

Developing high-throughput organ-on-a-chip models to investigate the effects of ionizing radiation on the central nervous system

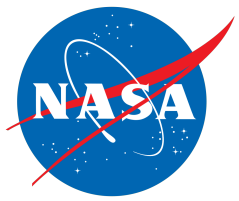
Sherina Malkani

Blue Marble Space Institute of Science

Space Biosciences Research Branch, NASA Ames Research Center



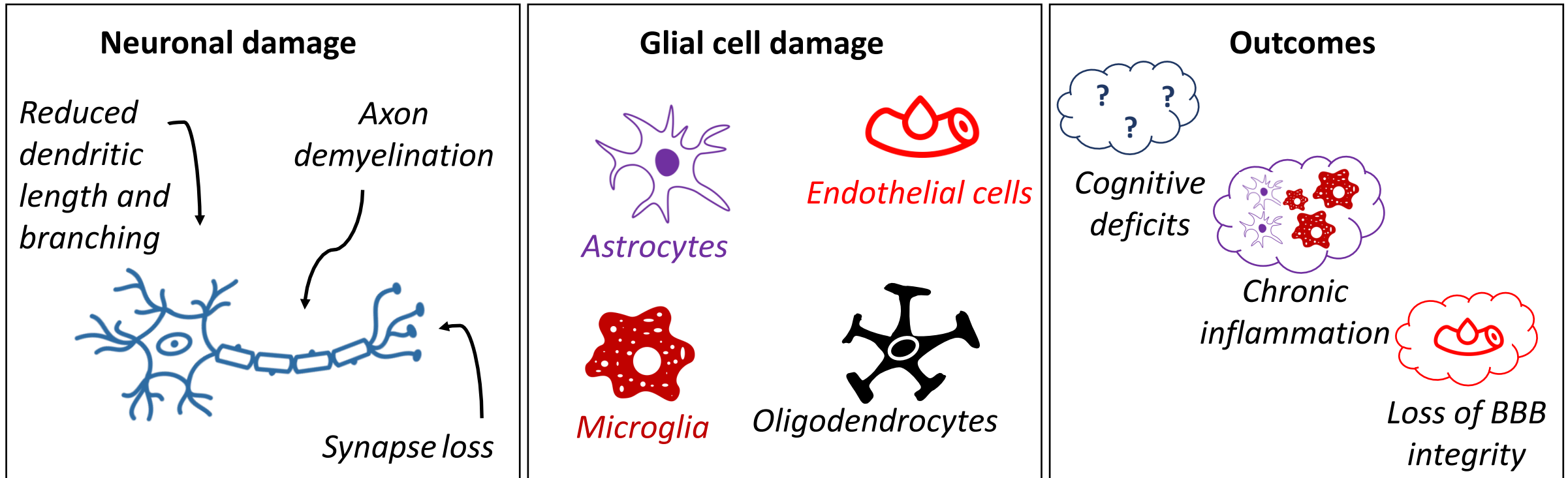
YOUNG SCIENTIST PROGRAM
BLUE MARBLE SPACE INSTITUTE OF SCIENCE

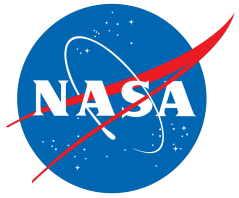


Ionizing radiation effects on the central nervous system (CNS)

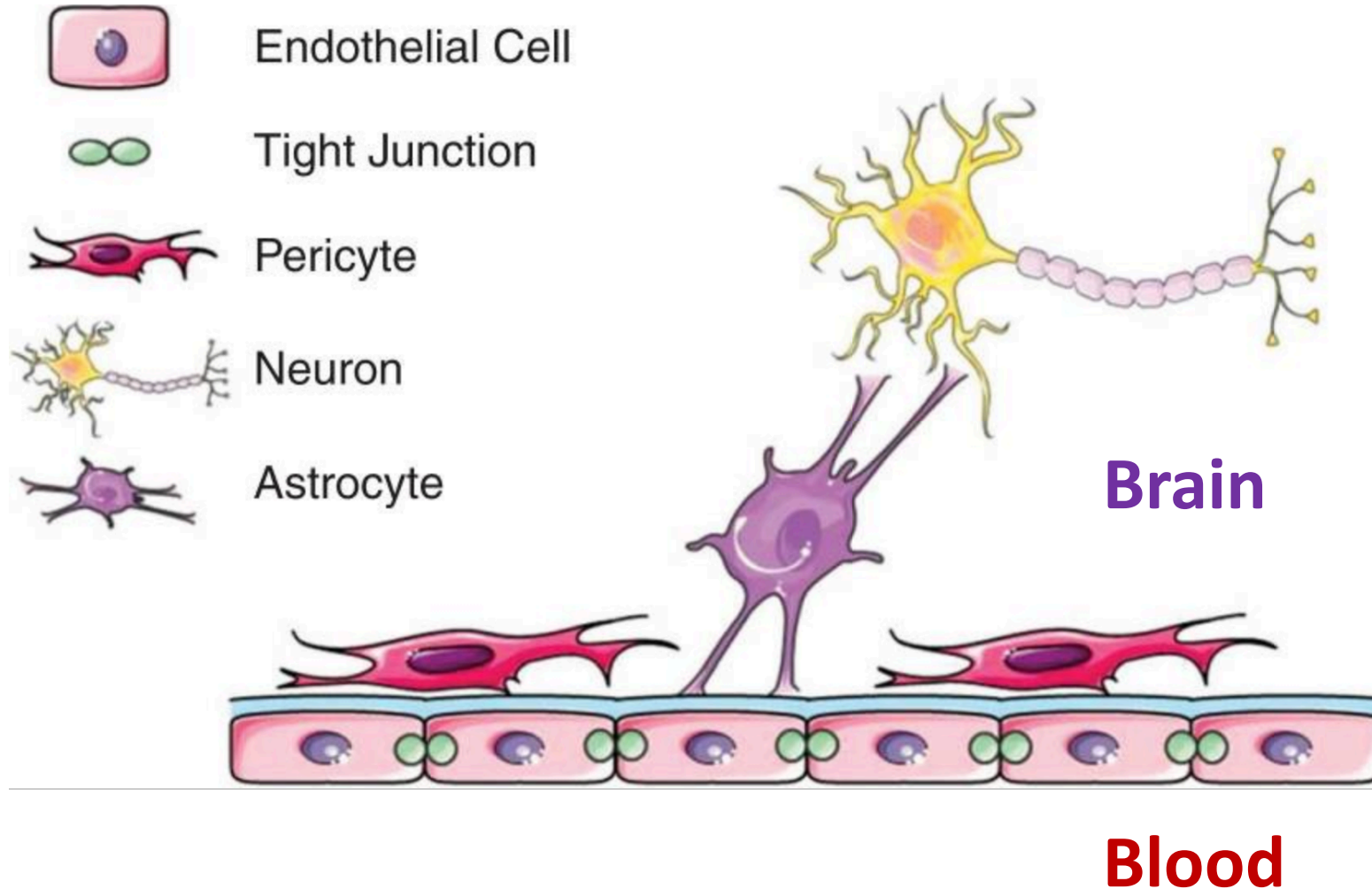


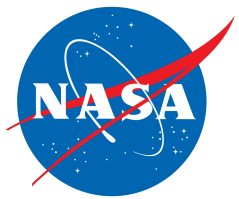
Ionizing Radiation
Galactic Cosmic Rays
Solar Particle Events





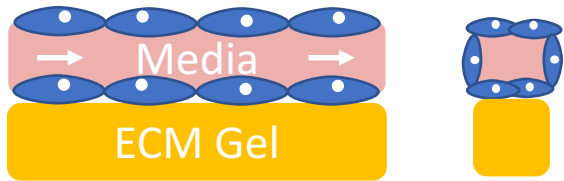
Role of the blood-brain barrier (BBB) in CNS



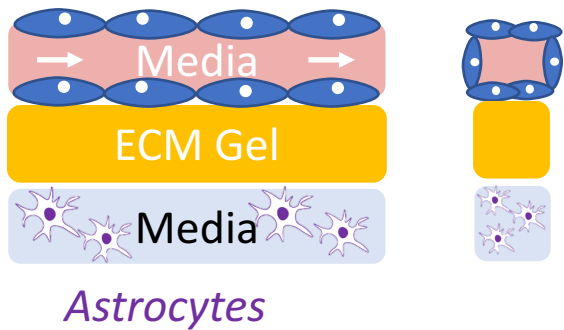


OrganoPlate system

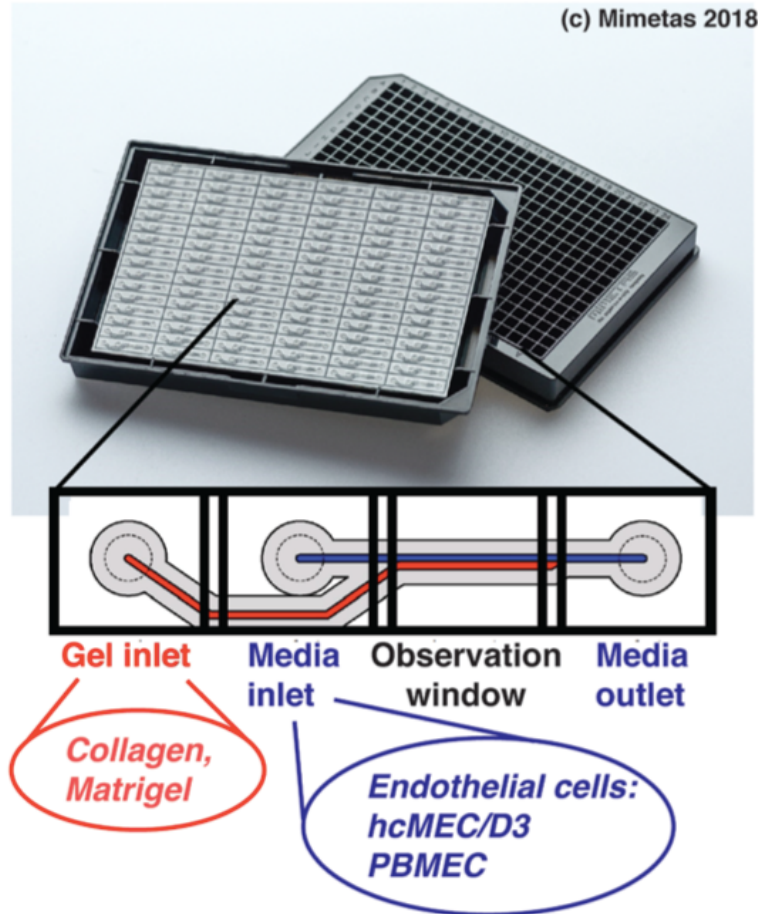
2-lane plate setup
Endothelial cells only



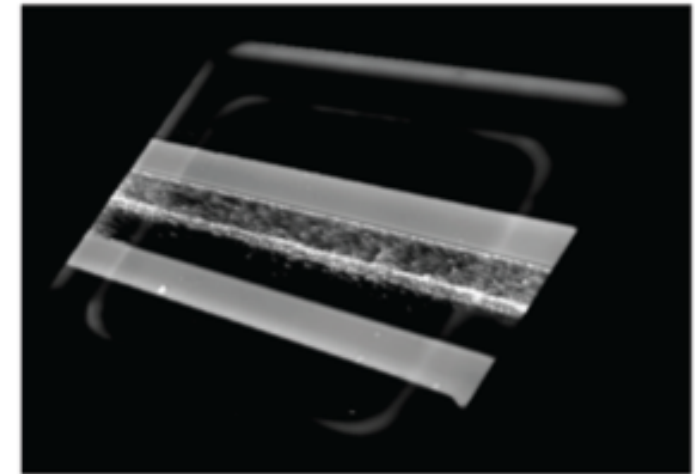
3-lane plate setup
Endothelial cells



Goal

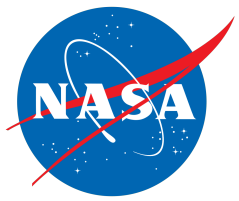


Platform



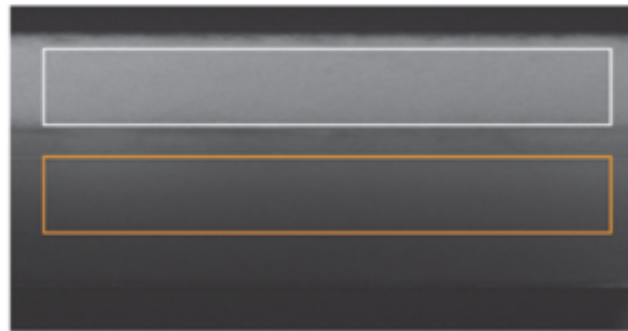
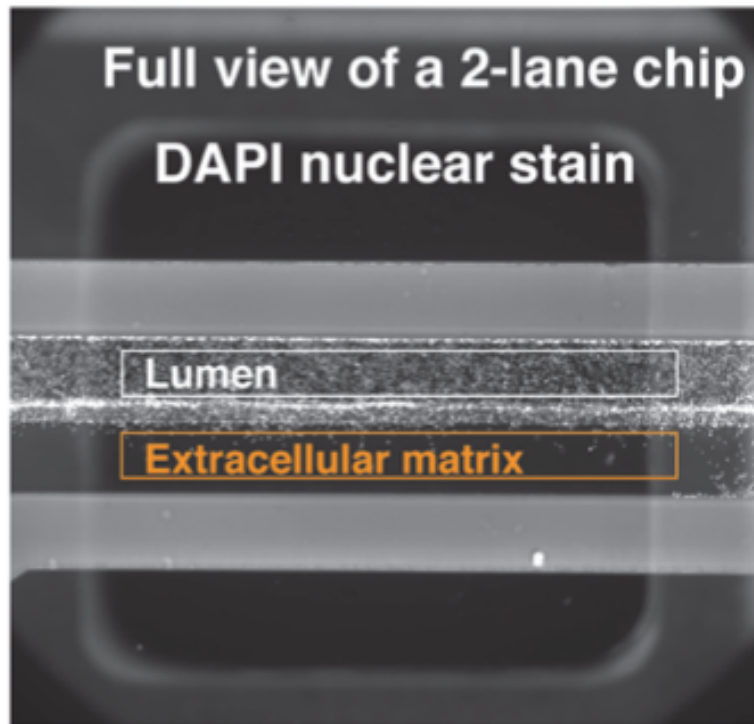
DAPI nuclear stain of endothelial cells on a chip in a 2-lane plate

Execution



Using OrganoPlates to measure human CNS responses to ionizing radiation

- BBB permeability and morphology and astrocyte activation after X-ray irradiation
- Immediate and delayed responses
- Oxidative stress and cytokine production

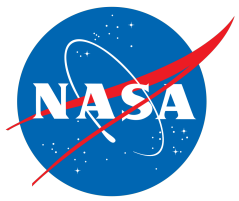


Non-leaky barrier



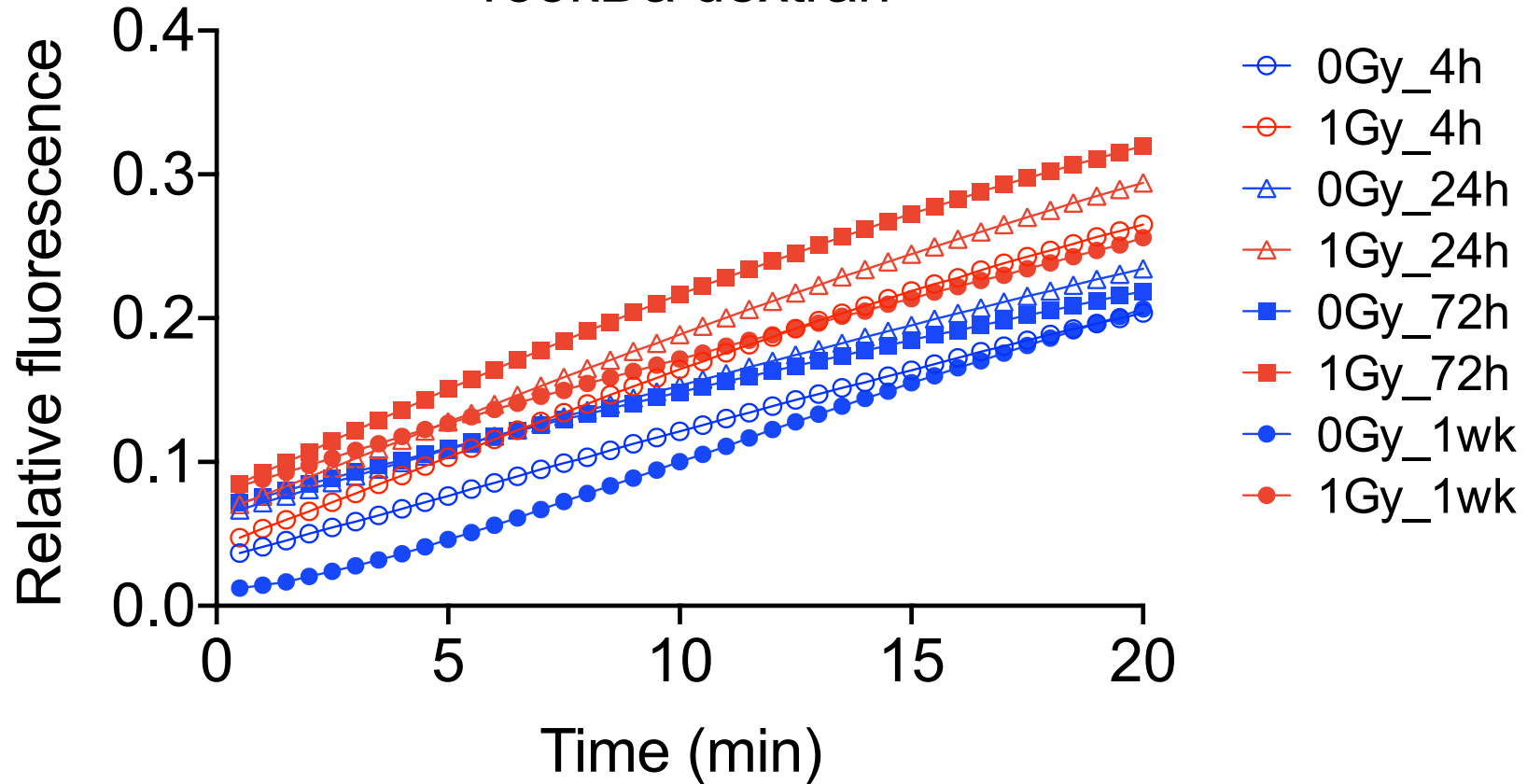
Leaky barrier

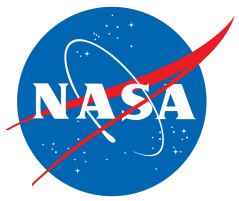
*Relative fluorescence of dye in
extracellular matrix channel / lumen channel*



1Gy X-ray irradiation increases BBB permeability

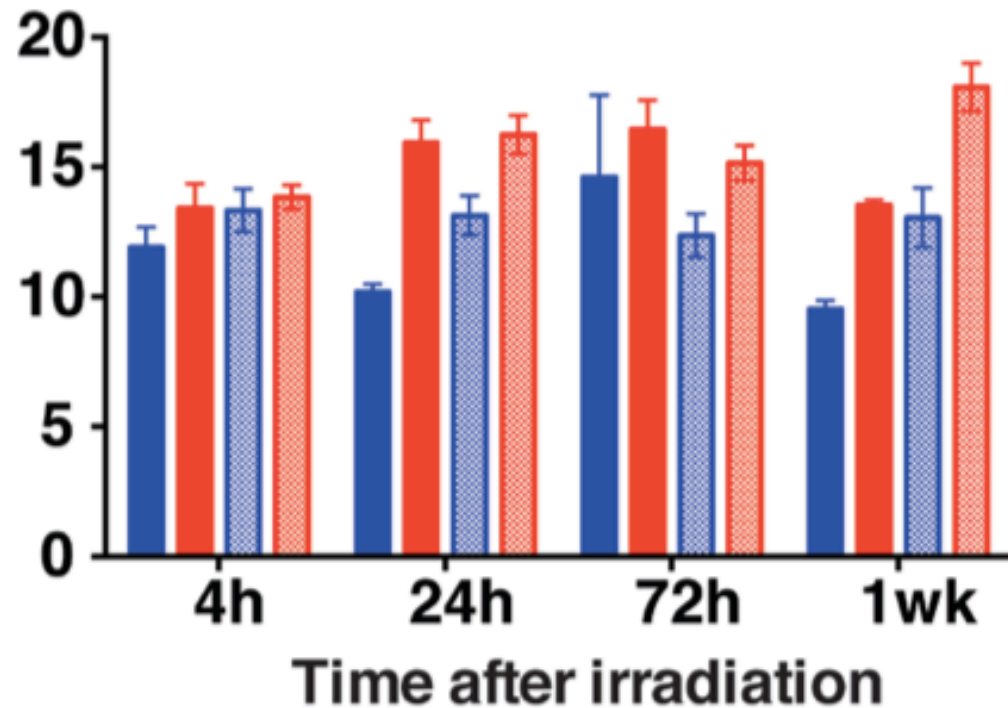
hCMEC/D3 endothelial cells
155kDa dextran



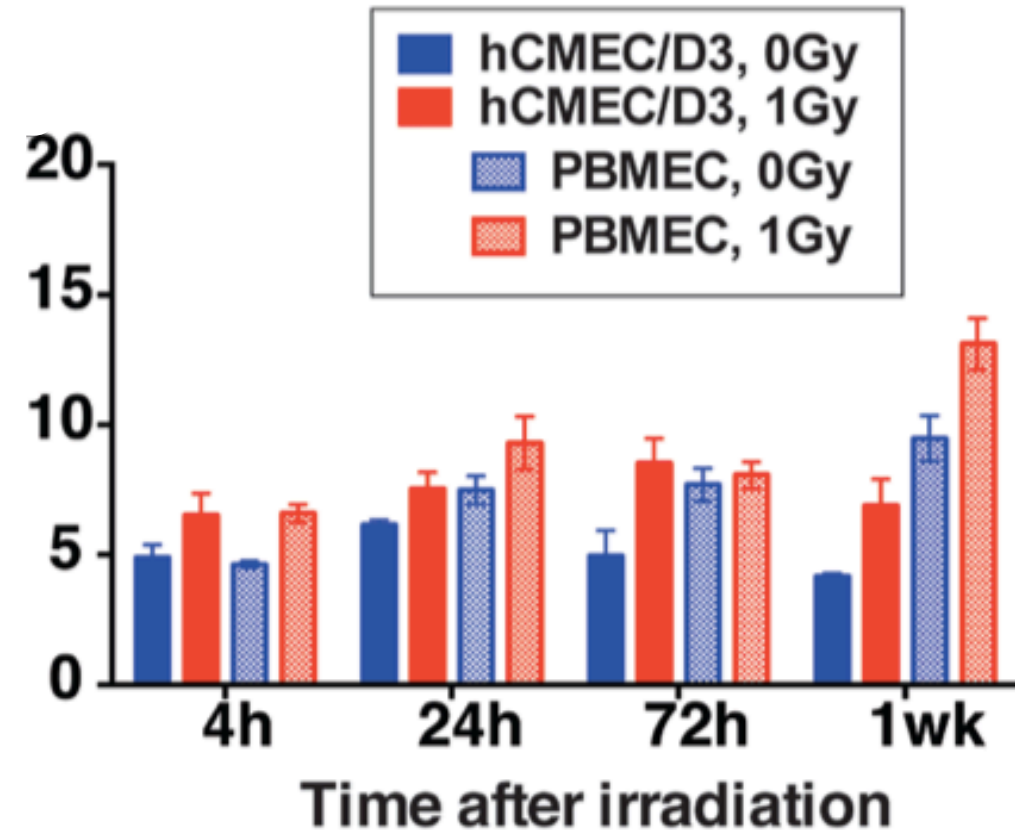


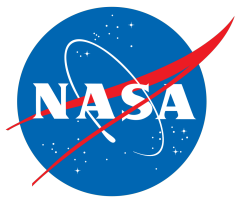
1Gy X-ray irradiation increases BBB permeability

Area under curve, 40kDa dextran

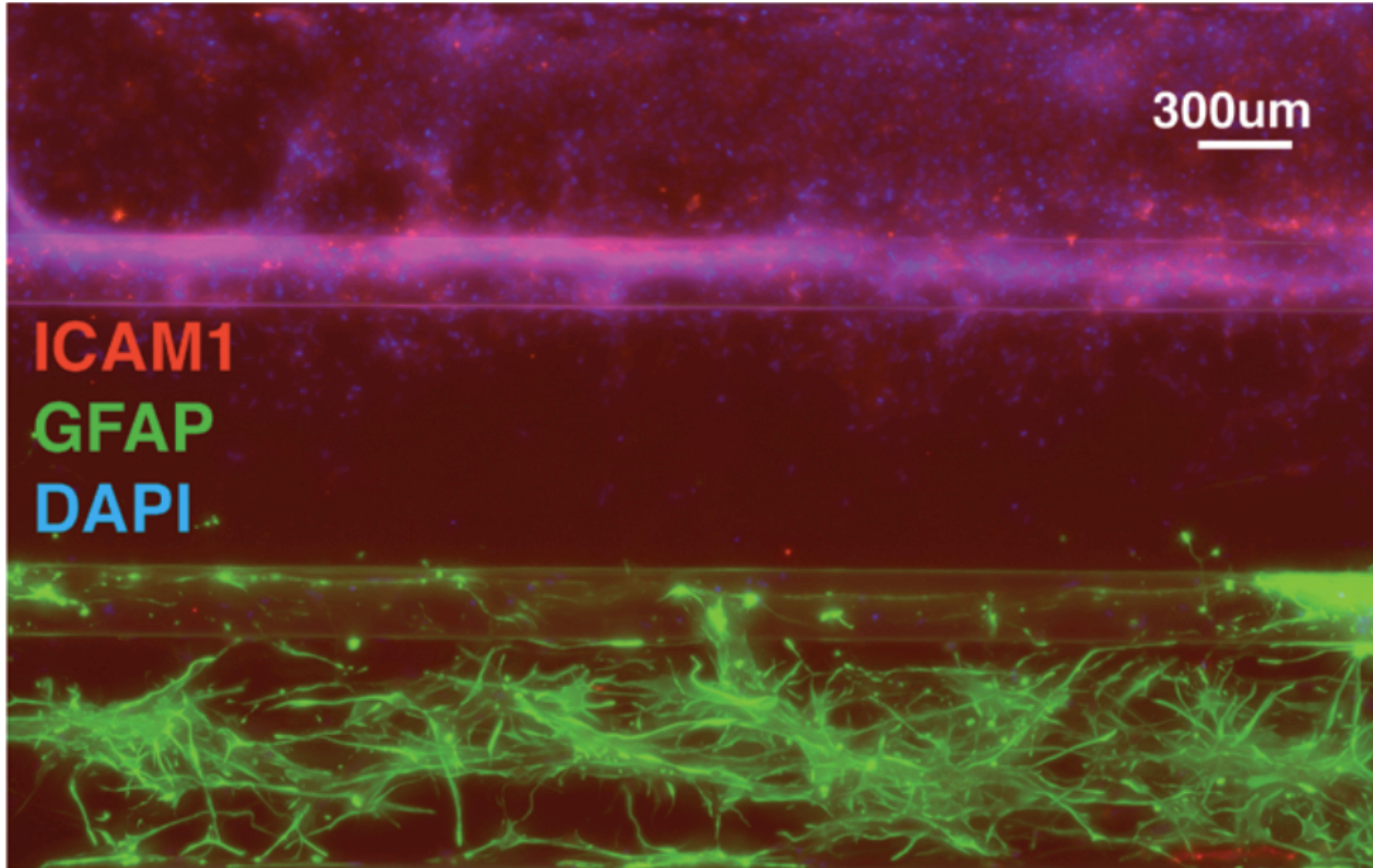


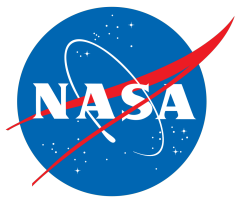
Area under curve, 155kDa dextran



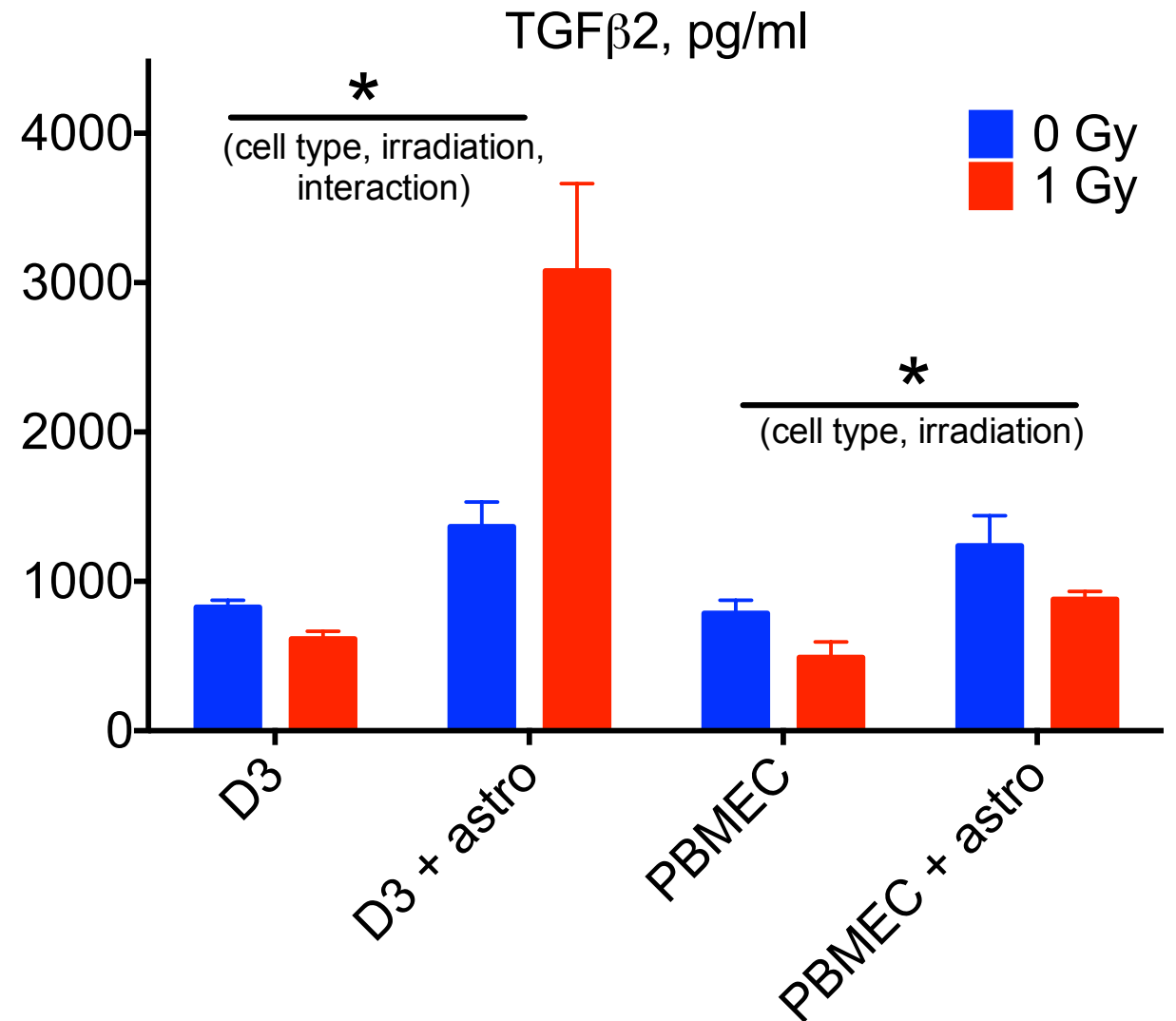
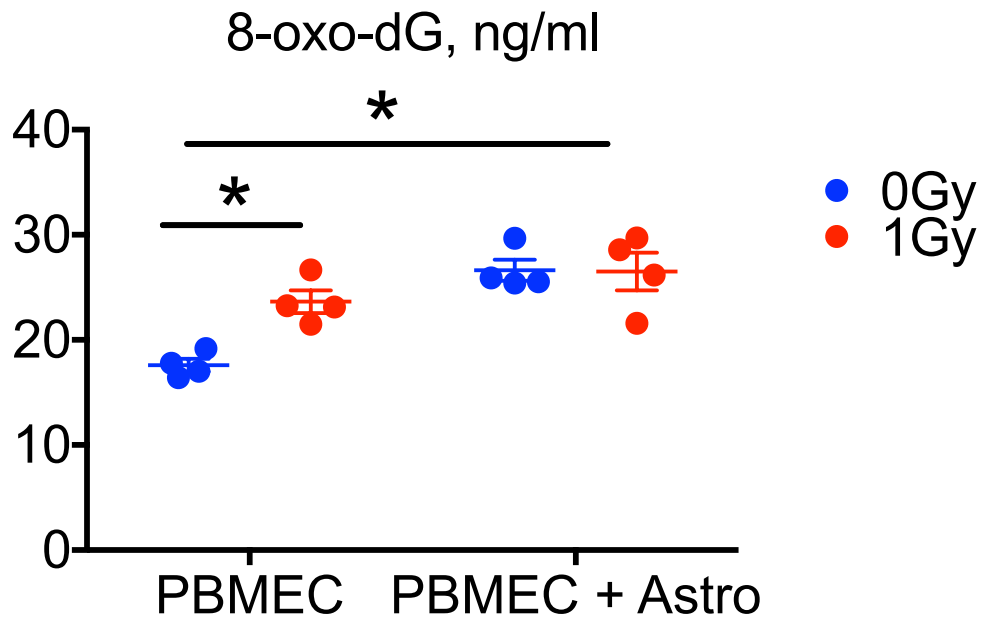


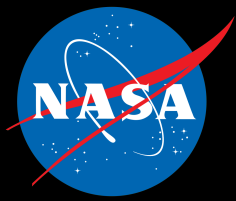
Astrocyte and endothelial cell co-cultures on OrganoPlate





Astrocytes change endothelial cell responses to 1 Gy X-ray irradiation





Future Directions

Immediate

More complex models (neurons, pericytes)
Explore NF κ B as a potential signaling pathway
Longer term cultures

In the coming year

Exposure to high-LET radiation via simulated GCRs
Compare high and low dose rate ionizing radiation responses
Transcriptomic analysis

Long-term

Adapting this platform for spaceflight!



Acknowledgments



Radiation Biophysics Lab at NASA Ames Research Center

Sylvain Costes

Egle Cekanaviciute

Eloise Pariset

Vanesa Gomez Gonzalez

Alejandra Lopez-Macha

Brookhaven National Laboratory

Adam Rusek

Peter Guida

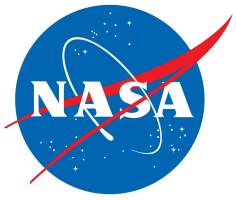
NSRL Support Staff



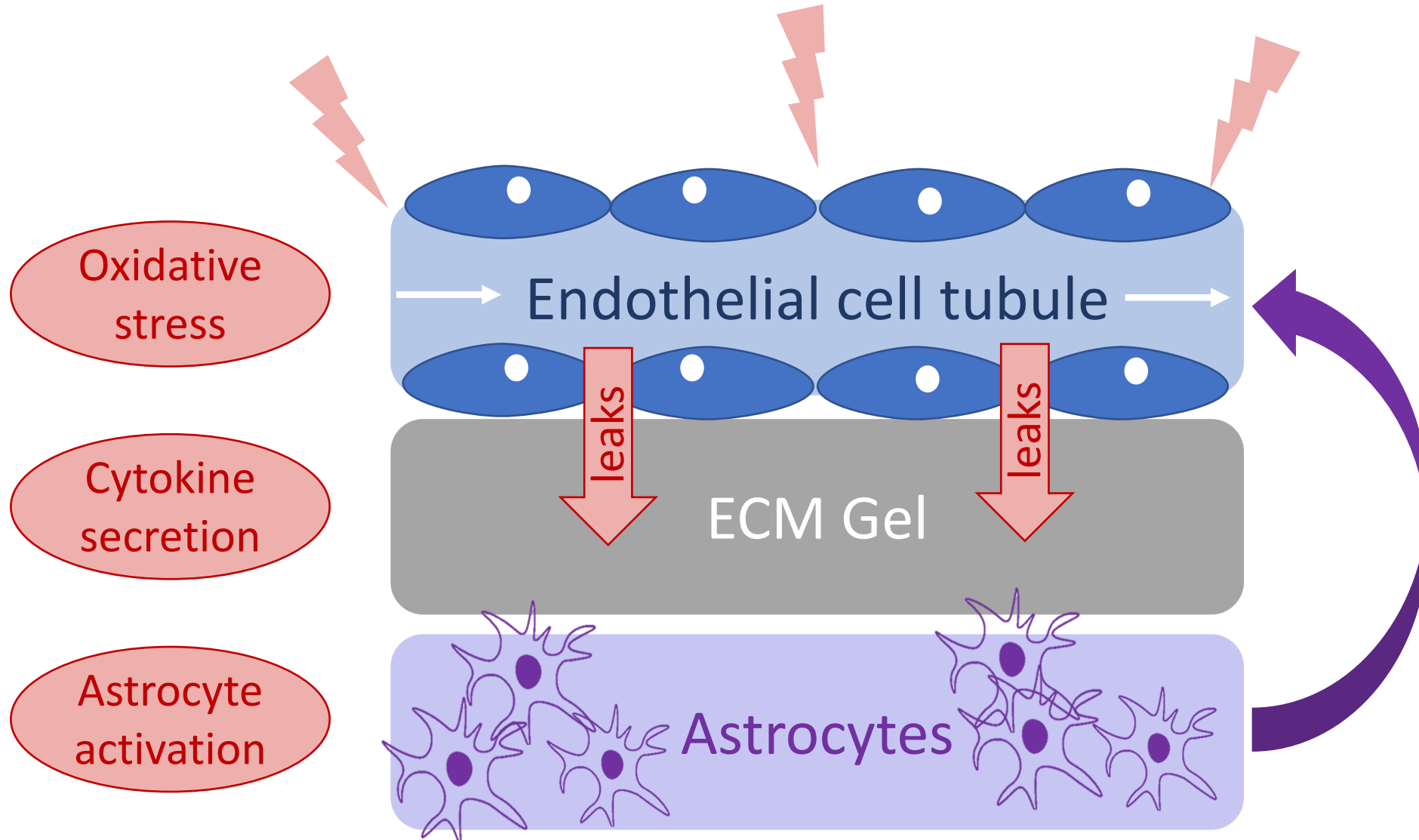
Funding

NASA HRP

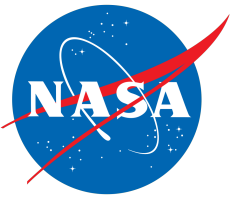
NASA Ames ARIA



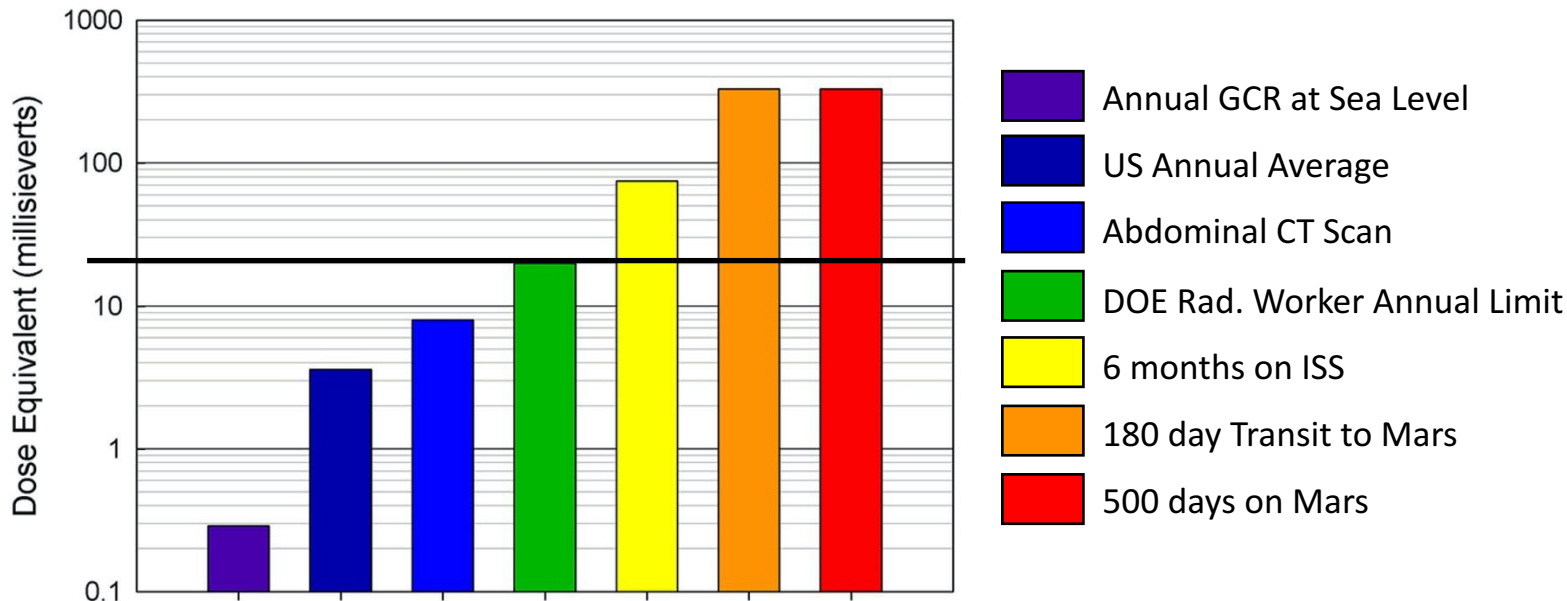
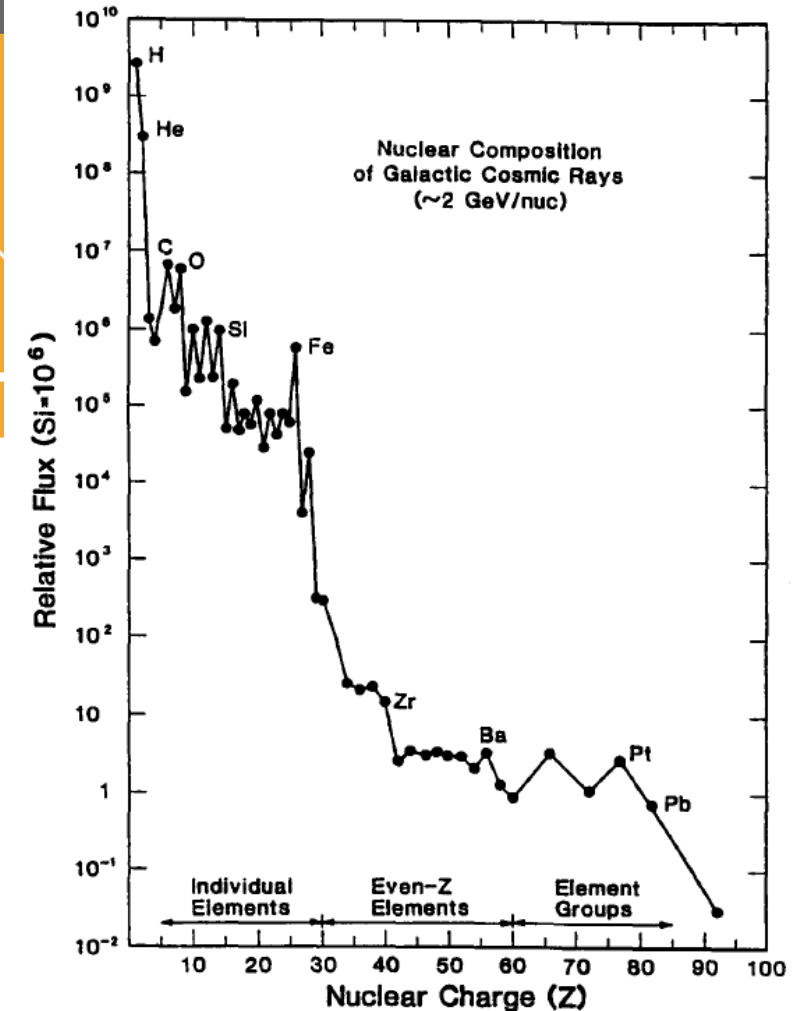
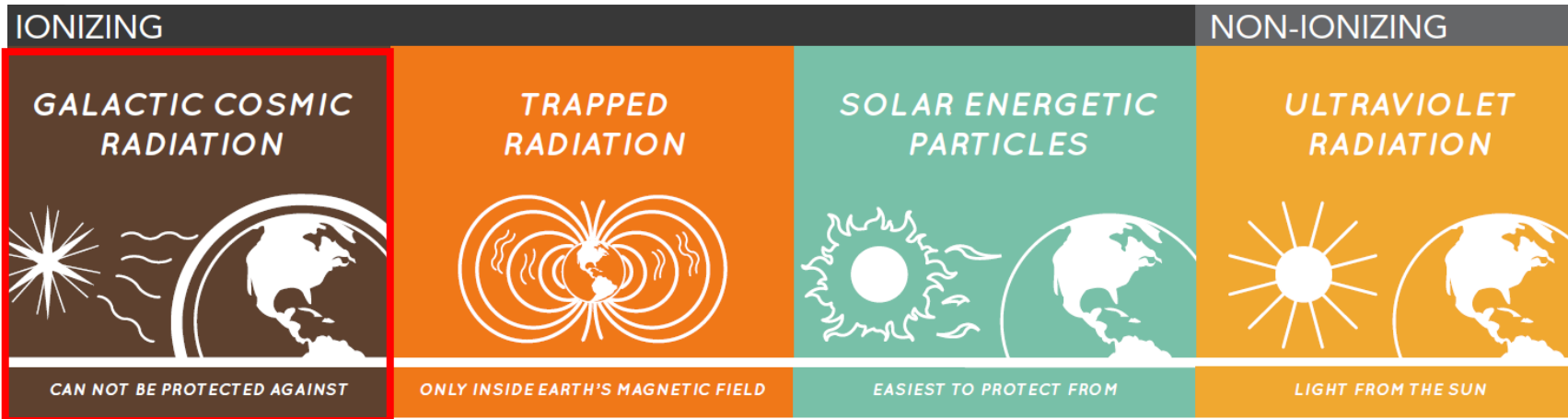
Human blood-brain barrier responses to ionizing radiation (thus far)



Supplementary Slides

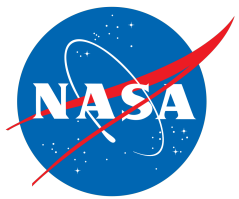


Hazardous Components of Space Radiation



Hassler et al., Science, 2014

Mewaldt, Adv. Space Res., 1994



Results TNFa

