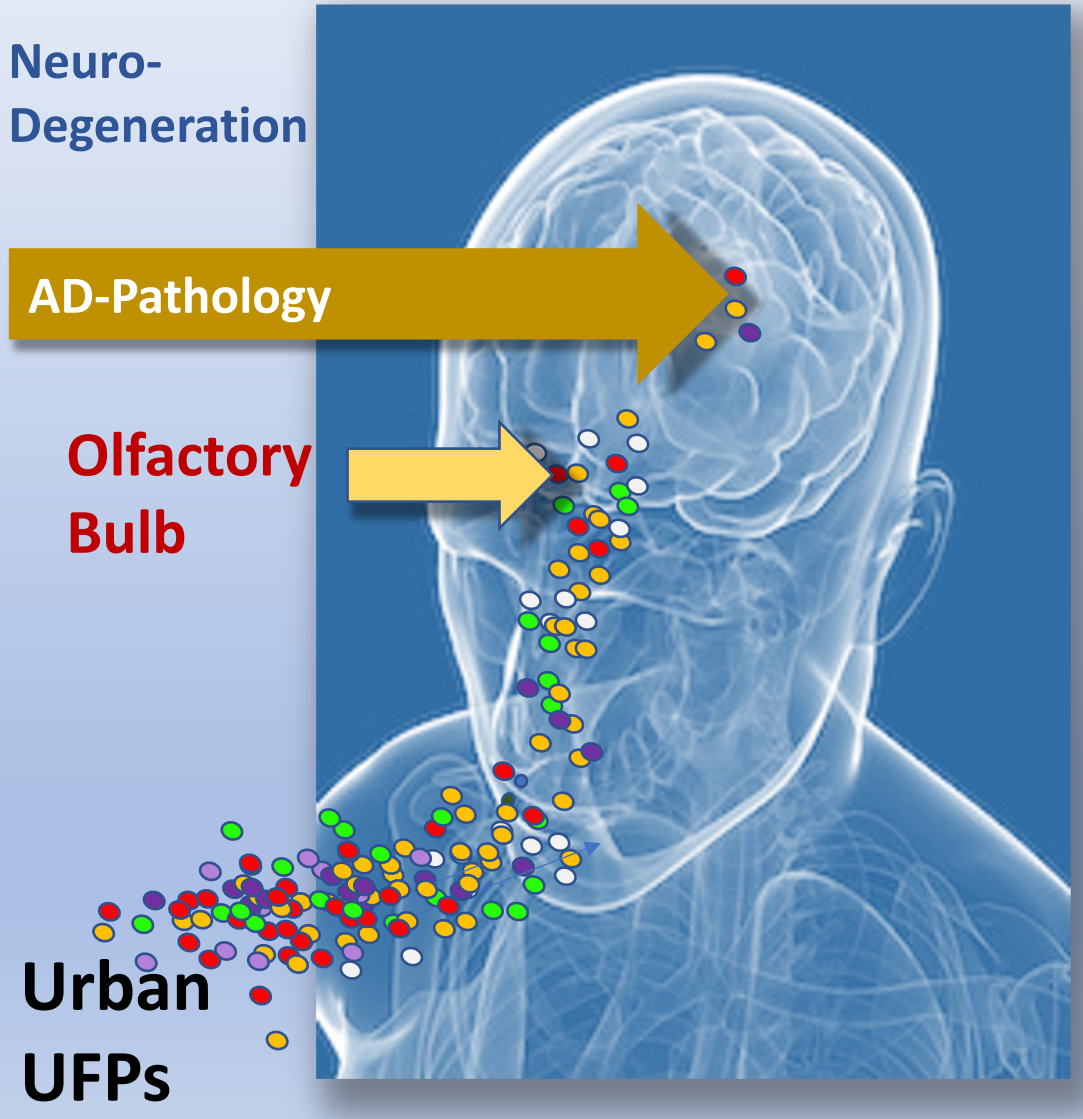
(of select Cohort Subjects)

Graham et al., 2020



High Resolution STEM/EELS/EDX:
Nanoparticle-Cell Interactions

What we presented at last year's ETH Conference:



Metal and Metal Oxide Nanoparticles can enter the Human Olfactory Bulb and Deeper Brain Regions using a Trojan Horse Mechanism.

ONGOING OBJECTIVES

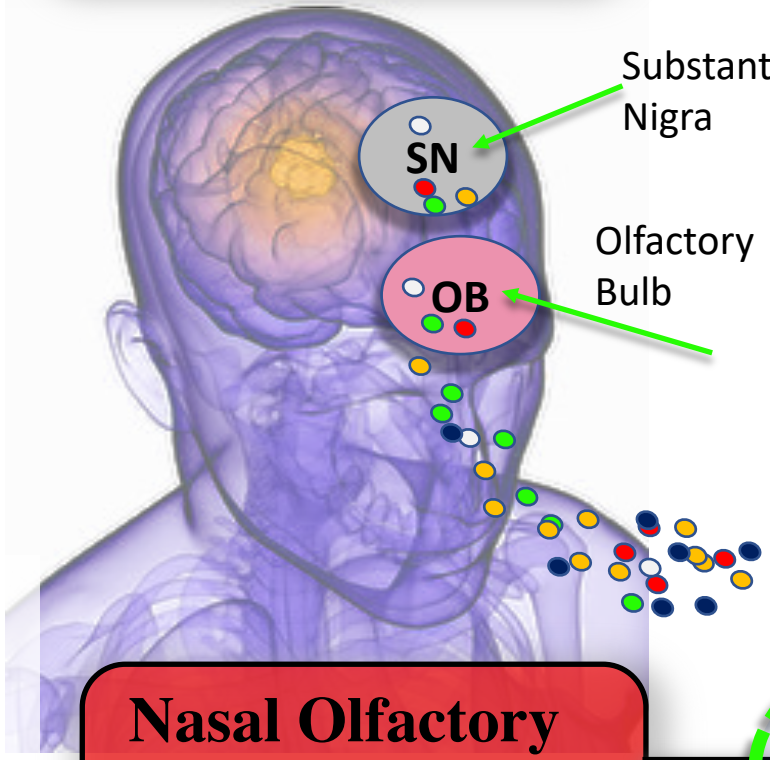
- Do inhaled NPs translocate to the OB?
- Which types of NPs?
- Do translocated NPs interact with cells in OB?
- Are NPs undergoing bioprocessing?
- More NPs cause more neurodegeneration?

From the Nose to the Brain, Neuronal Pathways for NPs?

Neocortex
Orbitofrontal Cortex

Olfactory Cortex
Piriform Cortex; Amygdala; Entorhinal Cortex

Mediodorsal Thalamus



Olfactory Tract
Axons of Mitral Neurons (Olfactory Striae)

Substantia Nigra
(basal ganglia; dopamine production)

Nasal Olfactory Mucosa
Olfactory Receptor Neurons

Olfactory Bulb
Glomeruli; Mitral Cells; Granular Cells

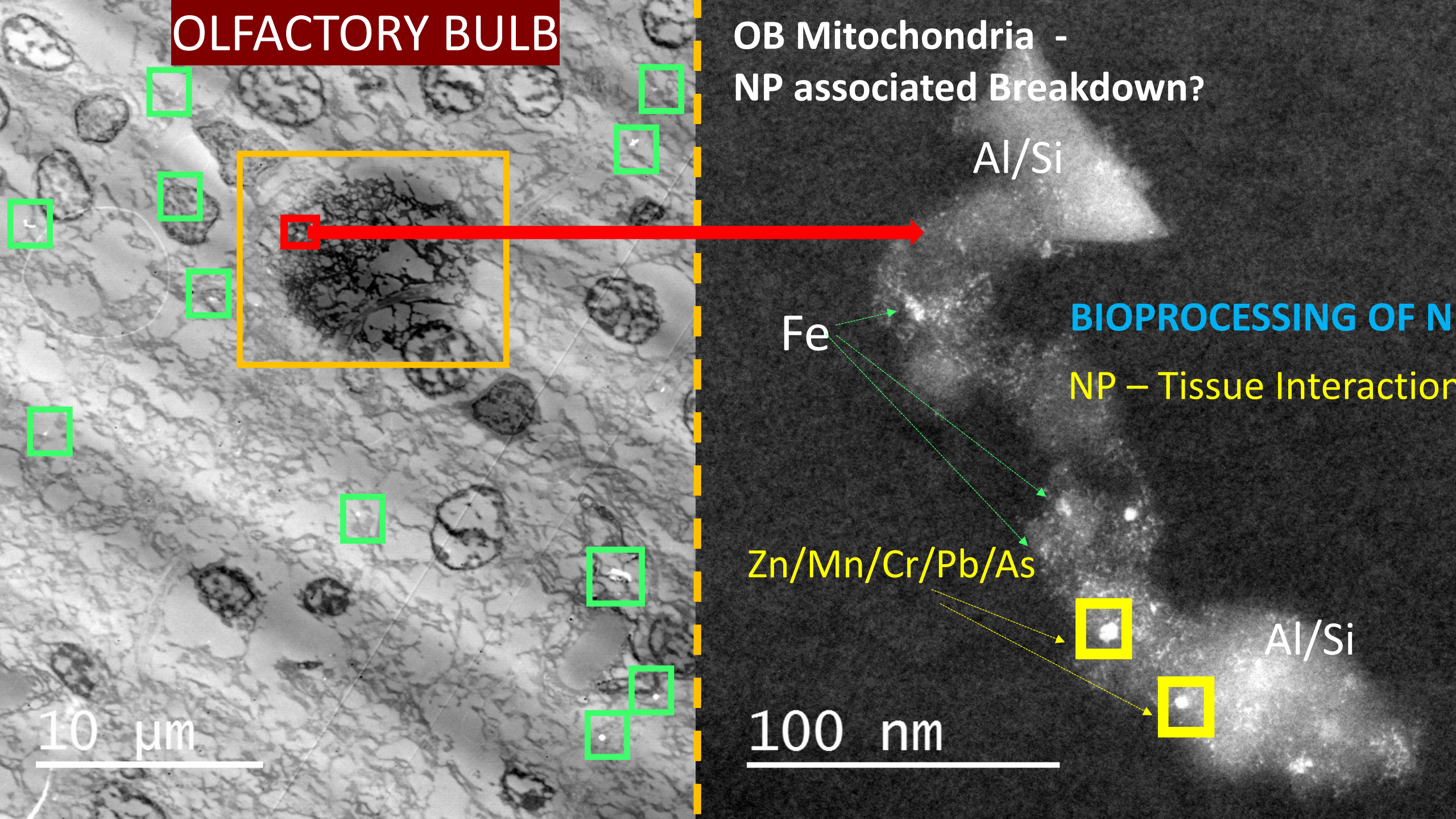
Striatum
(prosencephalon)

Multi-disciplinary Team

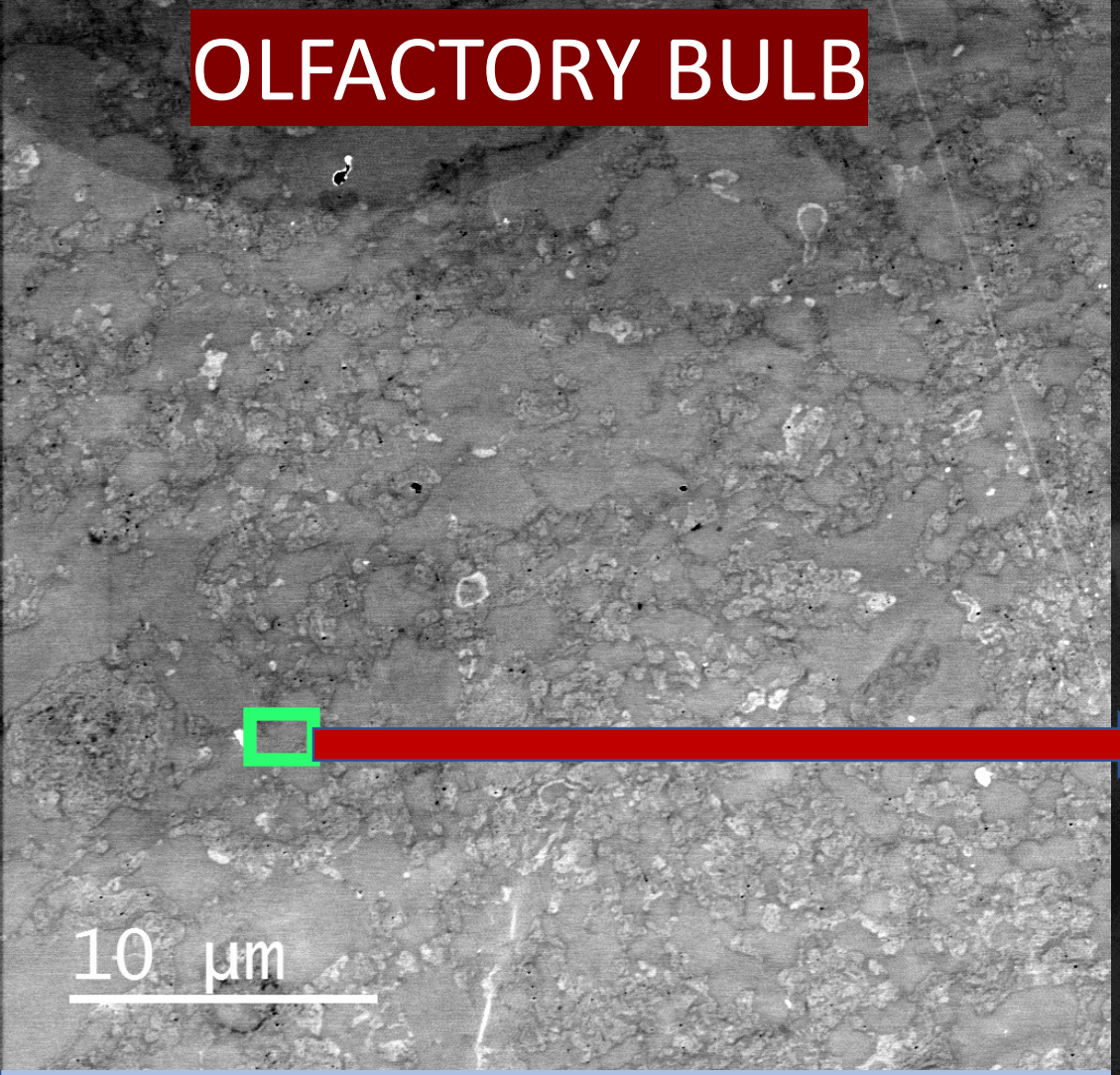
NEW PERSPCTIVES

- Brain Inflammation may be activated by Ultra-Fine Pollution Nanoparticles “UFP” that reach the Olfactory Bulb (OB).
- Nanoparticle Uptake to deeper brain regions may induce Neurodegeneration and potentially Glioblastoma Formation.
- **HYPOTHESIS**

Residents living close to Wildfire-caused air pollution and Veterans exposed to burn pit-UFPs may have a greater number of UFPs trapped in OB.

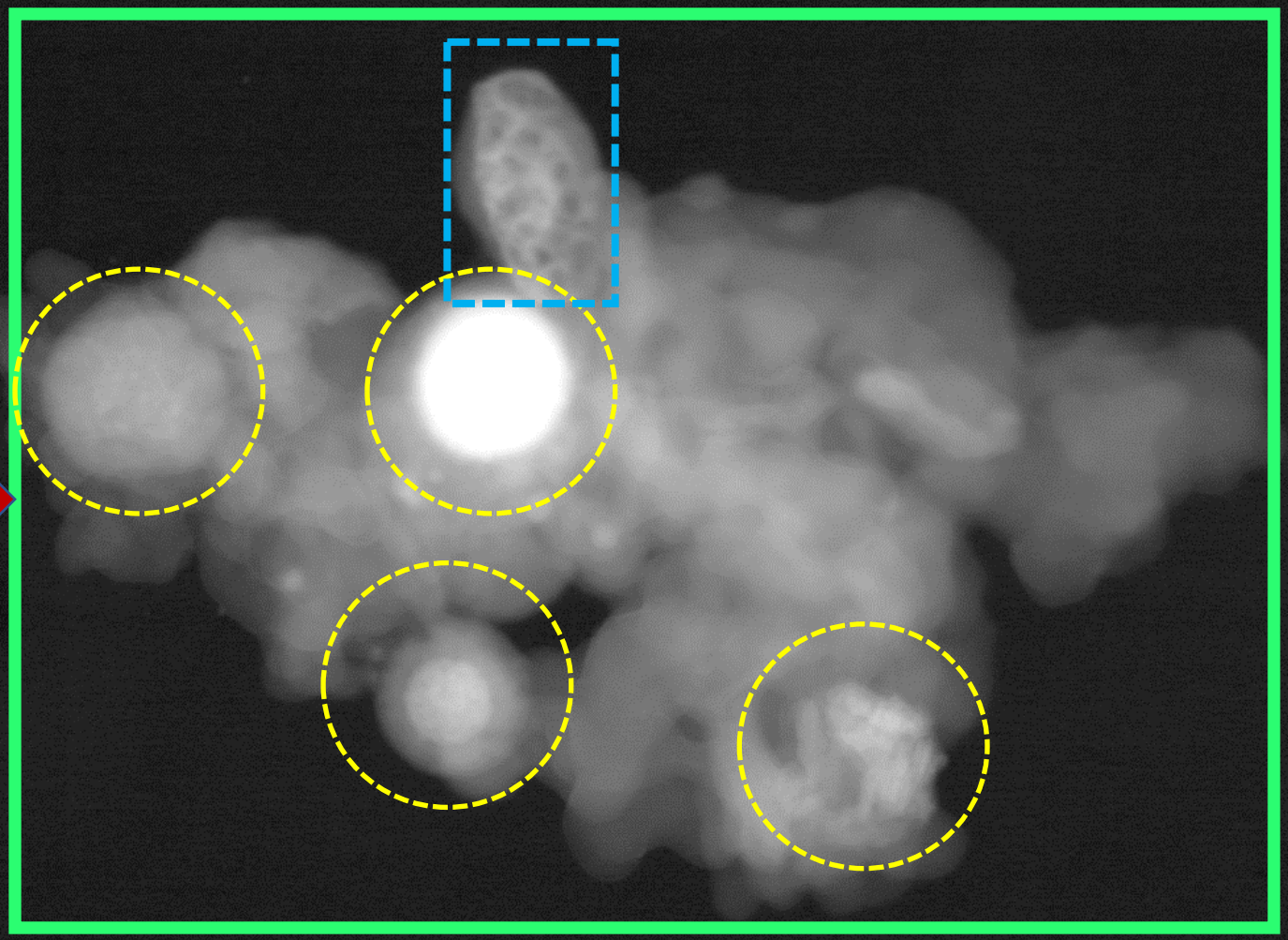

OLFACTORY BULB
10 µm
OB Mitochondria -
NP associated Breakdown?
Al/Si
Fe
BIOPROCESSING OF N
NP – Tissue Interaction
Zn/Mn/Cr/Pb/As
Al/Si
100 nm

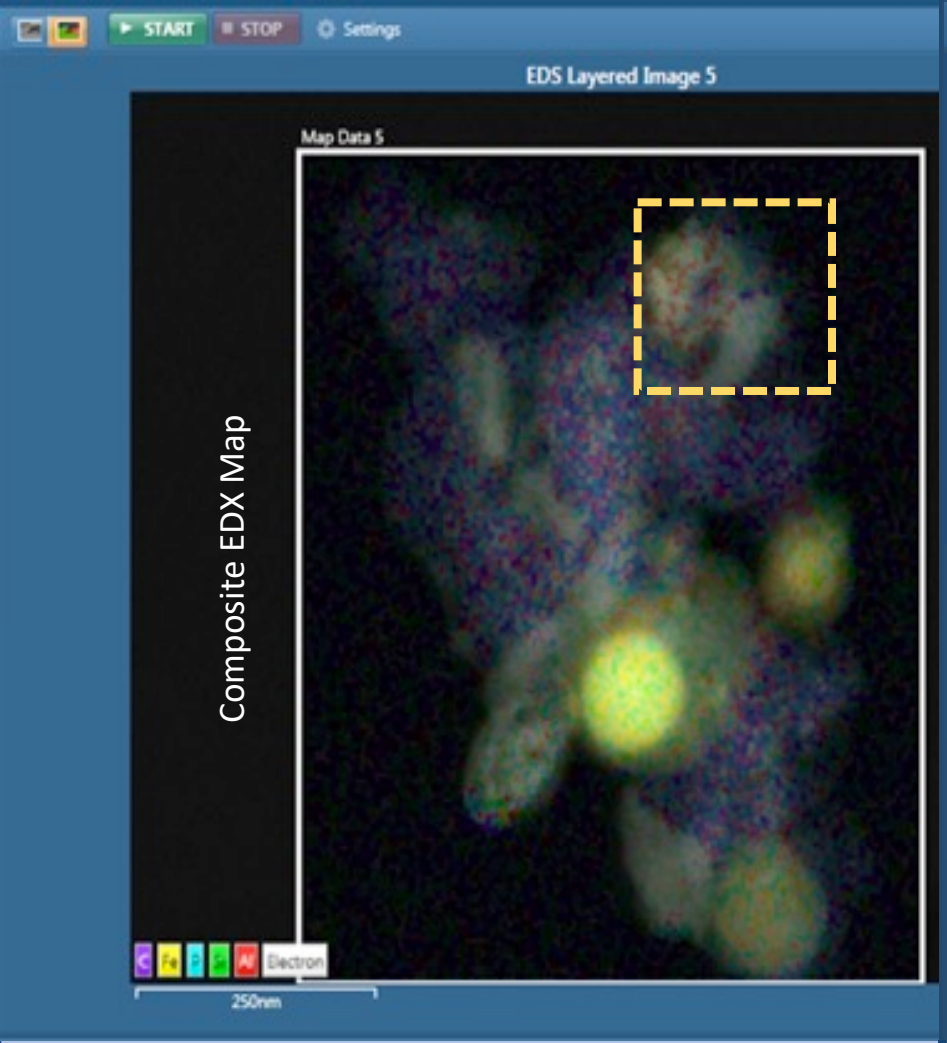
OLFACTORY BULB

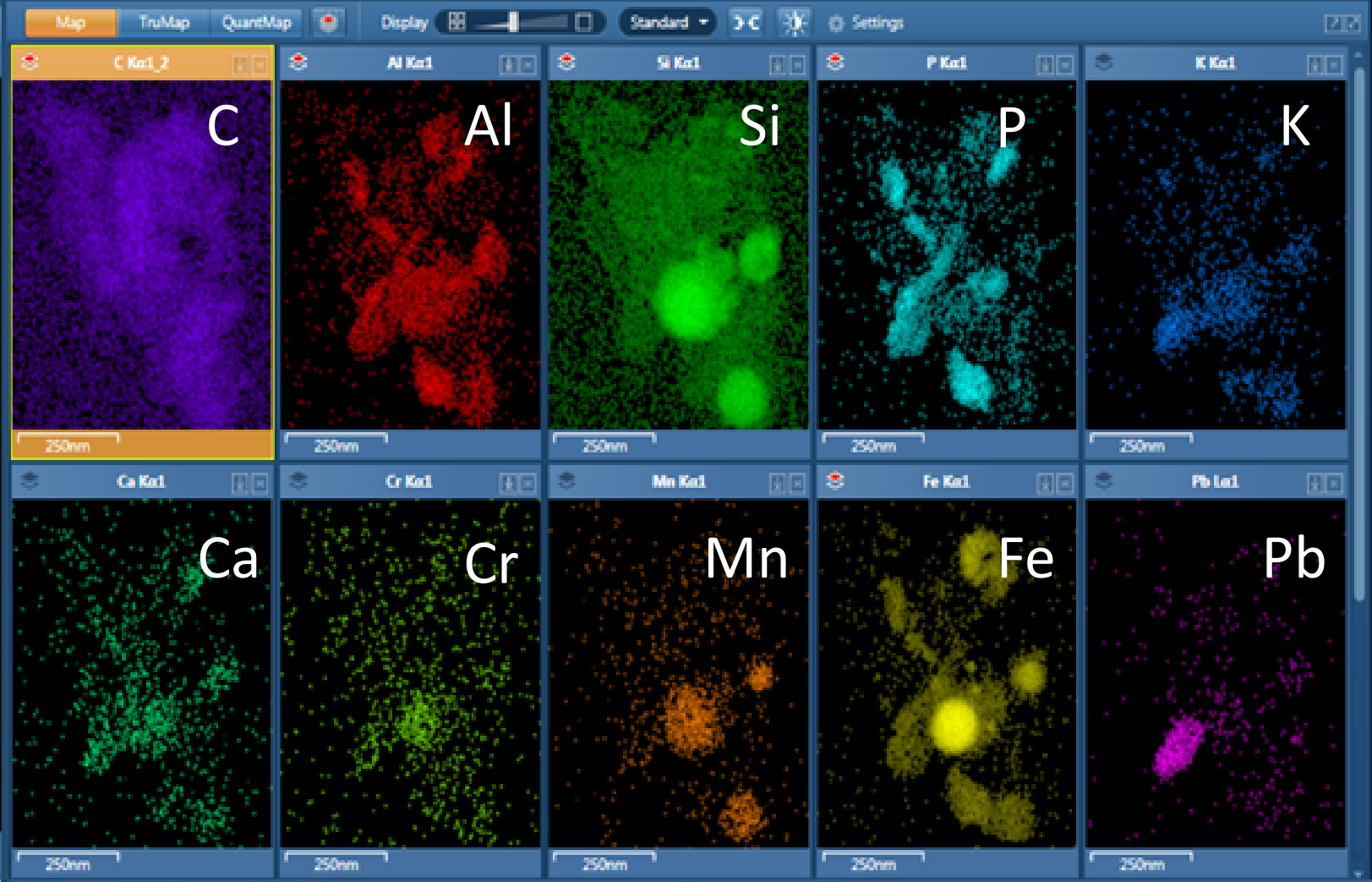


UFPs inside Olfactory Bulb

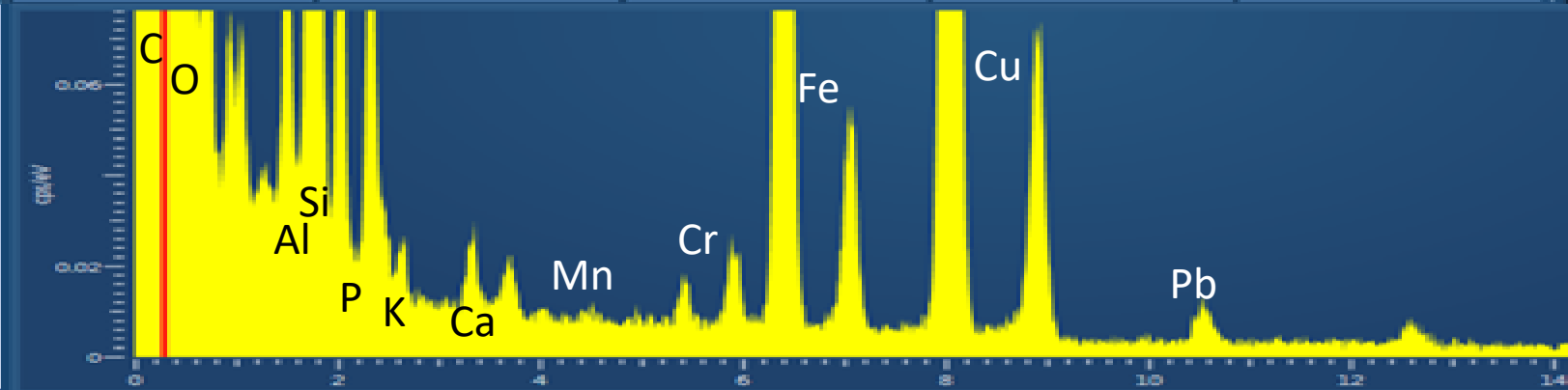
Combustion Particles “Spheres” with carbon Coatings



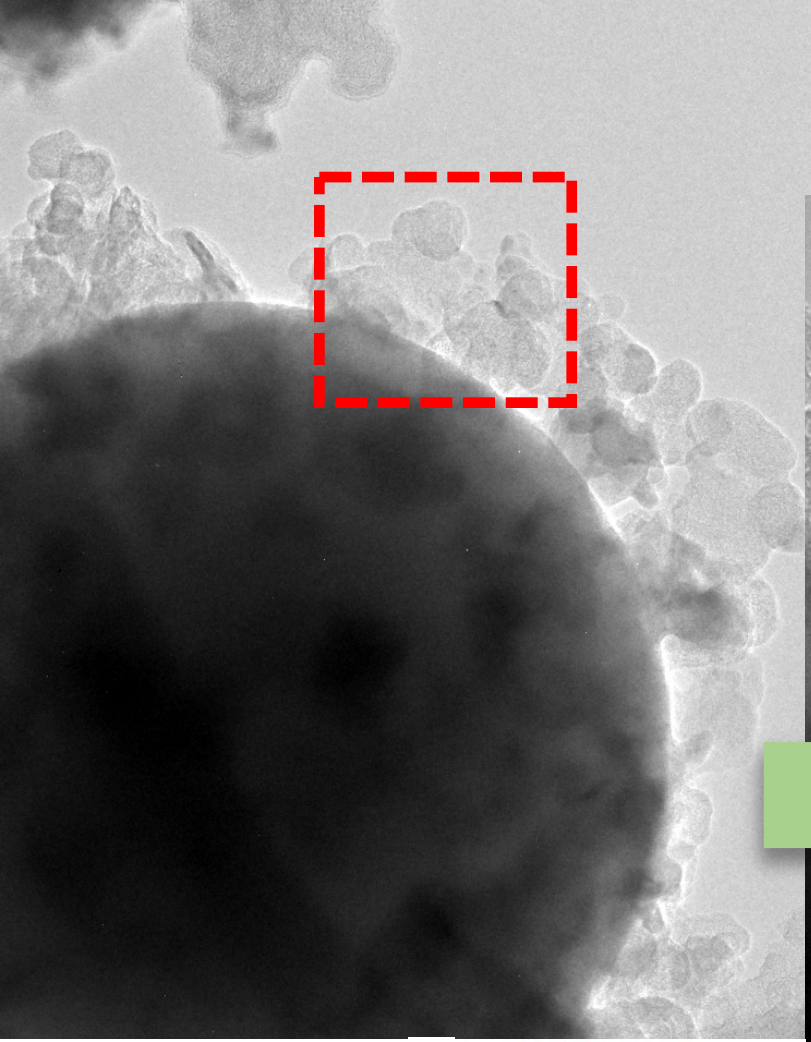


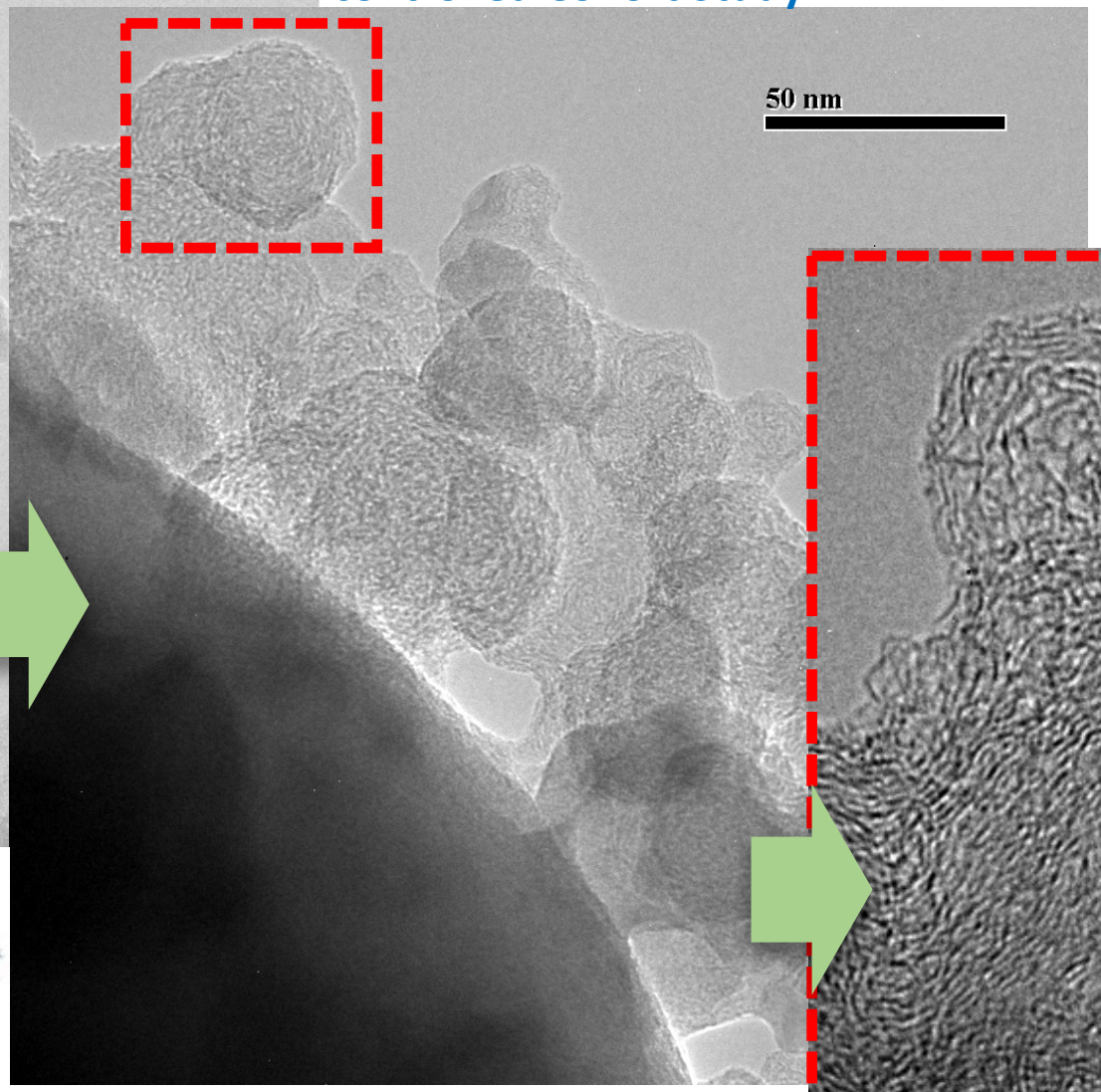


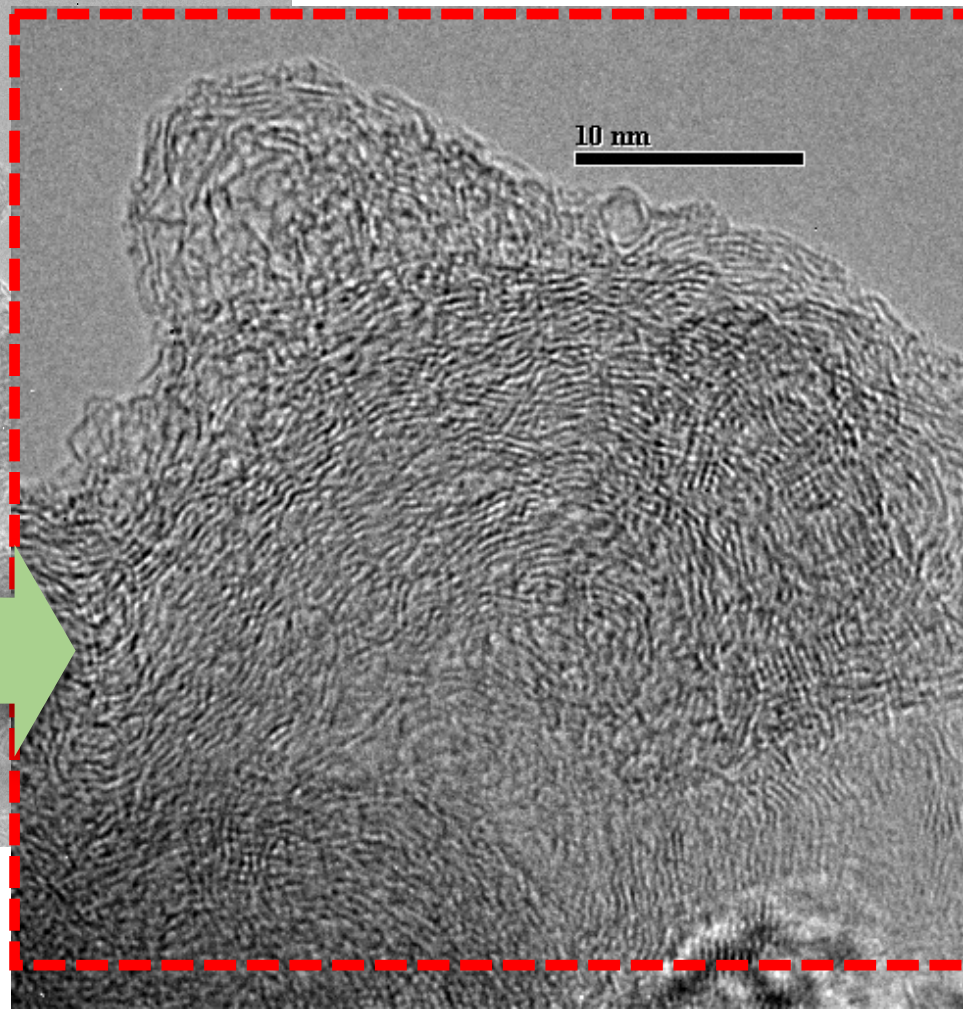
UFPs inside Olfactory Bulb

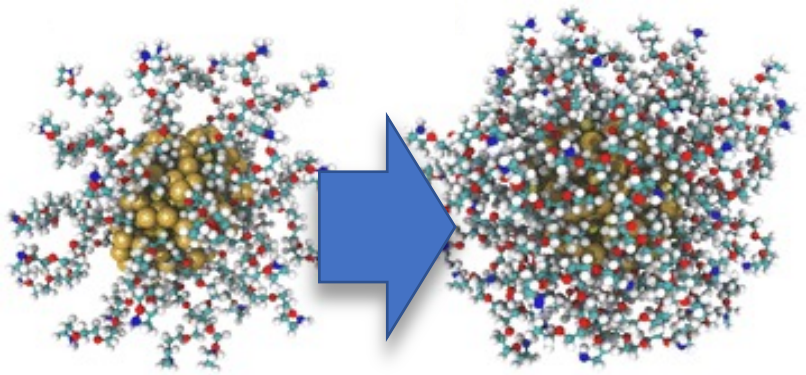


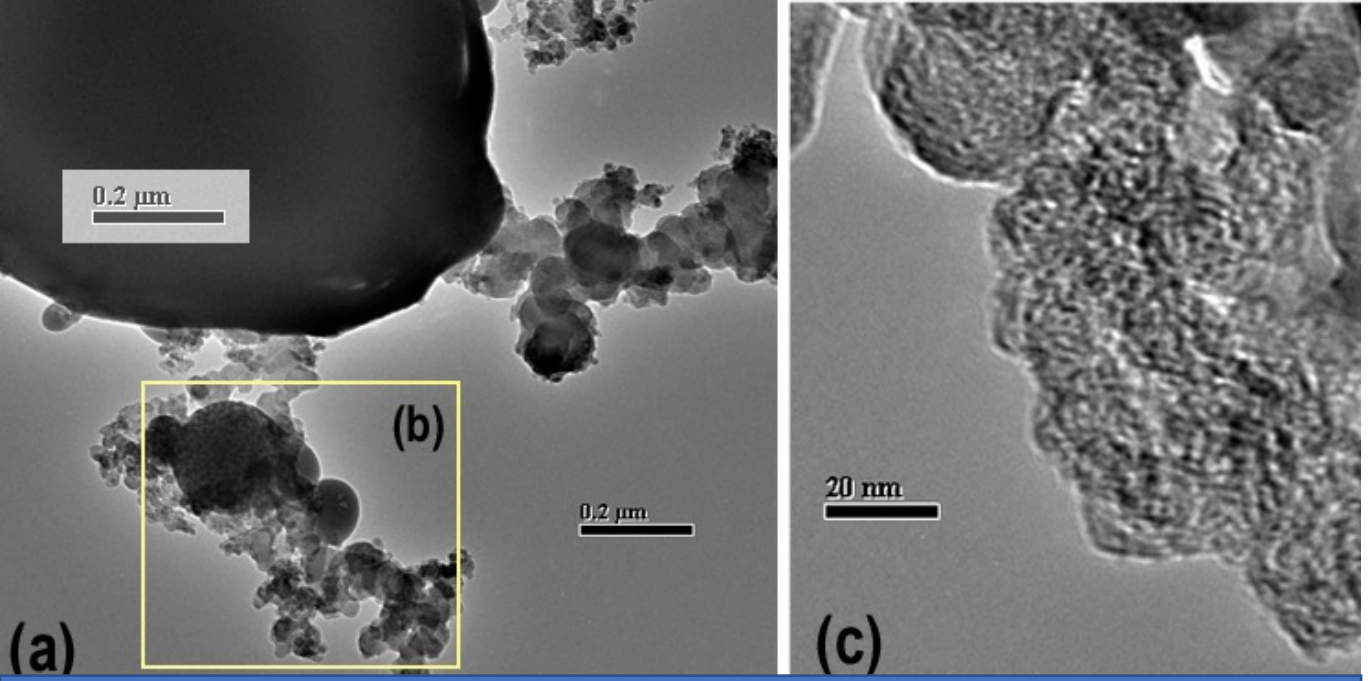
This is the first combustion-generated UFPs with carbon-coated Si/Al spheres located inside the OB of Alzheimer's Subject from a controlled Cohort Study



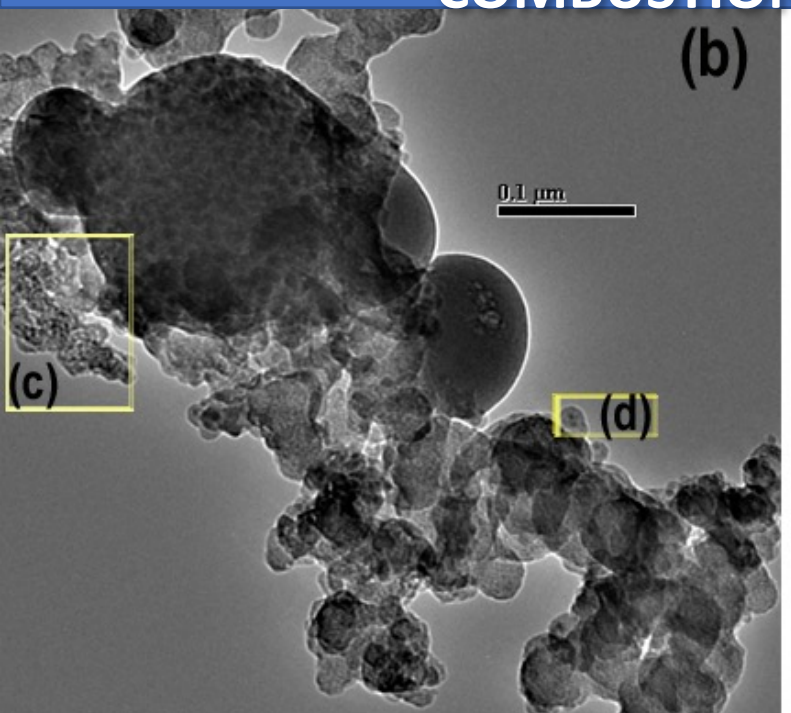


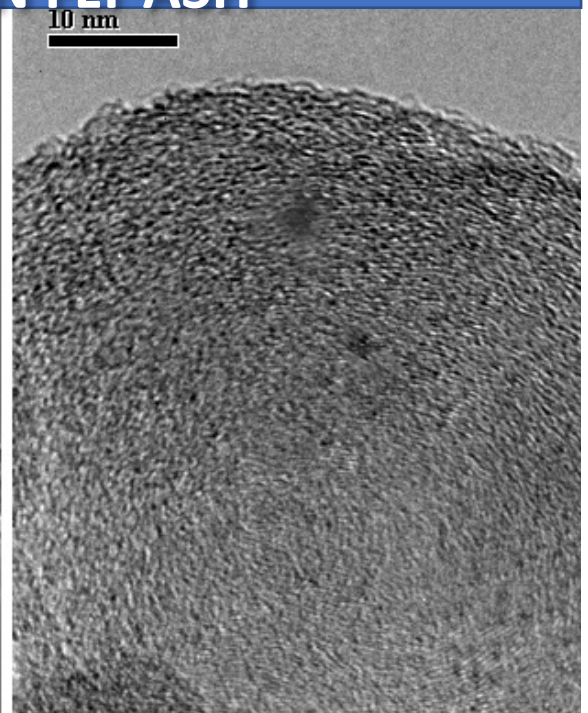


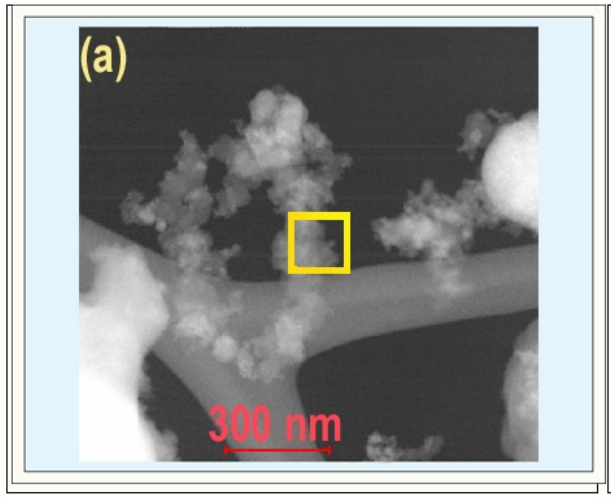


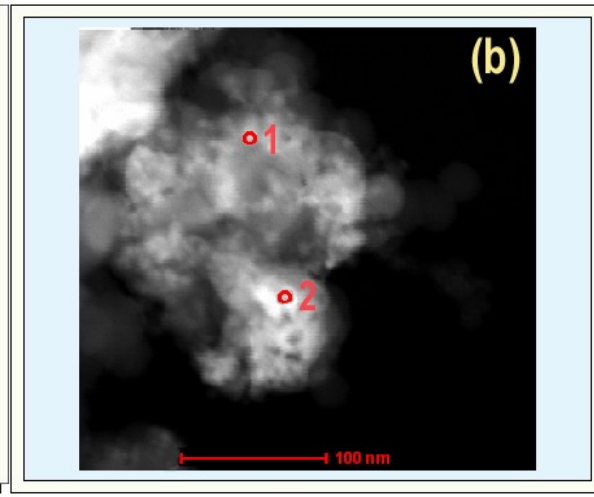


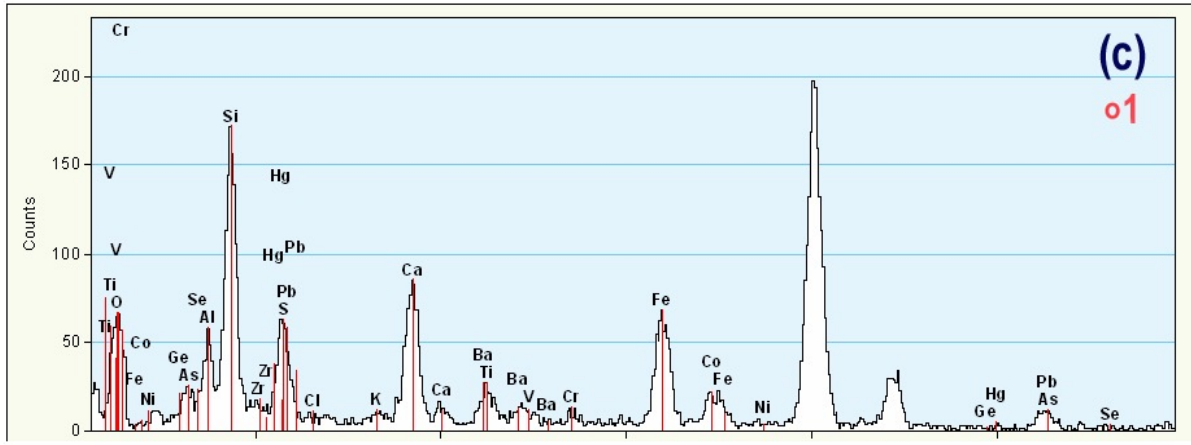
COMBUSTION FLY ASH

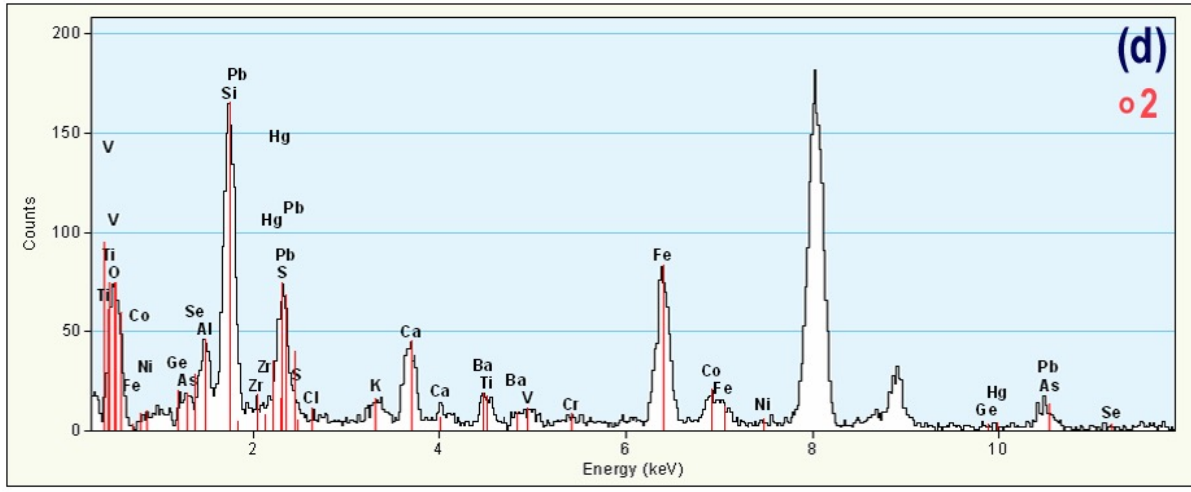










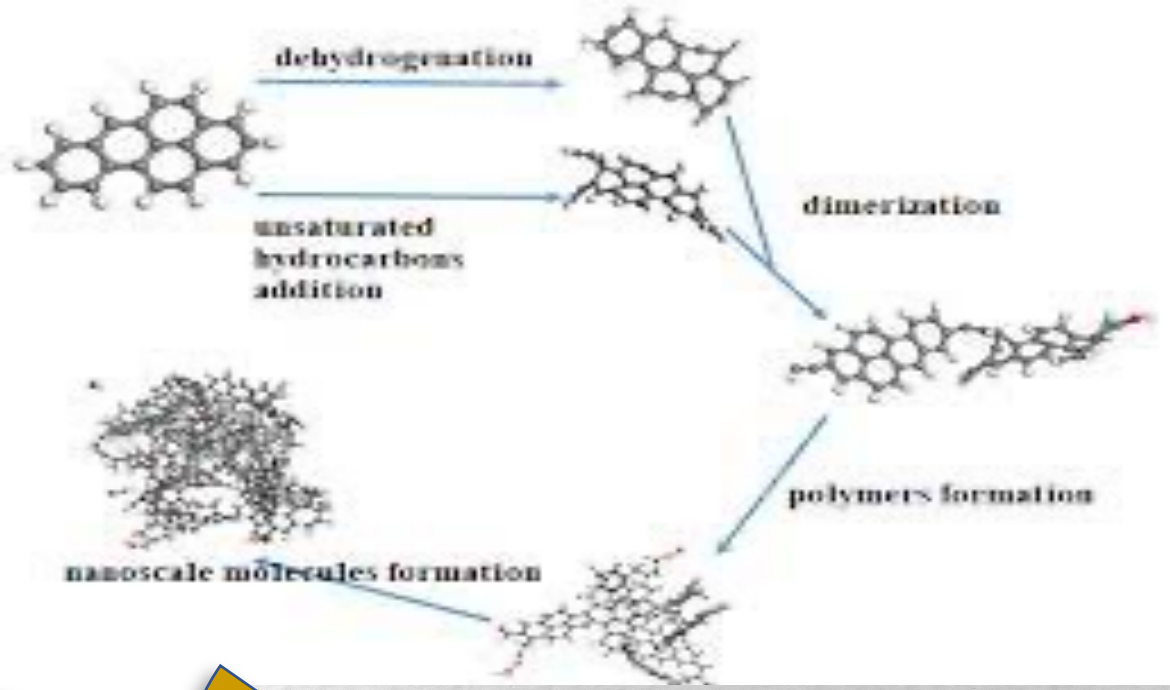


REACTIVE CARBON COATING

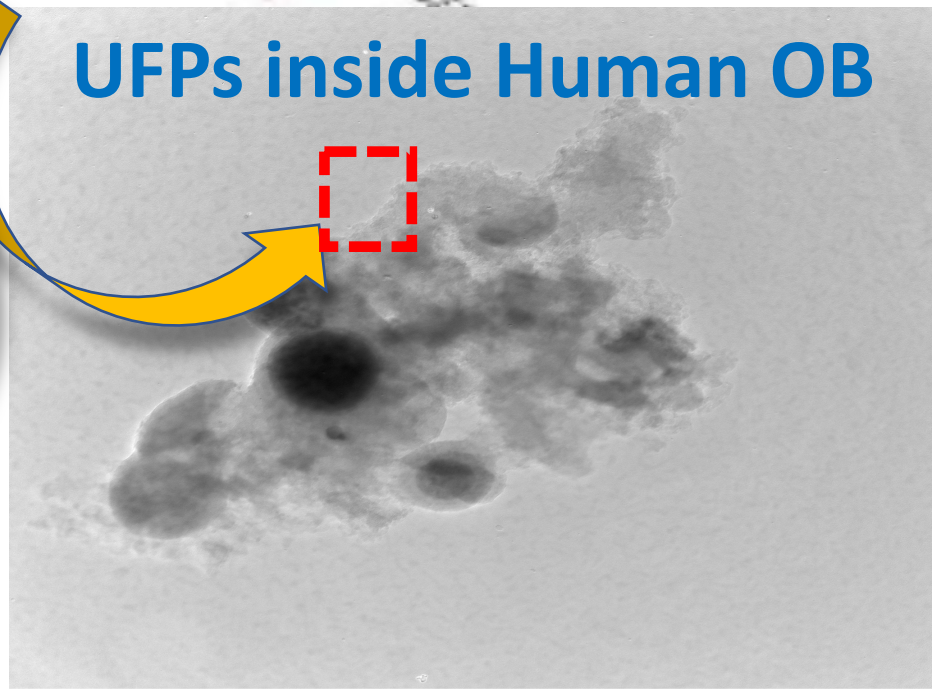
Soot nucleation and growth from PAHs

TEM11.tif
14:16 5/13/2022

5 nm
Direct Mag: 1500000 x
NIOSH



UFPs inside Human OB

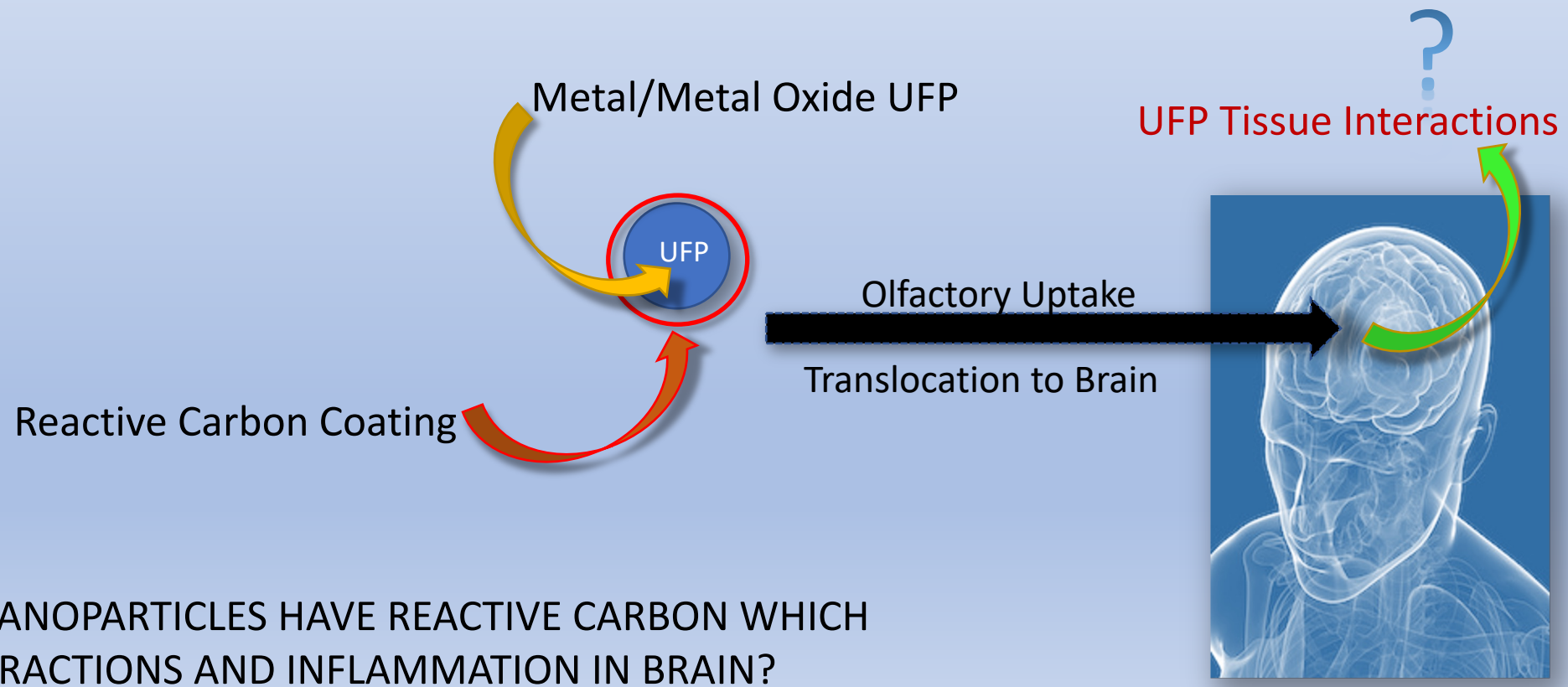


TEM6.tif
14:00 5/13/2022

100 nm
Direct Mag: 150000 x
NIOSH

DISCOVERY

We show for the first time the presence of carbon coatings on the surfaces of UFPs that translocated to the Human Olfactory Bulb (Cohort Subject with Neurodegeneration).

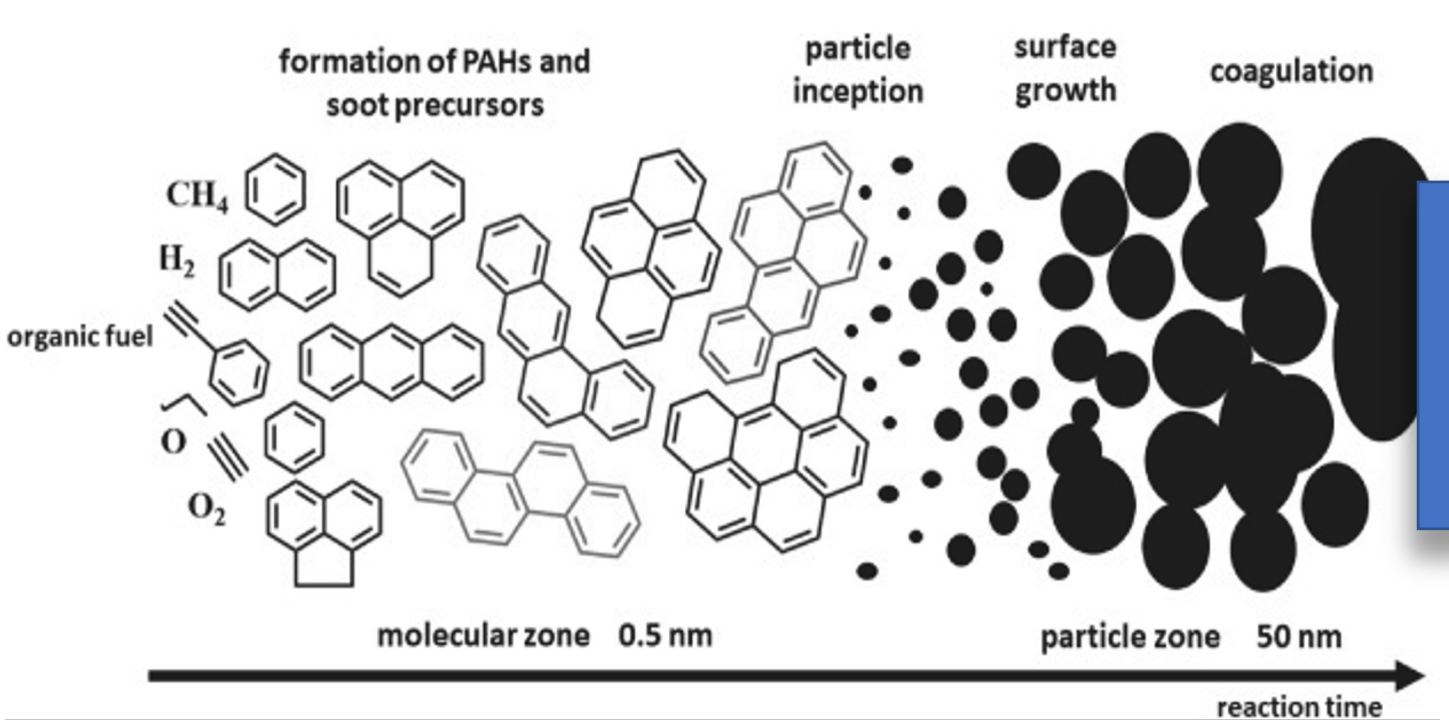


COMBUSTION DERIVED NANOPARTICLES HAVE REACTIVE CARBON WHICH MAY AFFECT TISSUE INTERACTIONS AND INFLAMMATION IN BRAIN?

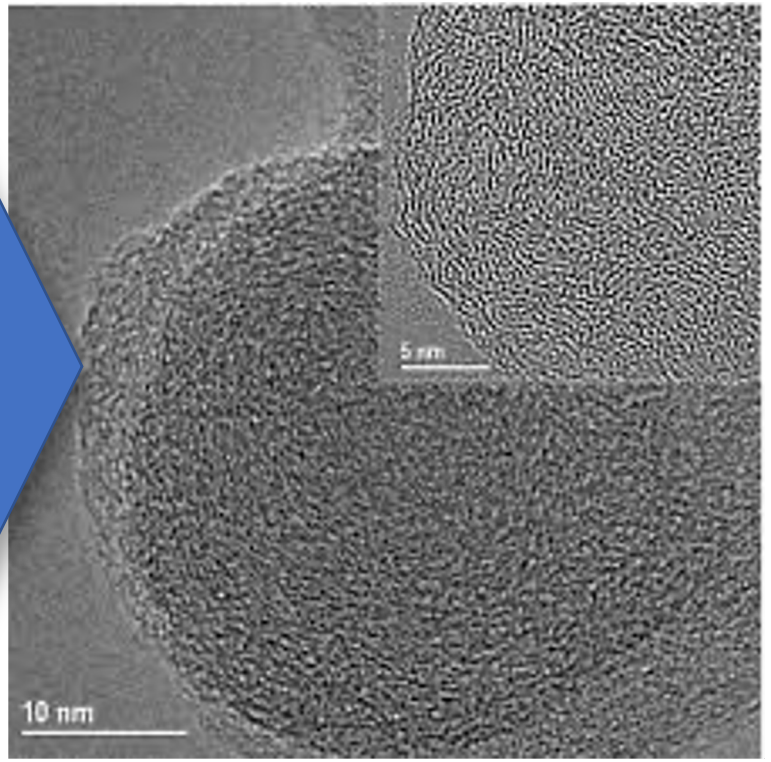
Unusual reaction pathways to hydrocarbon clusters formed in burn pits could bring a paradigm shift to the understanding of UFPs effects on neurodegeneration and neuro-oncology.

What is the significance of carbon or reactive carbon coatings on metal and metal oxide UFPs?

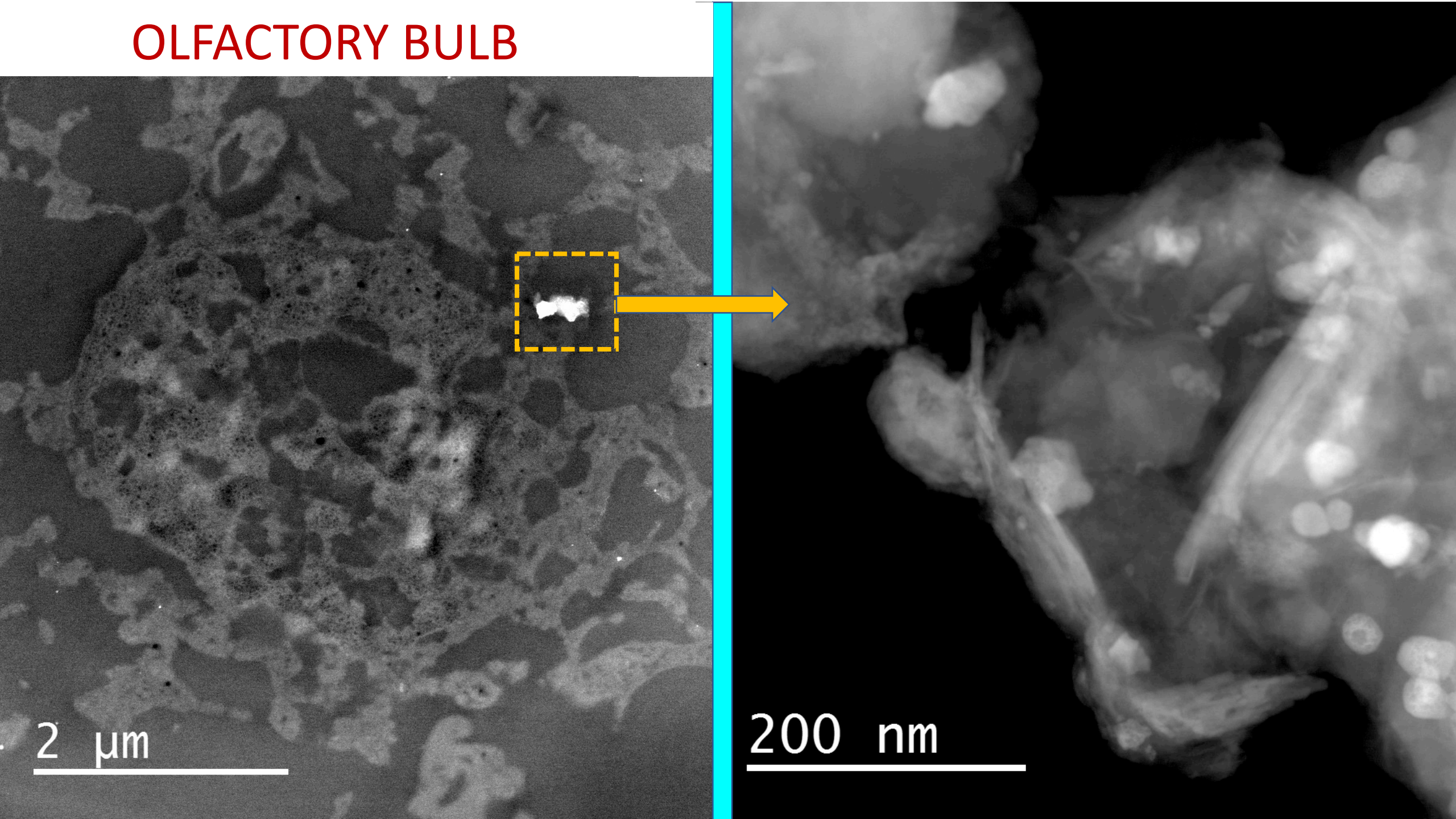
How does this affect potential toxicity and oxidative stress outcomes?



FORMATION OF POLYCYCLIC AROMATIC HYDROCARBONS AND CARBONACEOUS SOLIDS SURROUNDING INORGANIC UFPS



OLFACTORY BULB



AZtec® - Olfactory Bulb 2022

File View Techniques Tools Help

EDS-TEM | Map | Describe Specimen | Acquire and Construct | Analyze Phases | Report Results | Guided | Custom

START STOP Settings

EDS Layered Image 19

Map Data 19

K C Si Al Fe Electron

250nm

Map TruMap QuantMap Display Standard Settings

C Kα1_2 | Mg Kα1_2 | Al Kα1 | Si Kα1 | K Kα1 | Ca Kα1

Ti Kα1 | Fe Kα1 | Zn Kα1 | Pb Lα1 | Electron Image 53

100nm

Minimized Maps | Map Display Type: Weight % | Binning Factor: 1

Confirm Elements

Map Sum Spectrum | Compare... | At% | Copy | Powered by Tru-Q®

cps/eV

keV

Map Details

Save Settings to Profile | Apply Profile Settings

Selected Element Details

Element: Silicon

Label: Si Kα1

Energy Window Selection:

Automatic

Specify Line Series

Specify Energy Window

Lower Energy (keV): 1.688

Search Help

Project Data

Current Site | Data Tree

Site 48

Electron Ima...

Spectrum 45

Site 49

Electron Ima...

Spectrum 46

Spectrum 47

Spectrum 48

Site 50

Electron Ima...

Spectrum 50

Site 51

Step Notes

You can acquire, review, manipulate and process data in Acquire and Construct:

- The smart components, Scan Image, Acquire Map Data and Construct Maps are combined in the Custom mode to provide a single workspace called Acquire and Construct.
- The components are docked in the workspace in the four quadrants. Each component can be undocked in a free floating window. Each window can be dragged on to another monitor, resized and displayed in the full screen view or turned off and on as needed.

If you want to acquire an image, you must first ensure that the 'Acquire an

Mini View

Input Count Rate (cps) Total: 2171

Output Count Rate (cps) Total: 2130

Dead Time 0%

Recommended WD 0.0 mm

Process Time: 3

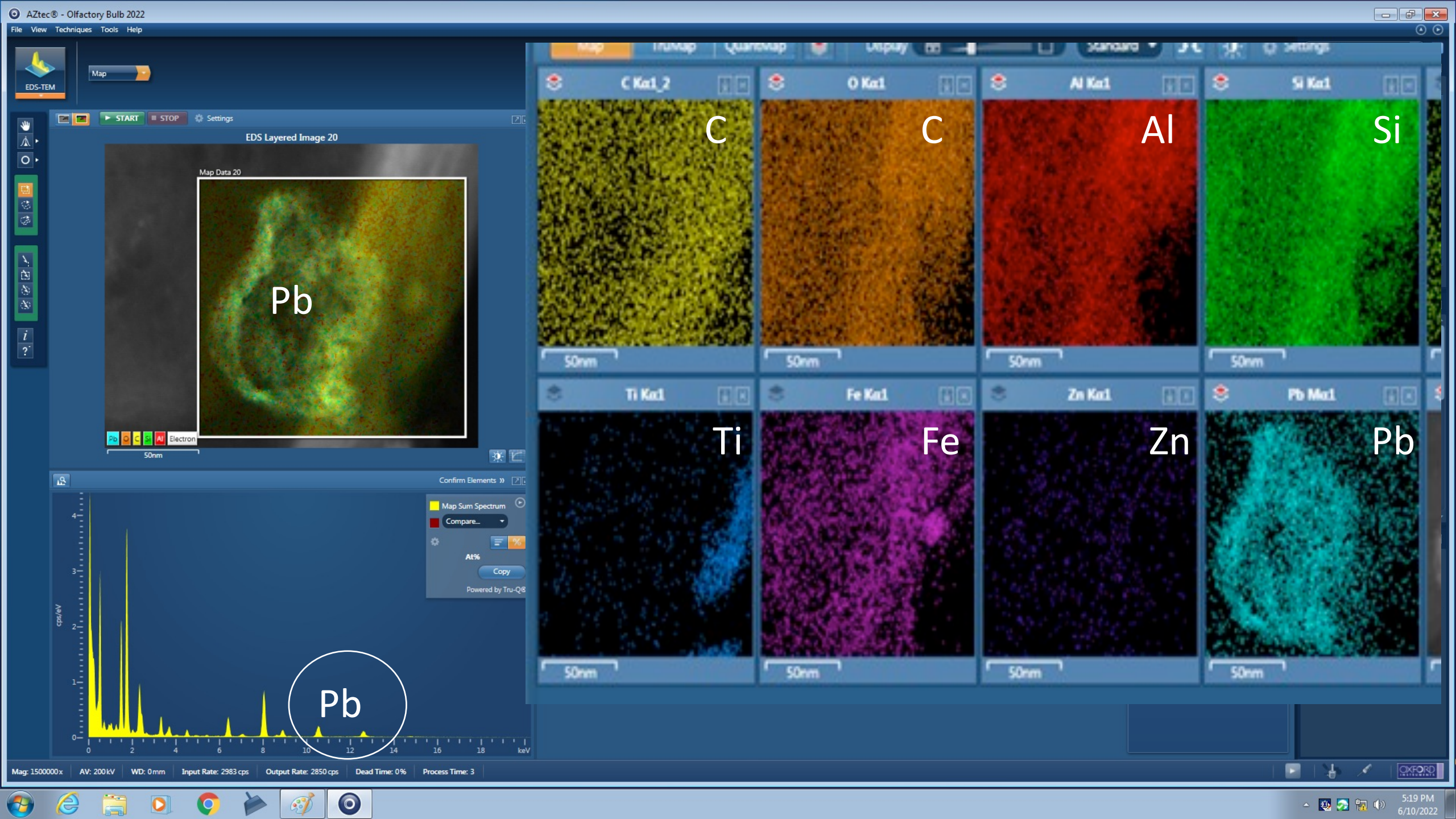
Accelerating Voltage (kV): 200.0

Information

Saved Olfactory Bulb 2022

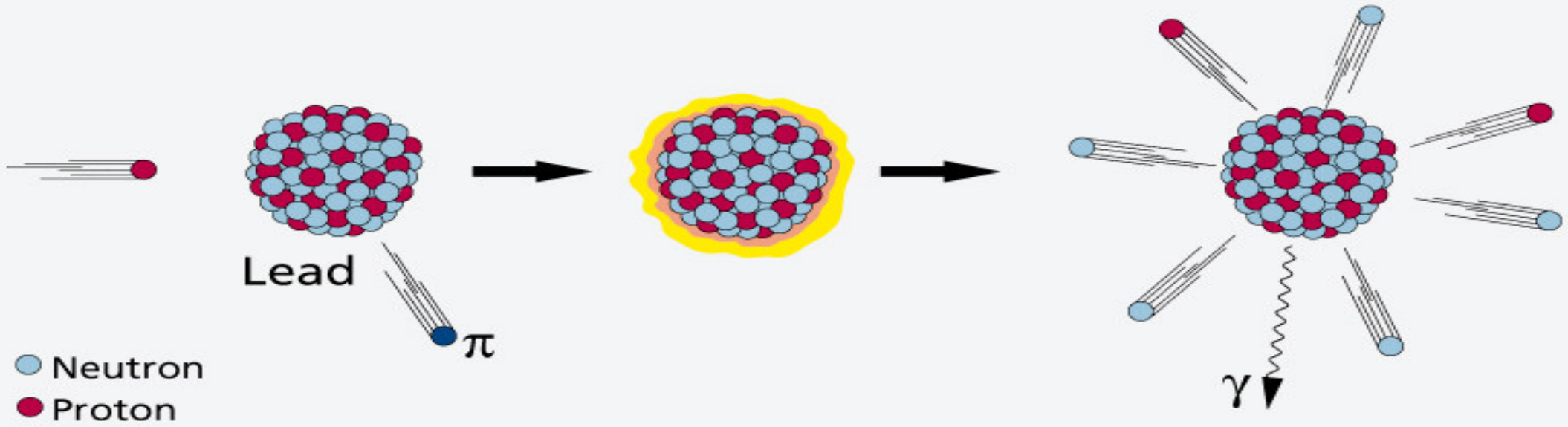
Mag: 250000 x | AV: 200 kV | WD: 0 mm | Input Rate: 2171 cps | Output Rate: 2130 cps | Dead Time: 0% | Process Time: 3

5:05 PM 6/10/2022

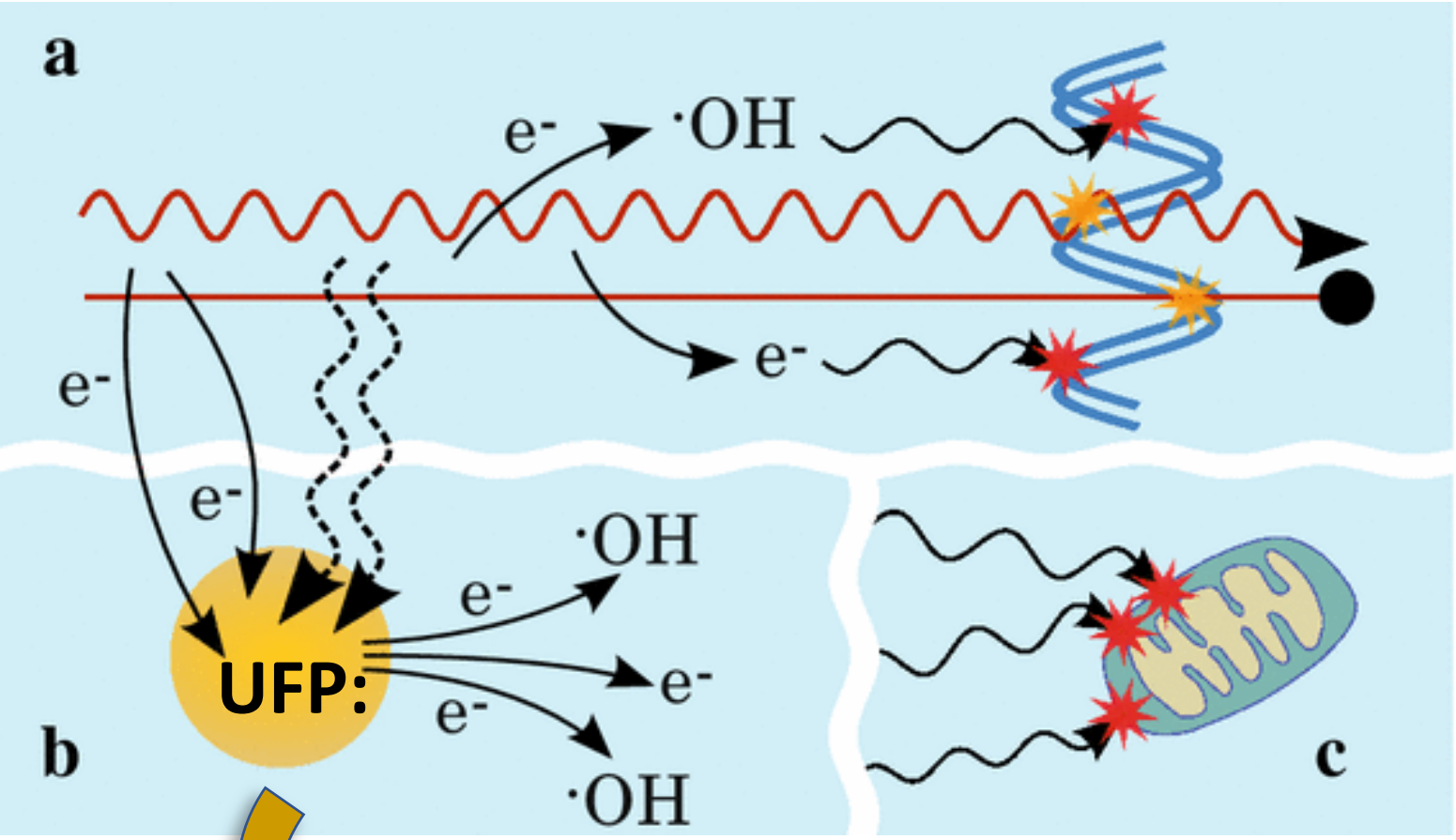

AZtec® - Olfactory Bulb 2022
File View Techniques Tools Help
EDS-TEM
Map
START
STOP
Settings
EDS Layered Image 20
Map Data 20
Pb
Electron
50nm
Confirm Elements
Map Sum Spectrum
Compare...
At%
Copy
Powered by Tru-Q®
cps/eV
keV
Pb
C Ka1_2
C
O Ka1
C
Al Ka1
Al
Si Ka1
Si
Ti Ka1
Ti
Fe Ka1
Fe
Zn Ka1
Zn
Pb Ma1
Pb
50nm
Mag: 1500000x
AV: 200 kV
WD: 0 mm
Input Rate: 2983 cps
Output Rate: 2850 cps
Dead Time: 0%
Process Time: 3
5:19 PM
6/10/2022

Pb-UFP

EXAMPLE:
Mechanisms for Glioblastoma after UFPs in OB?



Radiation interacts with lead nucleus the nucleus will be heated up and potentially alter tissue and cause DNA damage or mutations.



Mechanisms of cellular damage in the presence of nanoparticles.

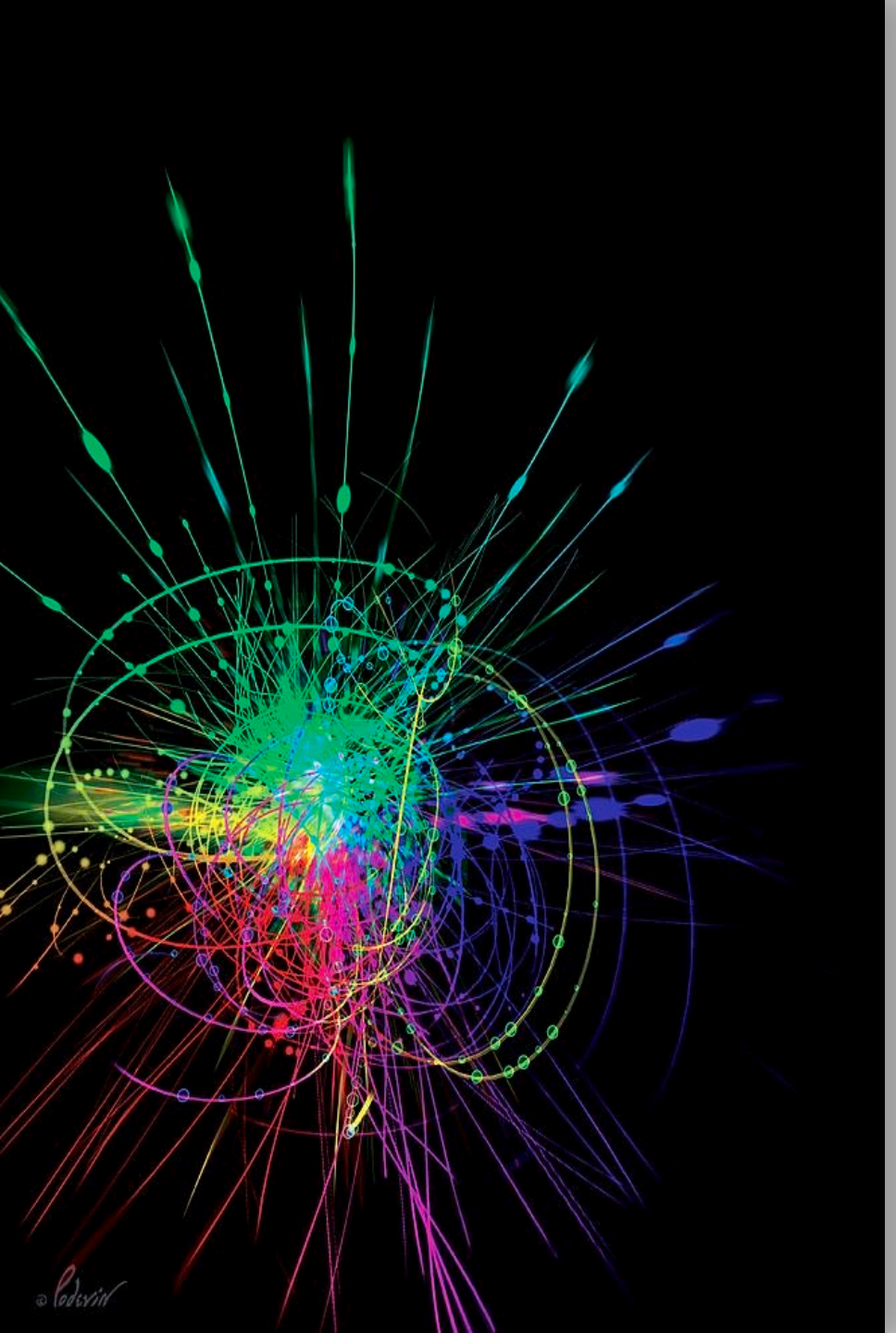
In addition to the direct and indirect damage to DNA or other parts of the cell,
there may also be an interaction of radiation with NPs.

Production of radicals and other reactive species (like ··OH radicals); secondary electrons produced by the radiation or by NPs may also induce further electron emission from NPs.

All the secondary species may diffuse and damage other parts of the cell (like **mitochondria**).

UFPs in OB and Brain

Oxidative stress and Inflammation

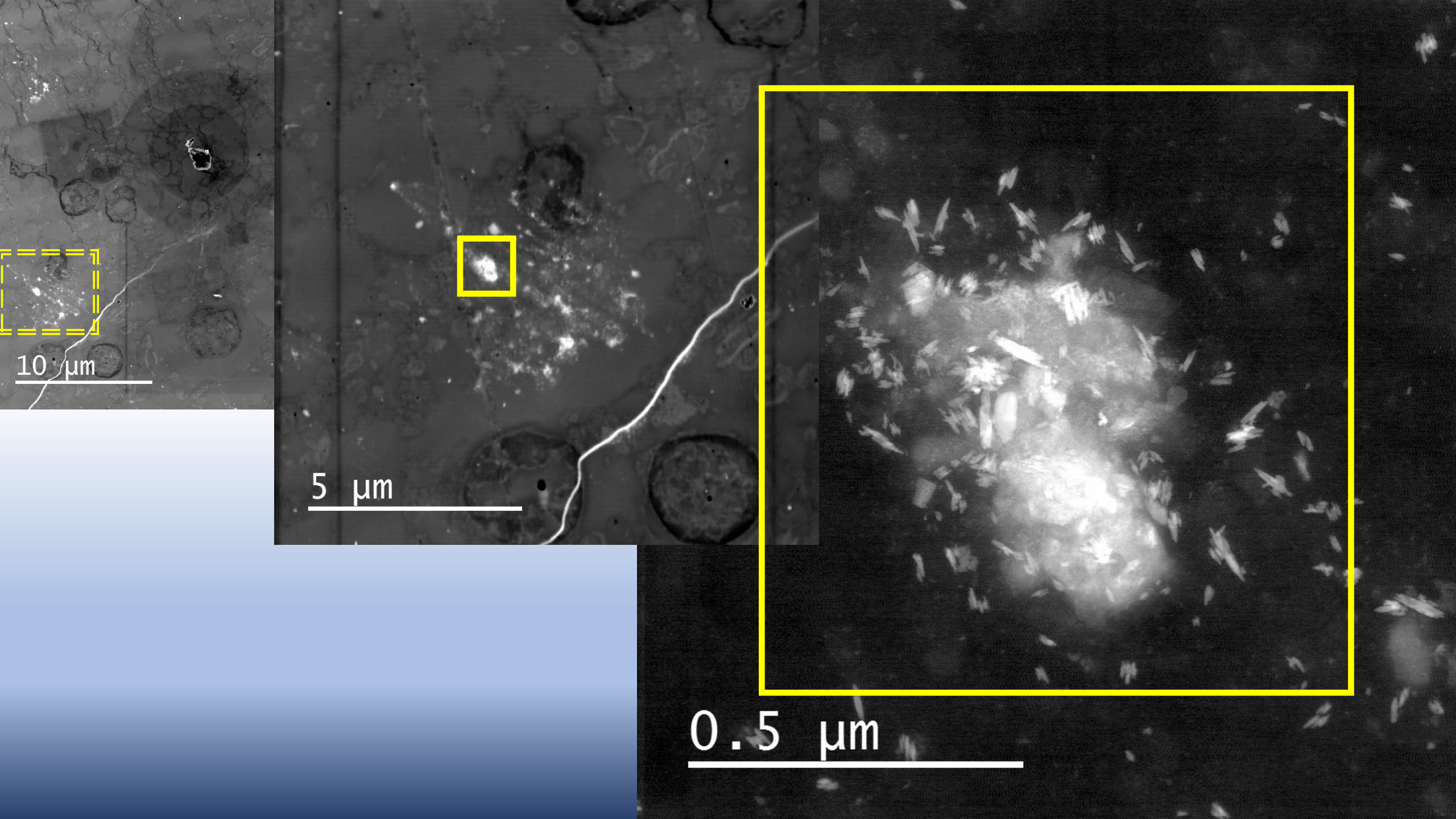


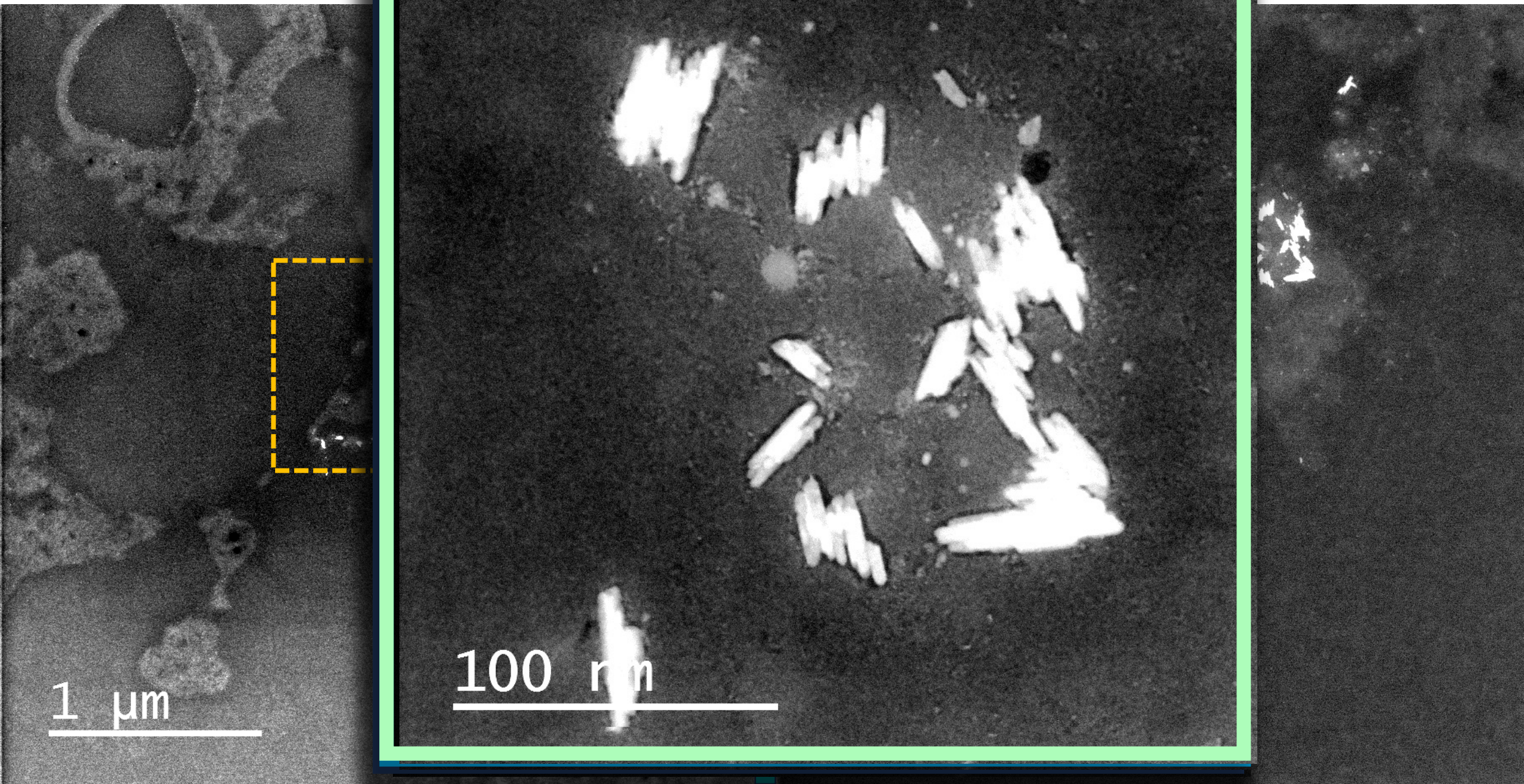
Ionizing Radiation

Ionizing Radiation: ➡ deposited energy can adversely affect healthy tissue, especially in the case of photon radiation (gamma and X-rays).

In addition to effects from IR, nanoparticles can locally increase the damaging effect of both photon and ion radiation.

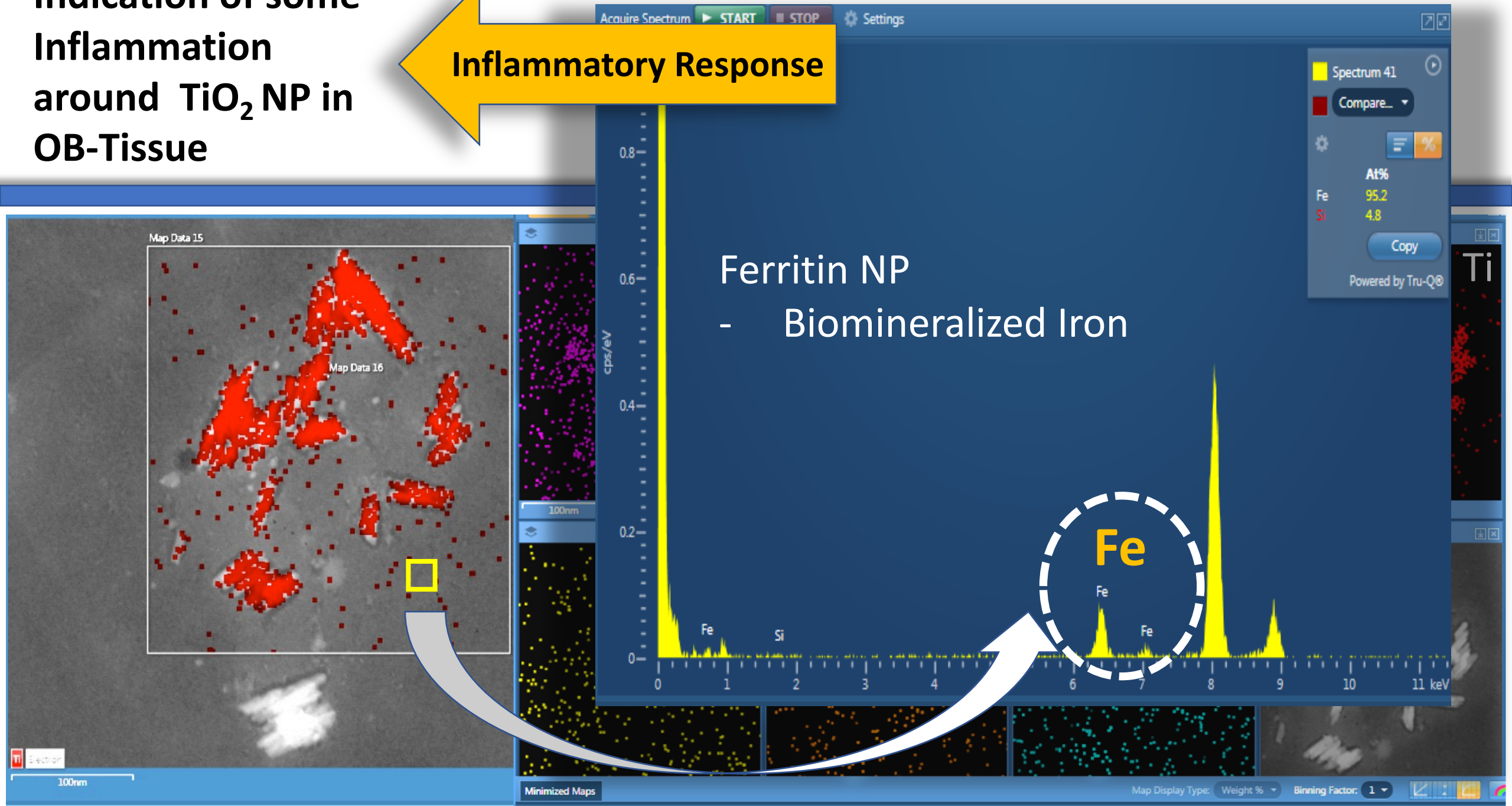
Mechanisms?
Ionizing Radiation "Photons and Ions" in the presence and absence of pollution–derived UFPs inside tissues.


10 µm
5 µm
0.5 µm


1 µm
100 nm

Indication of some Inflammation around TiO_2 NP in OB-Tissue

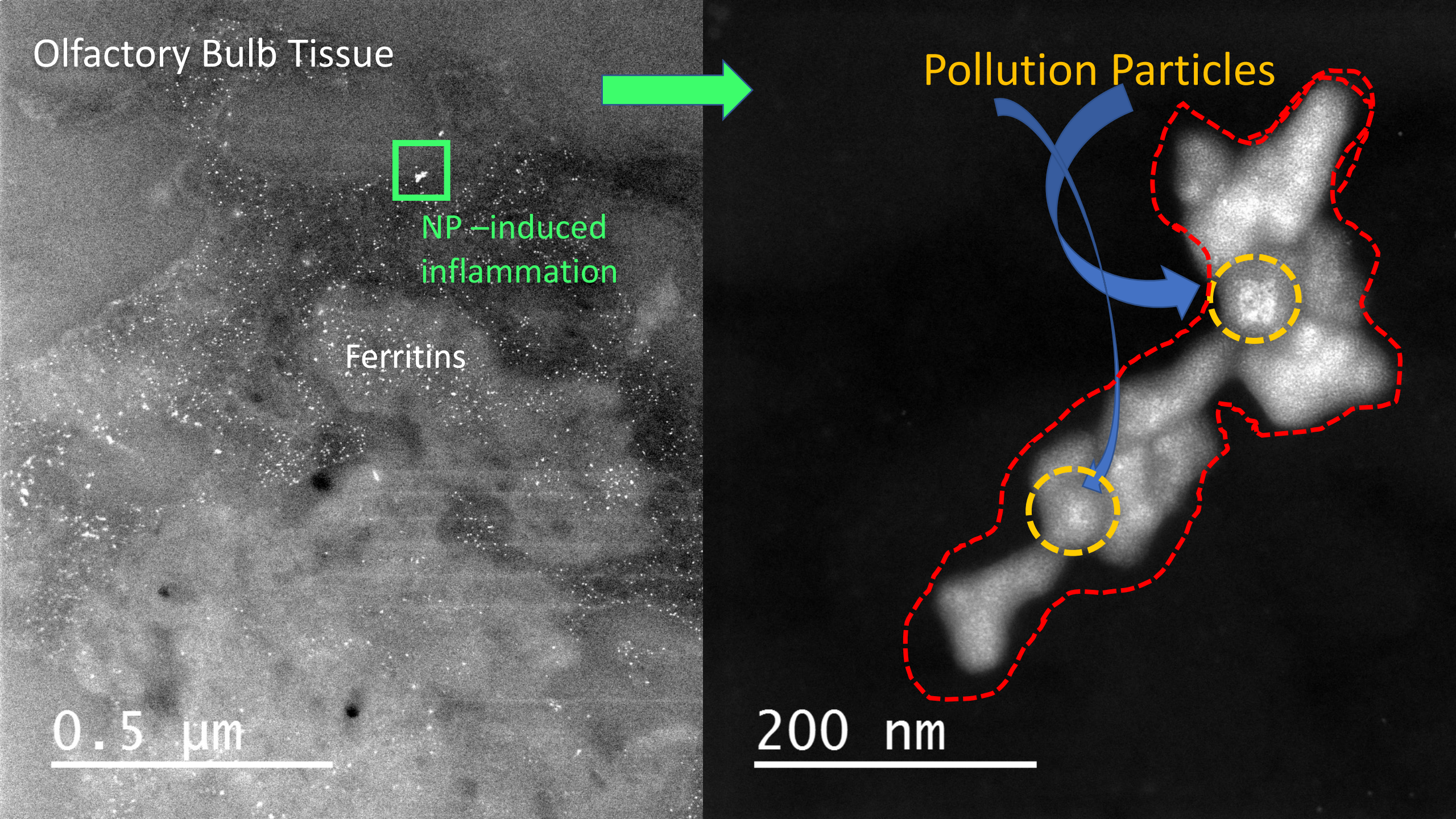
Inflammatory Response

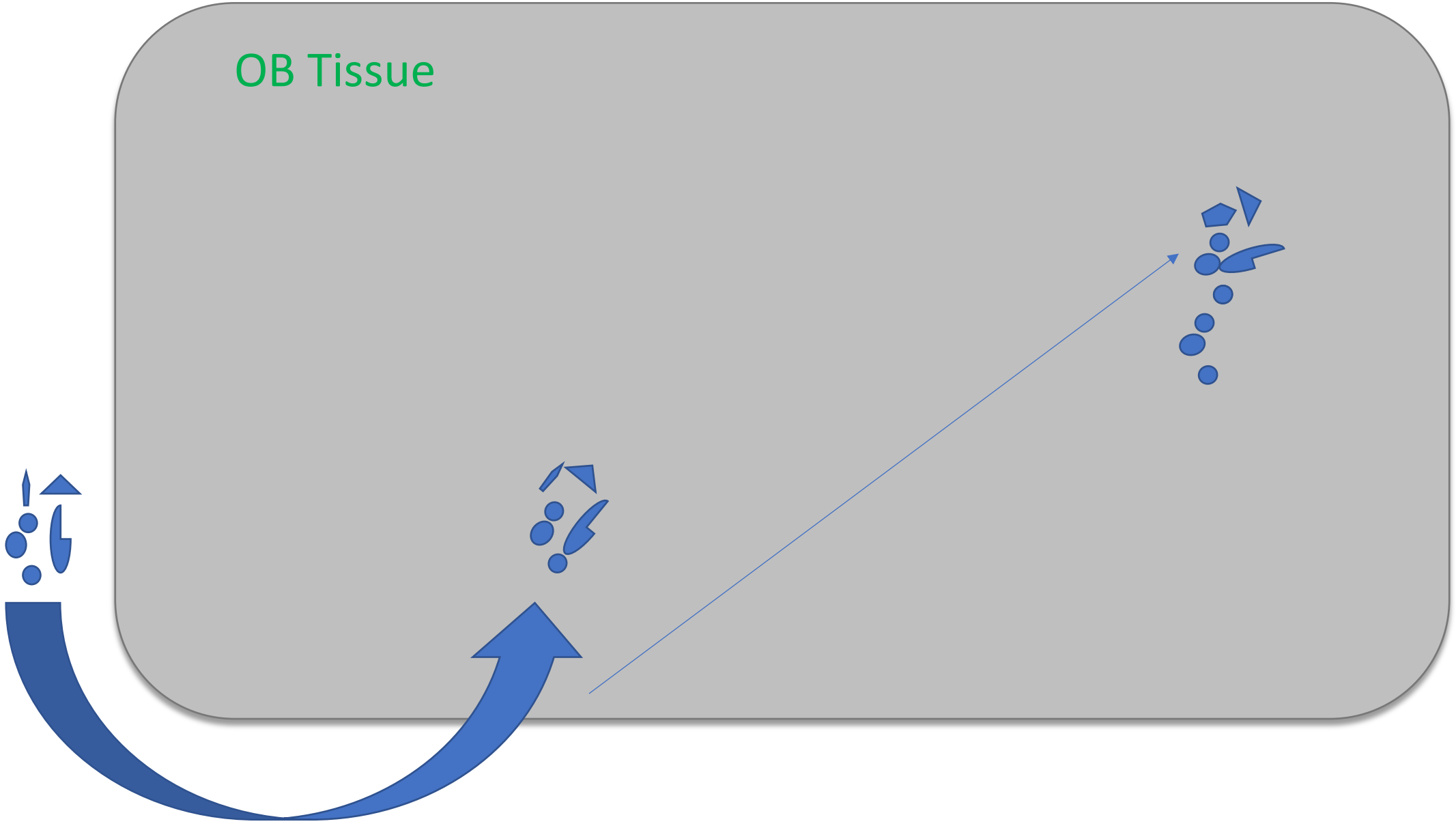


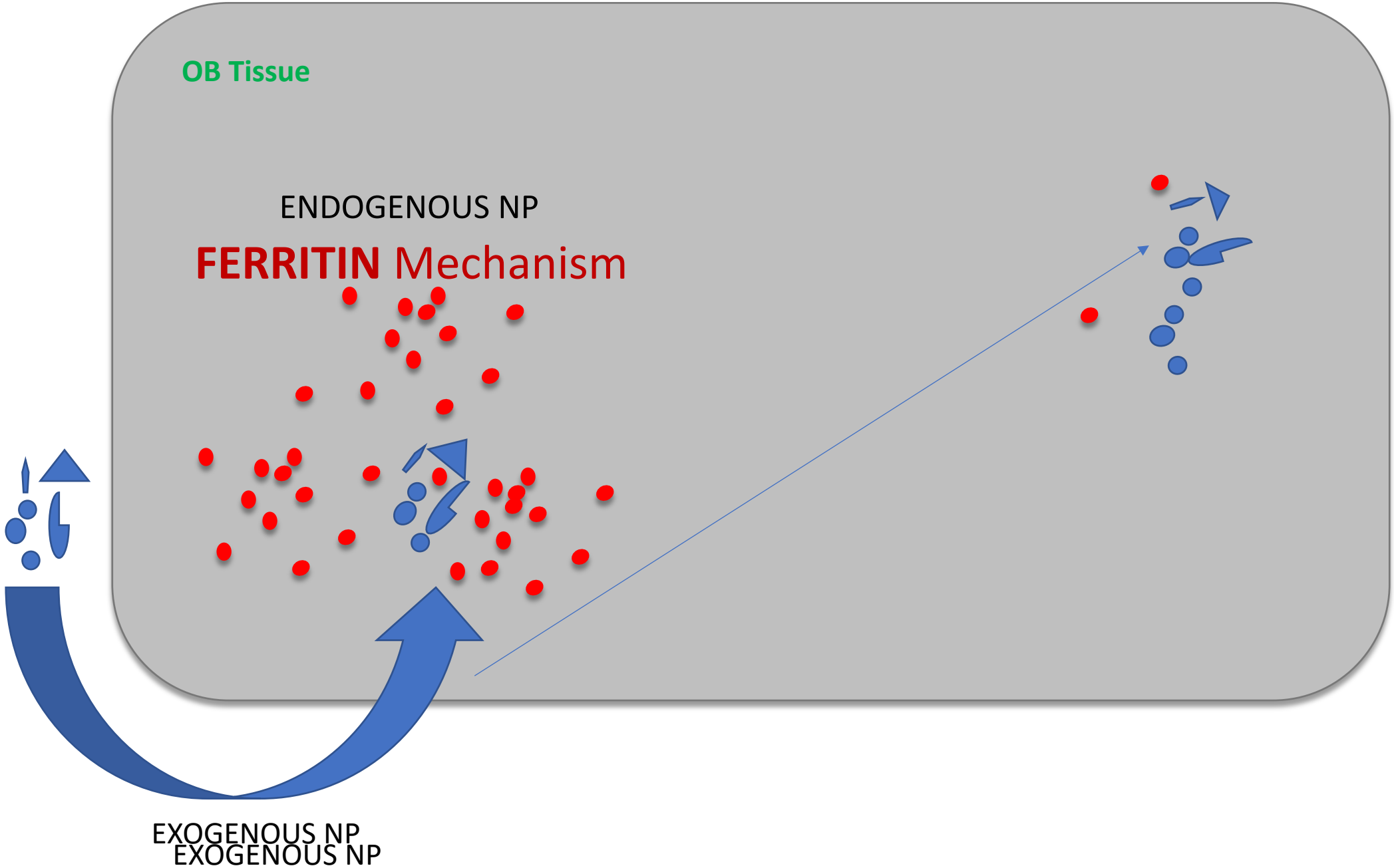
Ferritin NP

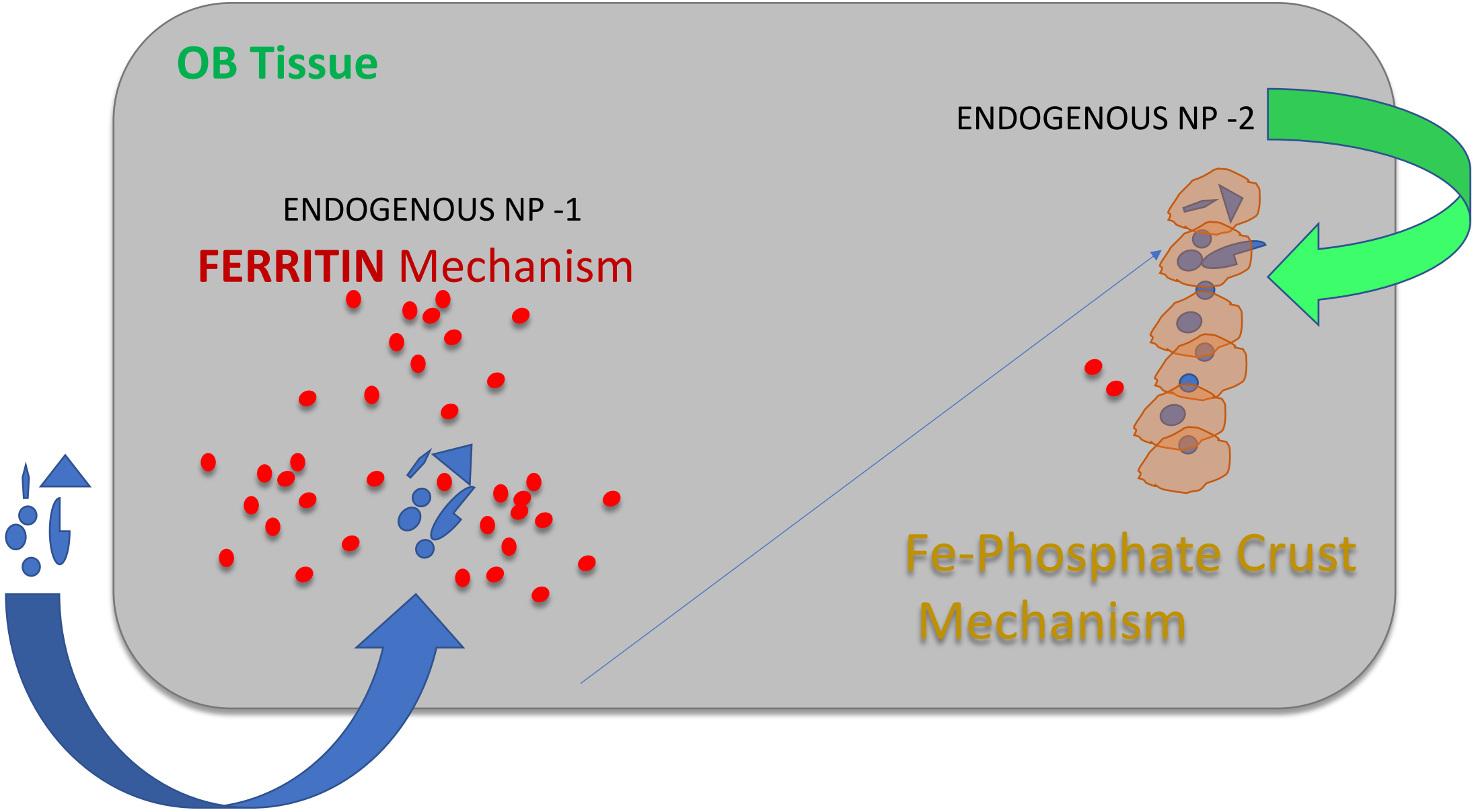
- Biomineralized Iron

EXOGENOUS Nanoparticle Transport to OB and Tissue Interaction with Ferritin Mechanism

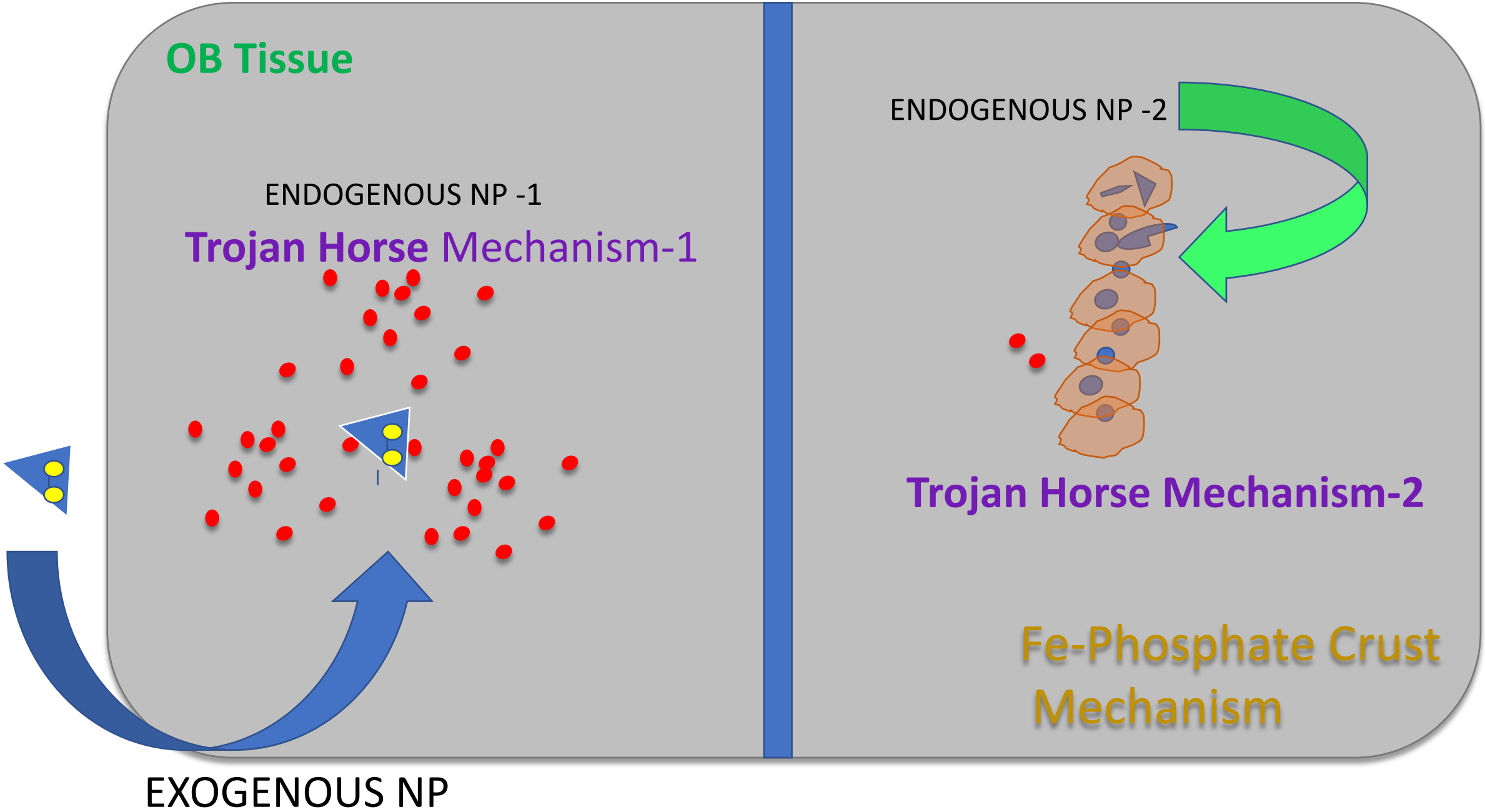

Olfactory Bulb Tissue
NP –induced inflammation
Ferritins
0.5 µm
Pollution Particles
200 nm

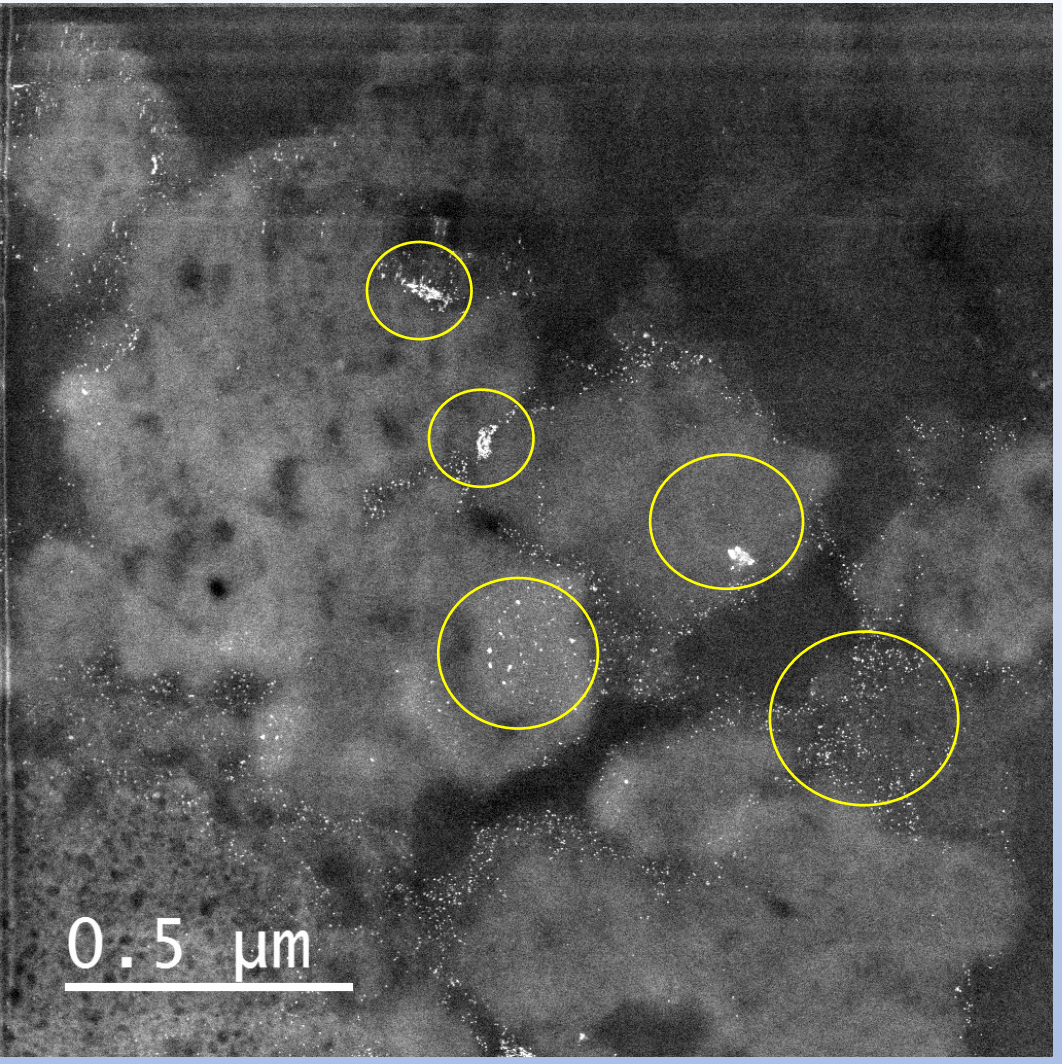

OB Tissue
EXOGENOUS NP


OB Tissue
ENDOGENOUS NP
FERRITIN Mechanism
EXOGENOUS NP
EXOGENOUS NP

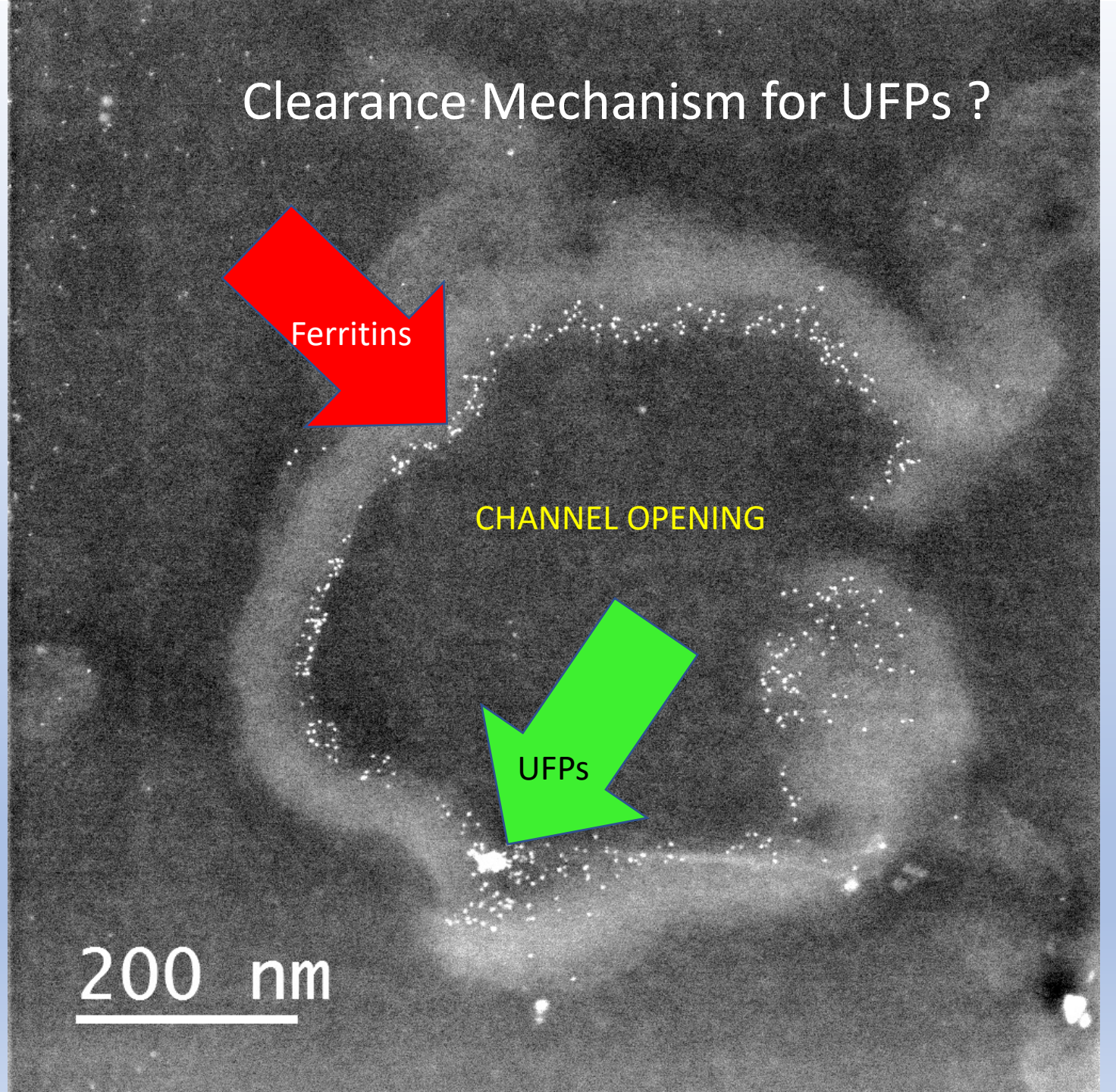

OB Tissue
ENDOGENOUS NP -2
ENDOGENOUS NP -1
FERRITIN Mechanism
Fe-Phosphate Crust Mechanism
EXOGENOUS NP

2 Distinct TROJAN-HORSE MECHANISMS



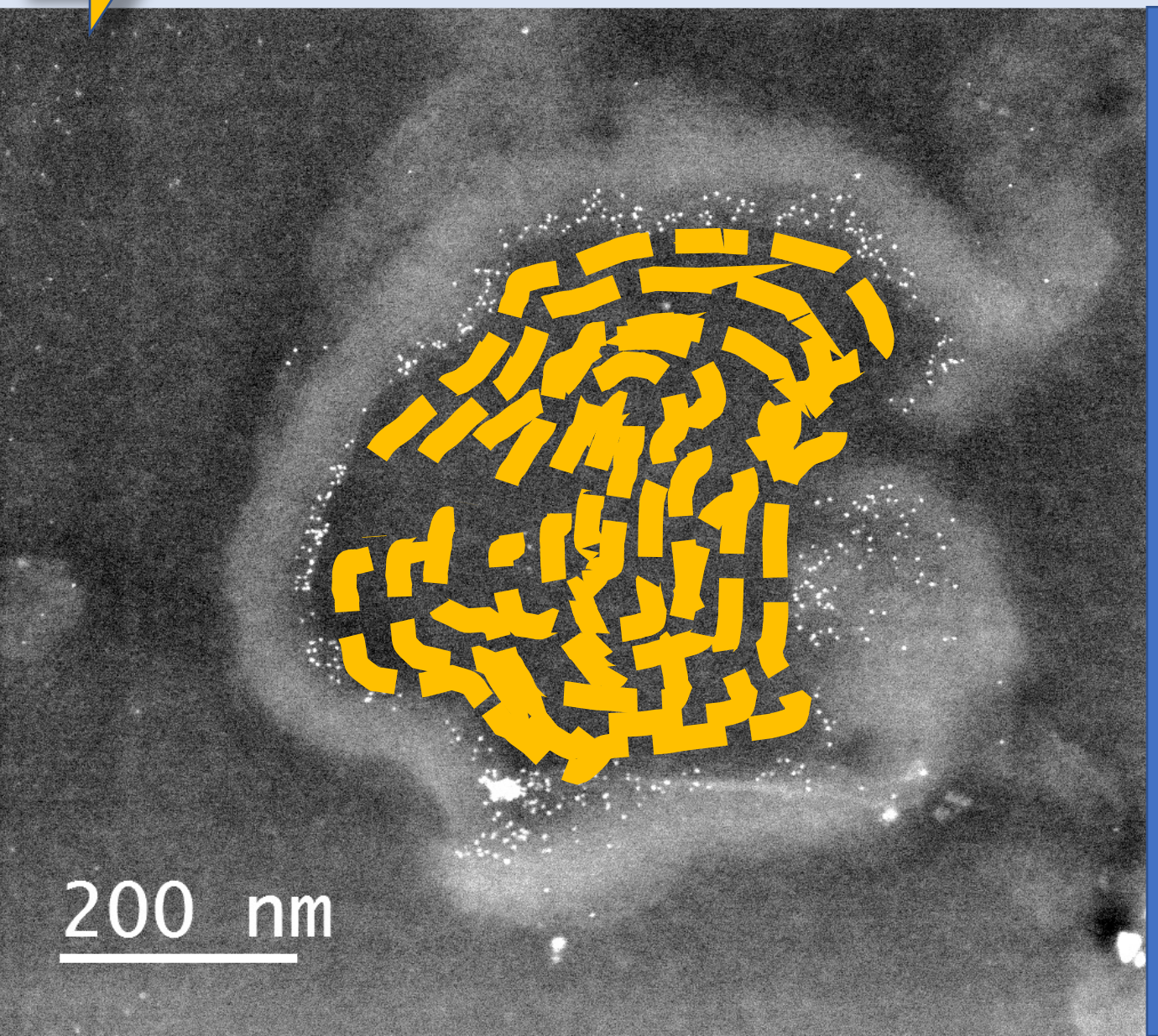


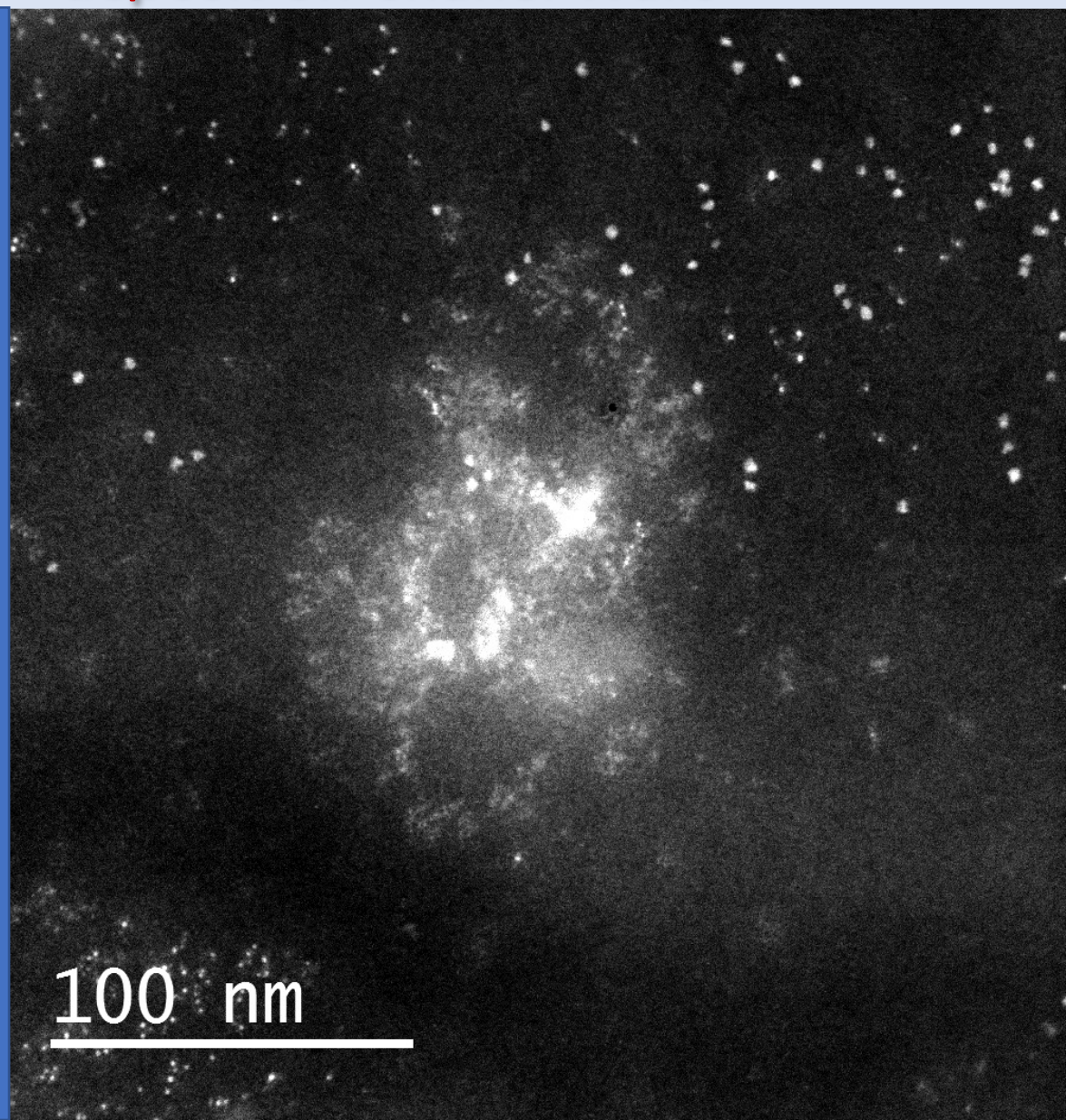
Microglia and Glymphatic Channels for Clearance of Debris from Brain?

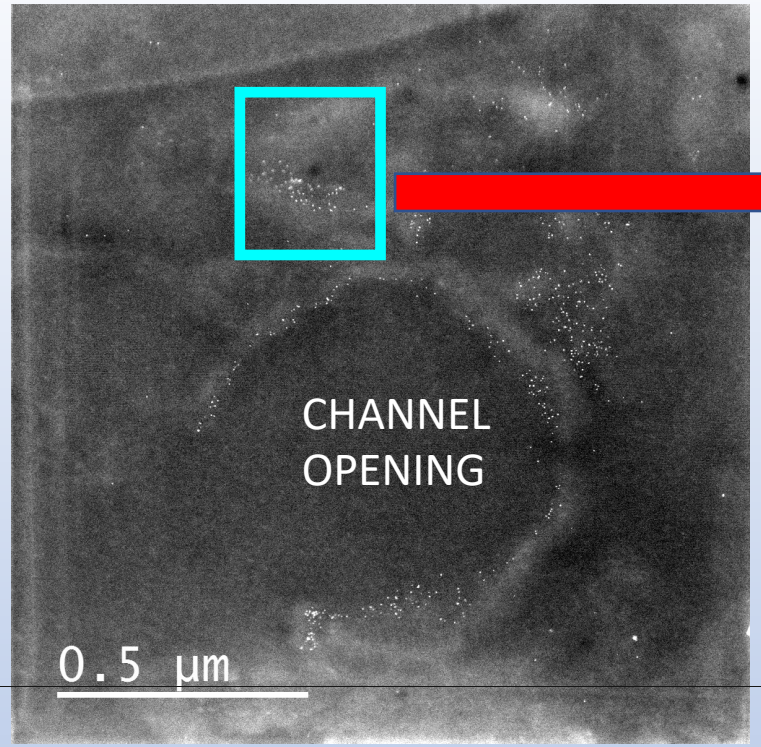


Glymphatic Drainage Mechanisms:

Invader UFPs and Ferritin NPs deposit on Chanel Walls



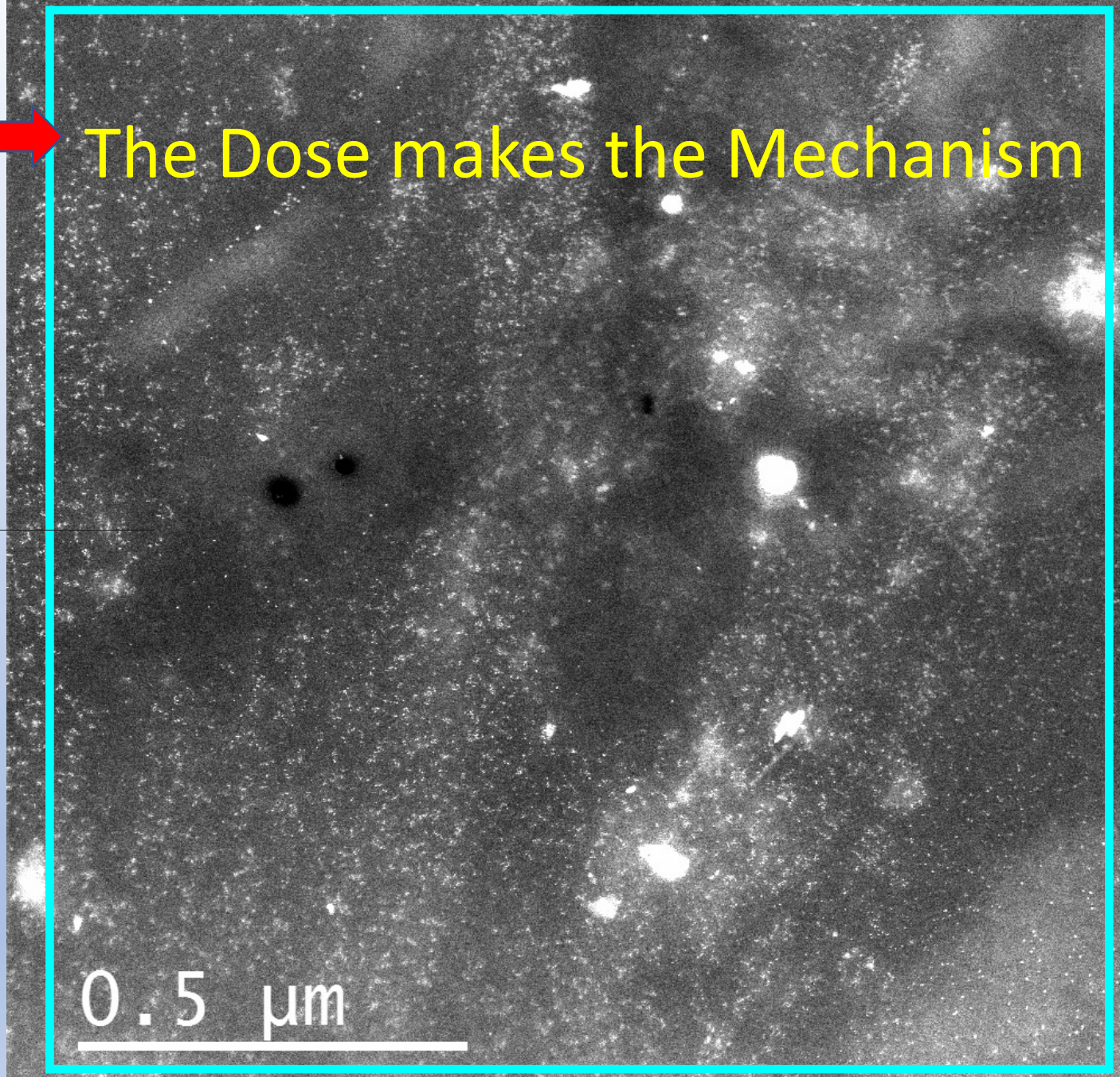


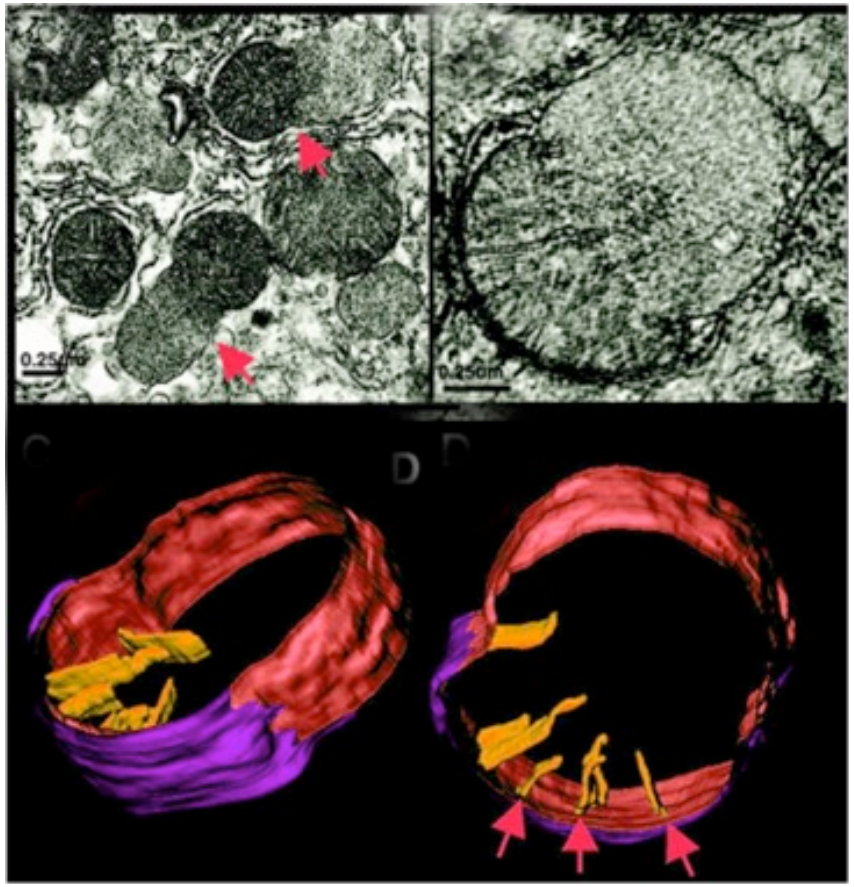


"The Dose makes the Poison"

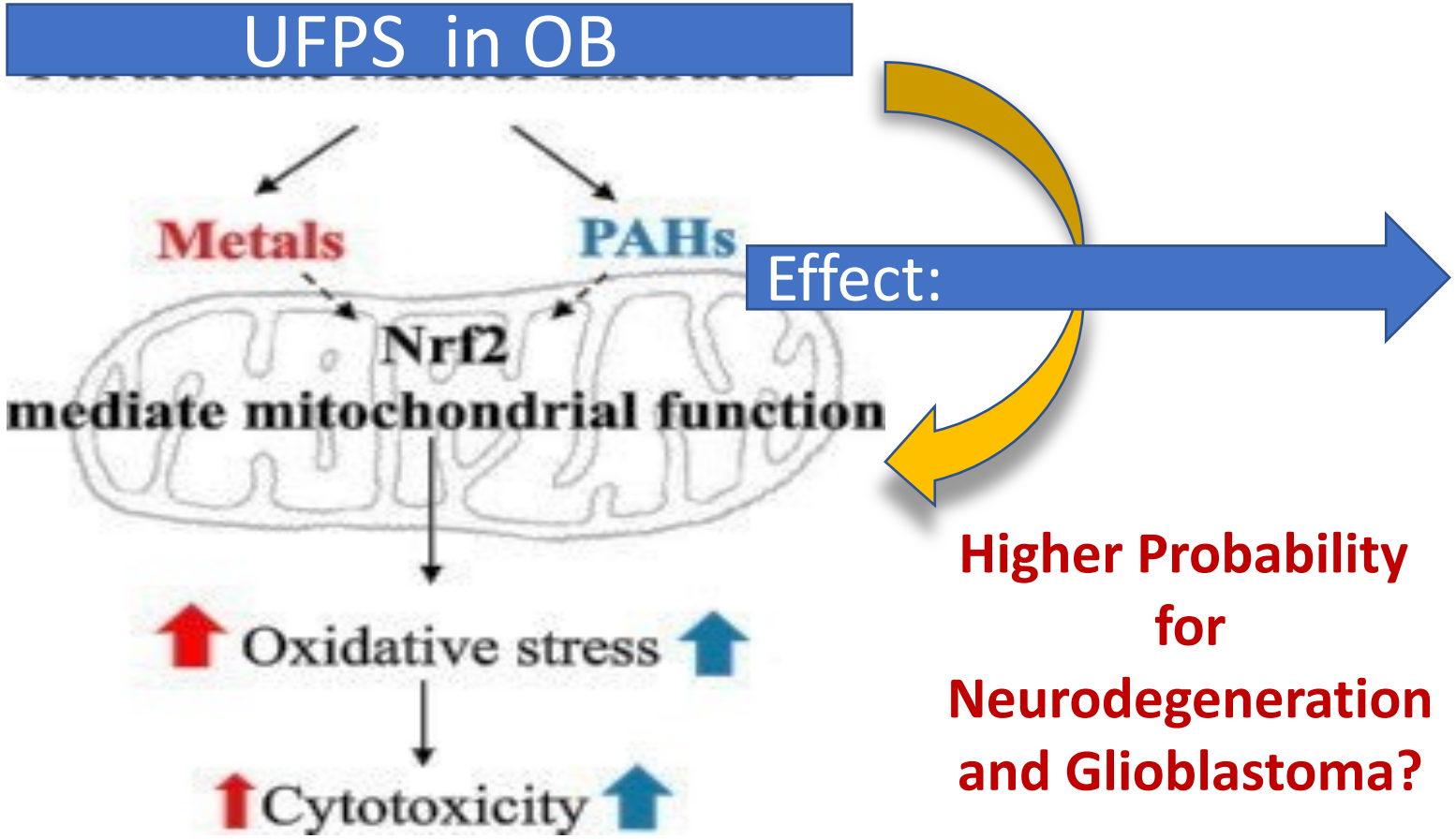
(Paracelsus)

Metal Buildup in Tissue after Ferritin Biomineralization triggered by Invader UFPs and Inflammation



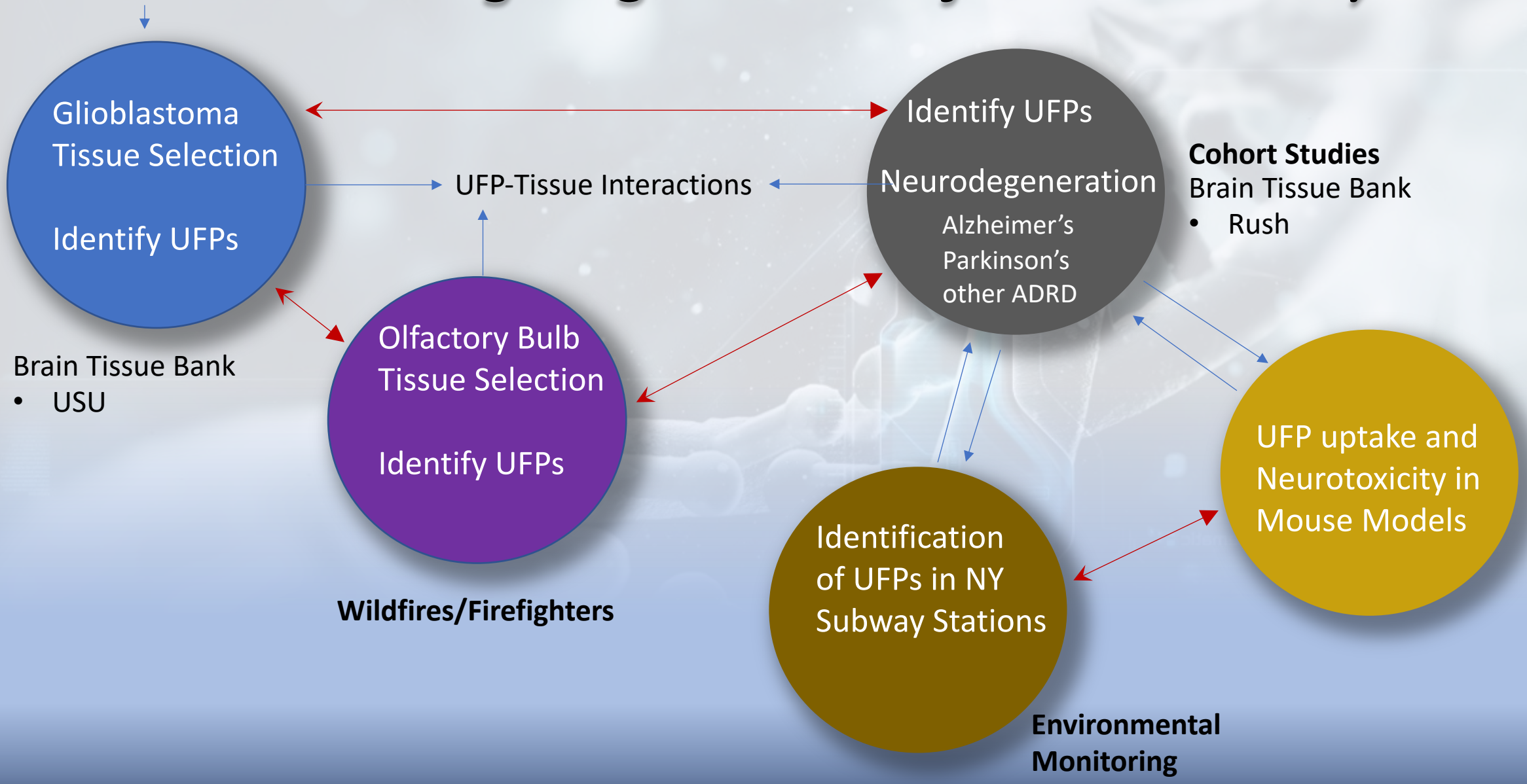


Cells interact with UFPs and damage other parts of the cell (like **mitochondria**).



Cell interaction with UFPs in tissues (OB and Brain) need to be further investigated to better understand how pollution (burn pits emissions) exposure to Vets may influence medical outcomes from ionizing radiation exposure.

Ongoing Studies of UFPs Toxicity



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Air Pollution and Alzheimer's Dementia: Neuropathologic and Olfactory Mechanisms in Multi-Ethnic Longitudinal Cohorts

Epidemiology	Surgery	Neurology	Pathology	Nanotoxicology	Nanotechnology
J Weuve	**JJ Pinto**	**DA Bennett**	**J Schneider**	**G Oberdorster**	**UM Graham**
Boston University	The University of Chicago	Rush	Rush	University of Rochester Medical Center	University of Kentucky

‘THE DOSE IS THE POISON’

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