



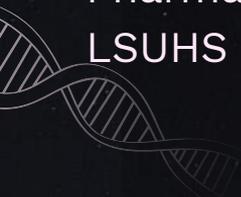
Decoding and Targeting “Space Fog”: Genomic Instability Bridges the Space Exposome and Neurocognitive Dysfunction

Katelyn Lofton

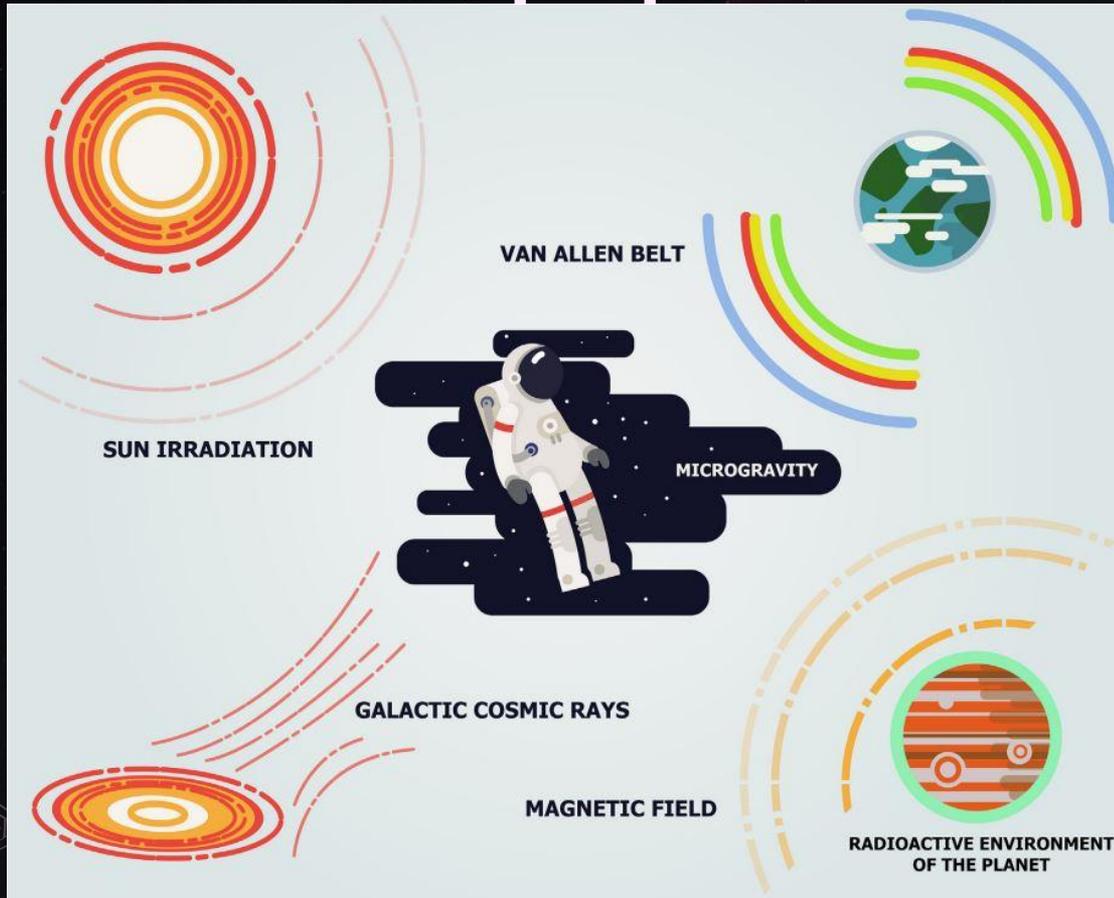
Dr. Xiao-Hong Lu Lab

Pharmacology, Toxicology, and Neuroscience

LSUHS



Sources of Deep Space Radiation



Effects of Deep Space Radiation



Image credit Cortese et. al, 2018

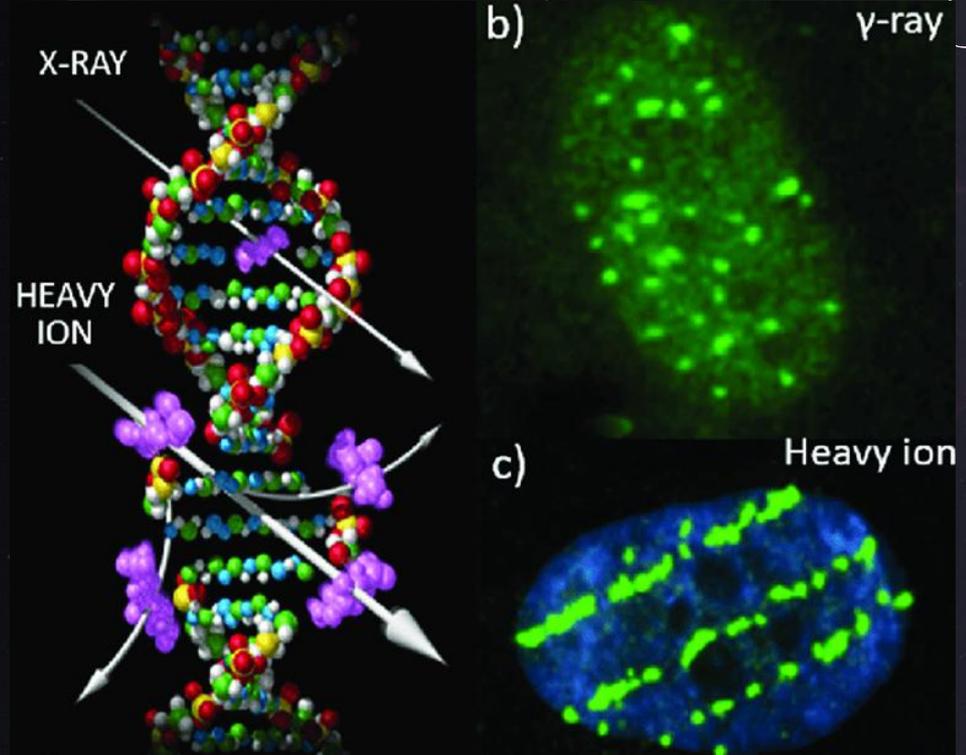
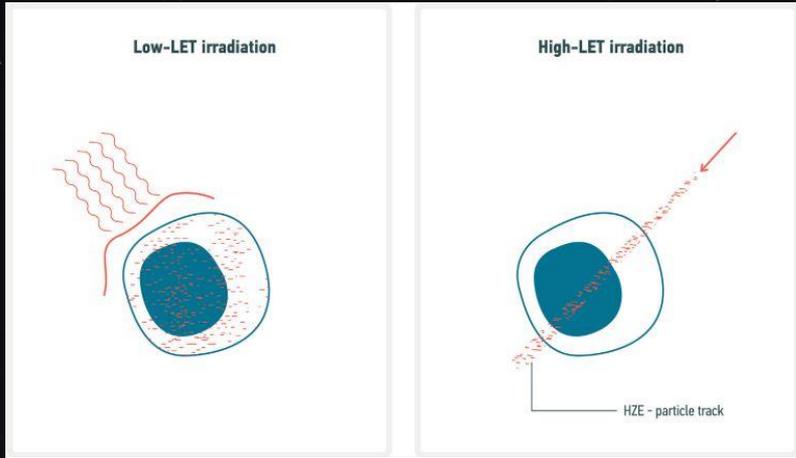
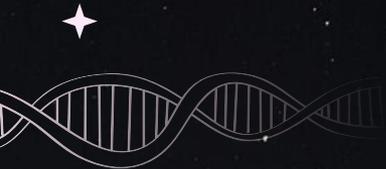
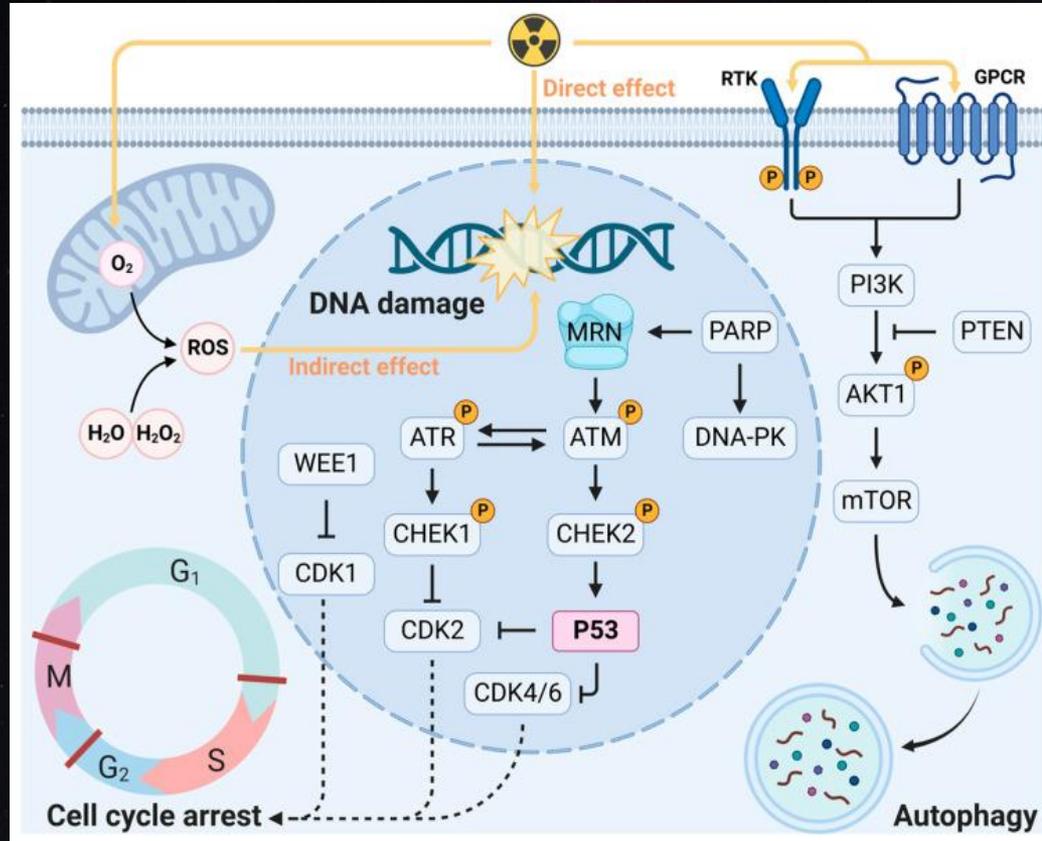


Image credit NASA



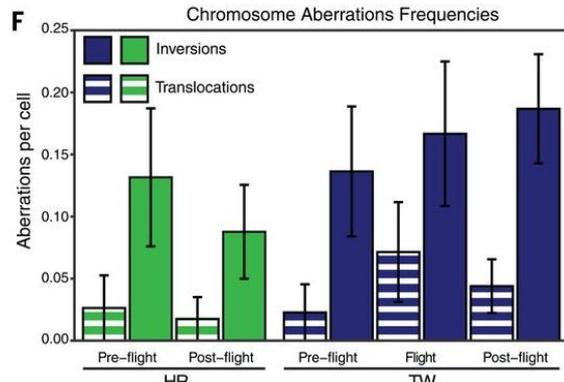
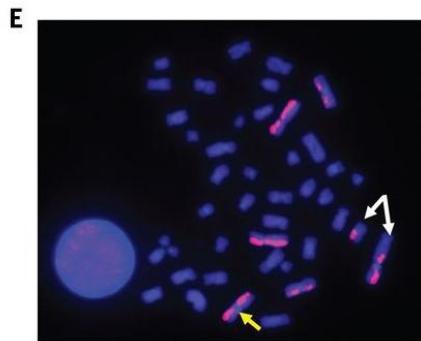
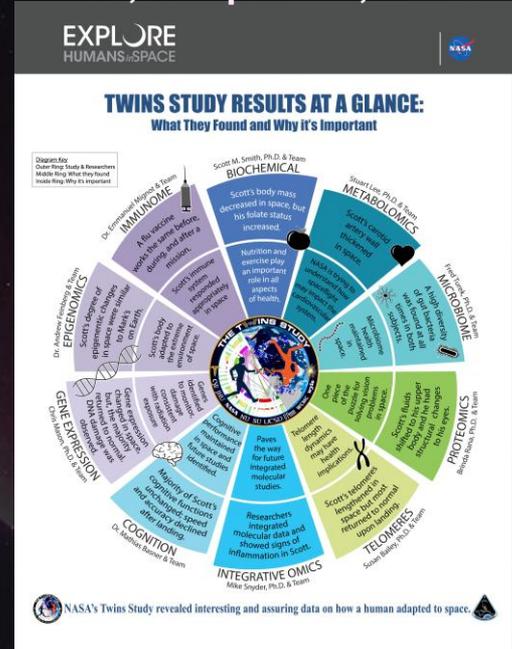
DNA Damage Response



Phytomedicine,
Volume 47, 1
August 2018,
Pages 192-200

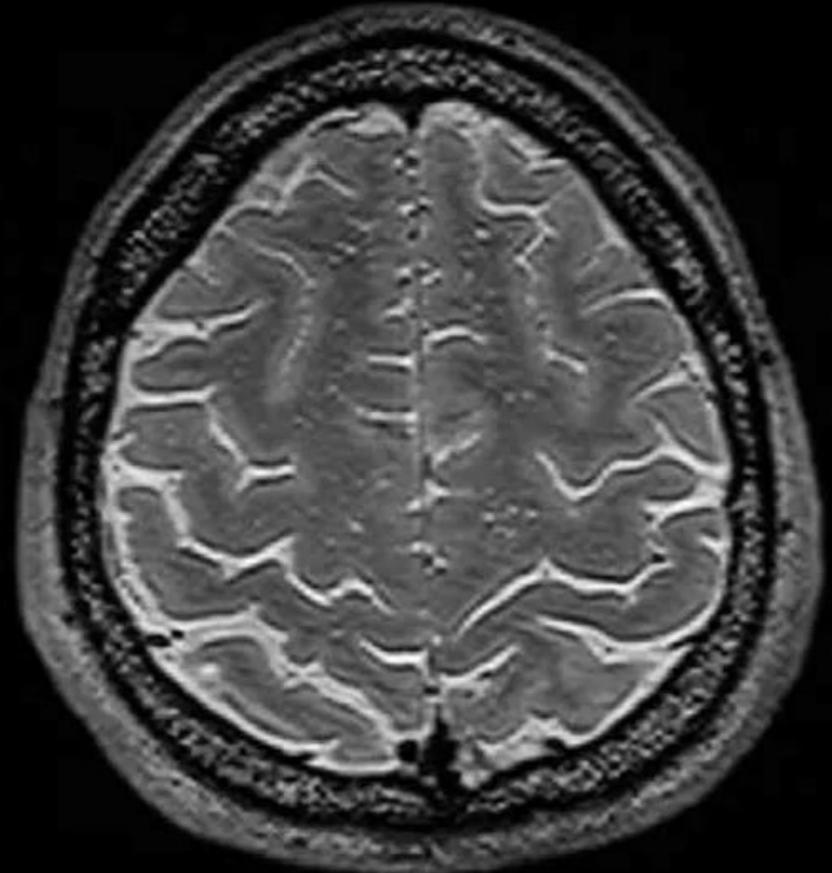
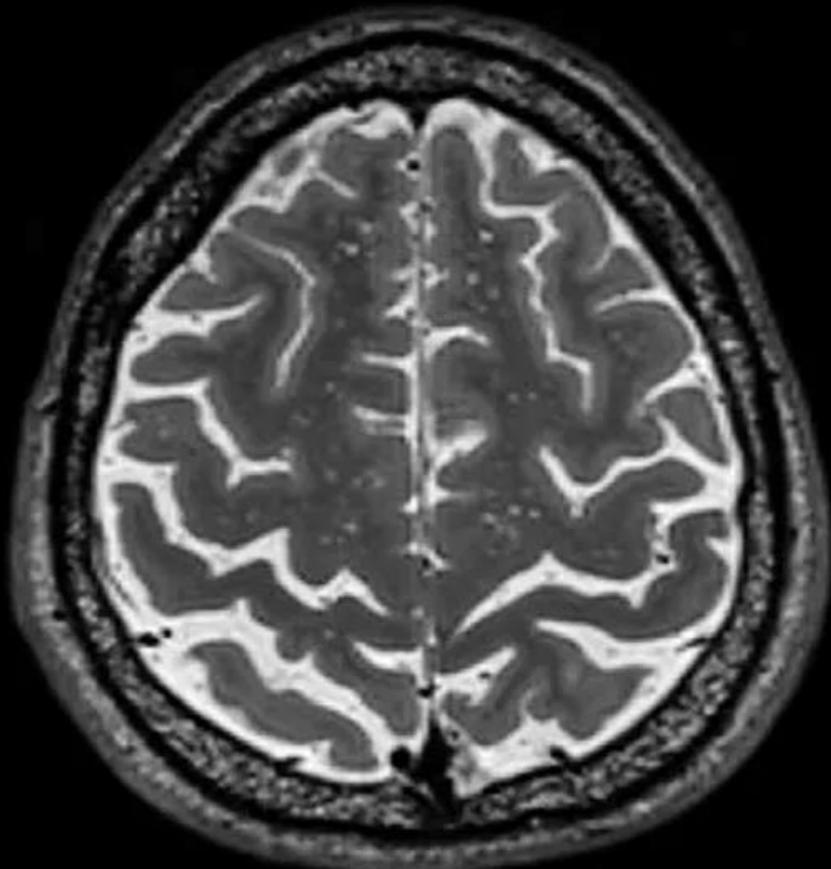
The NASA Twins Study

A multidimensional analysis of a year-long human spaceflight, *SCIENCE*, 12 Apr 2019, Vol 364, Issue 6436



“Also consistent with IR exposure, genes whose expression was altered inflight were significantly enriched in pathways related to DNA damage responses in LD, CD4, CD8, and PBMCs”

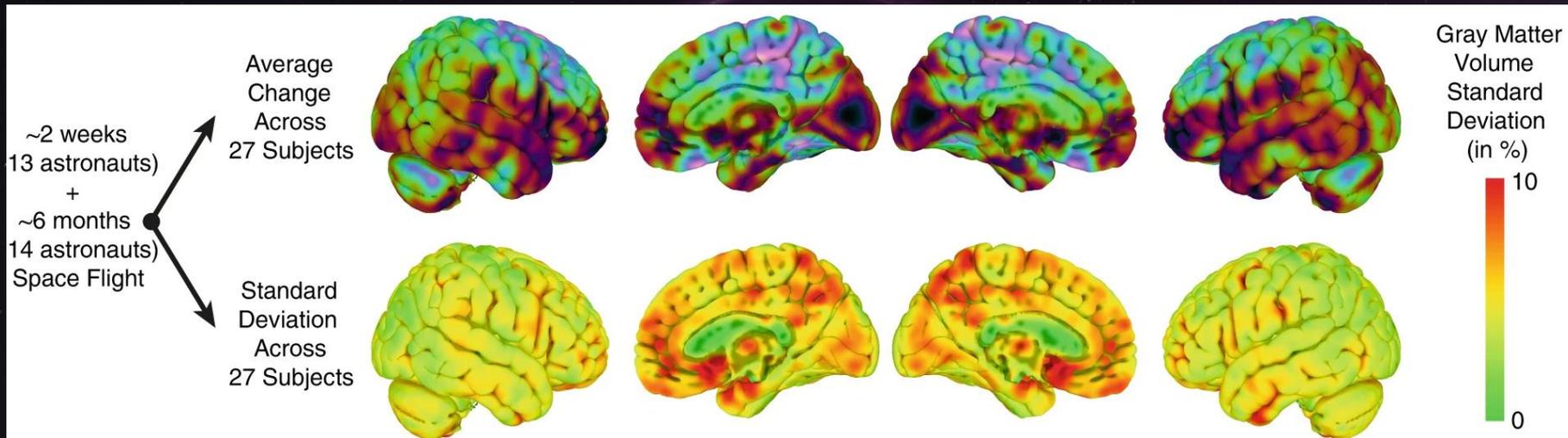
Long duration trip to the ISS had a “squeezing” effect on the brain



Rezaei S. et al. Effect of spaceflight experience on human brain structure, microstructure, and function: systematic review of neuroimaging studies. *Brain Imaging Behav.* 2024 Oct.

Gray Matter Changes from Pre to Post Flight in 27 astronauts

Wuyts, F.L., Deblieck, C.,
Vandevoorde, C. *et al.* *Nat.*
Rev. Neurosci. (2025).



A Case of the "Space Stupids" - actual term coined by US

Symptoms of Brain Fog

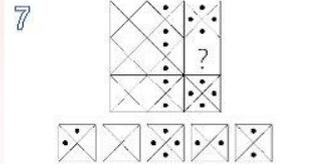
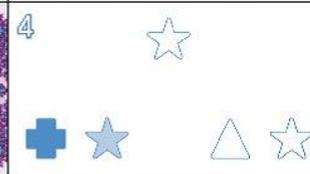
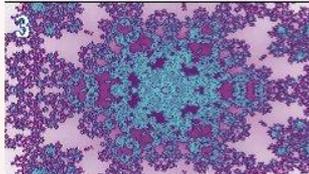
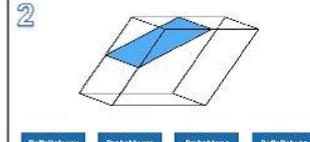
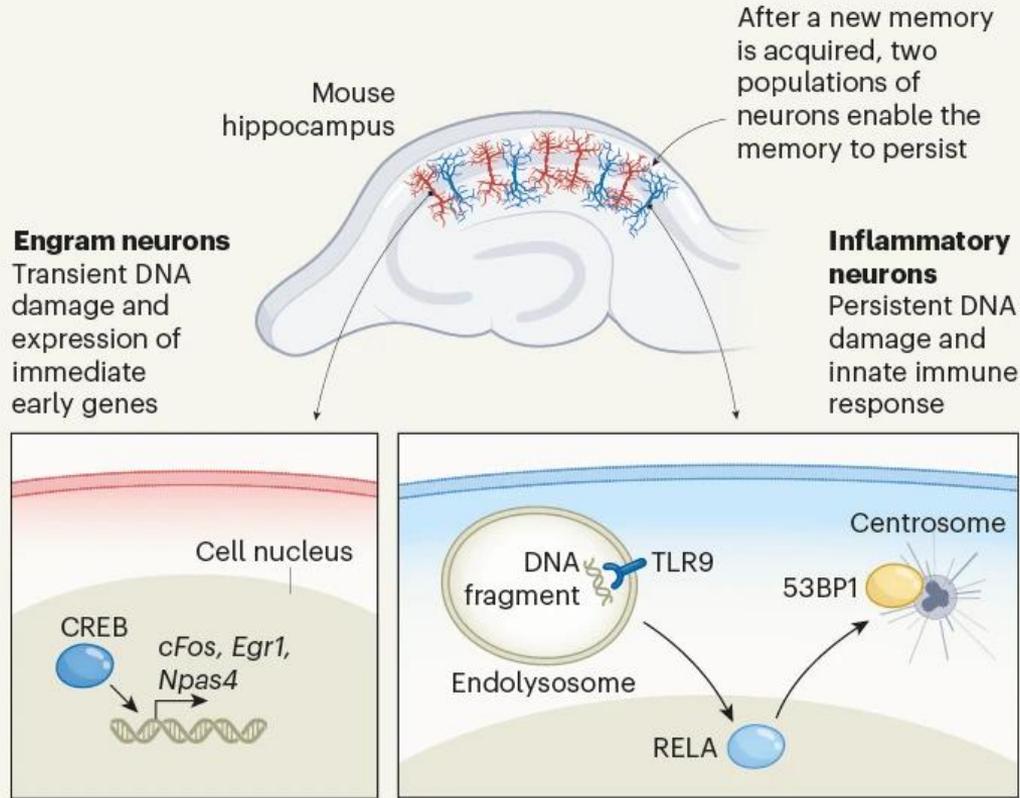


Image Credit NASA

DNA Damage and Memory Formation



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Formation of memory assemblies through the DNA-sensing TLR9 pathway

[Vladimir Jovasevic](#), [Elizabeth M. Wood](#), [Ana Cicvaric](#), [Hui Zhang](#), [Zorica Petrovic](#), [Anna Carboncino](#), [Kendra K. Parker](#), [Thomas E. Bassett](#), [Maria Moltesen](#), [Naoki Yamawaki](#), [Hande Login](#), [Joanna Kalucka](#), [Farahnaz Sananbenesi](#), [Xusheng Zhang](#), [Andre Fischer](#) & [Jelena Radulovic](#)

[Nature](#) **628**, 145–153 (2024) | [Cite this article](#)

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Brookhaven
National Laboratory

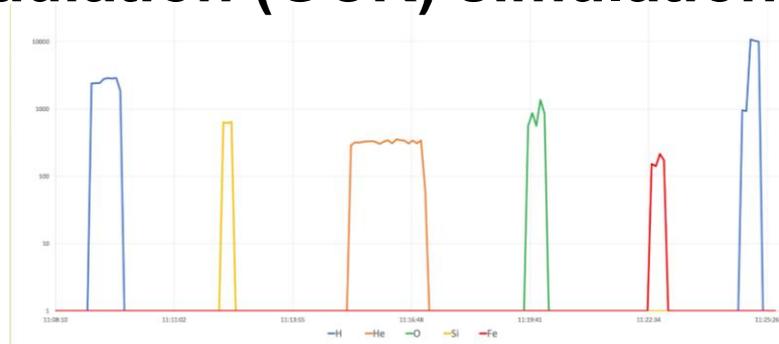




Galactic Cosmic Radiation (GCR) simulation

In order of delivery

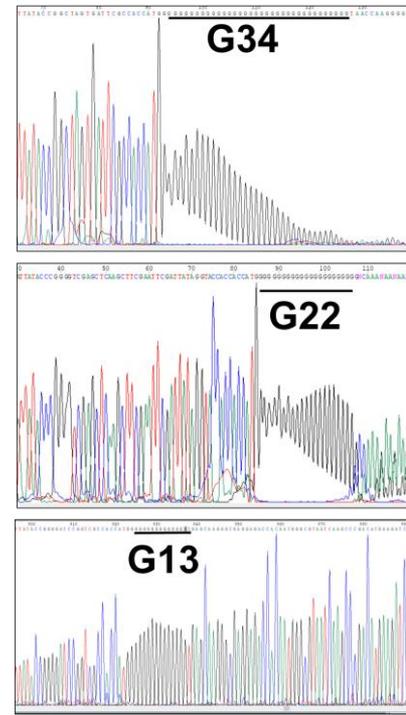
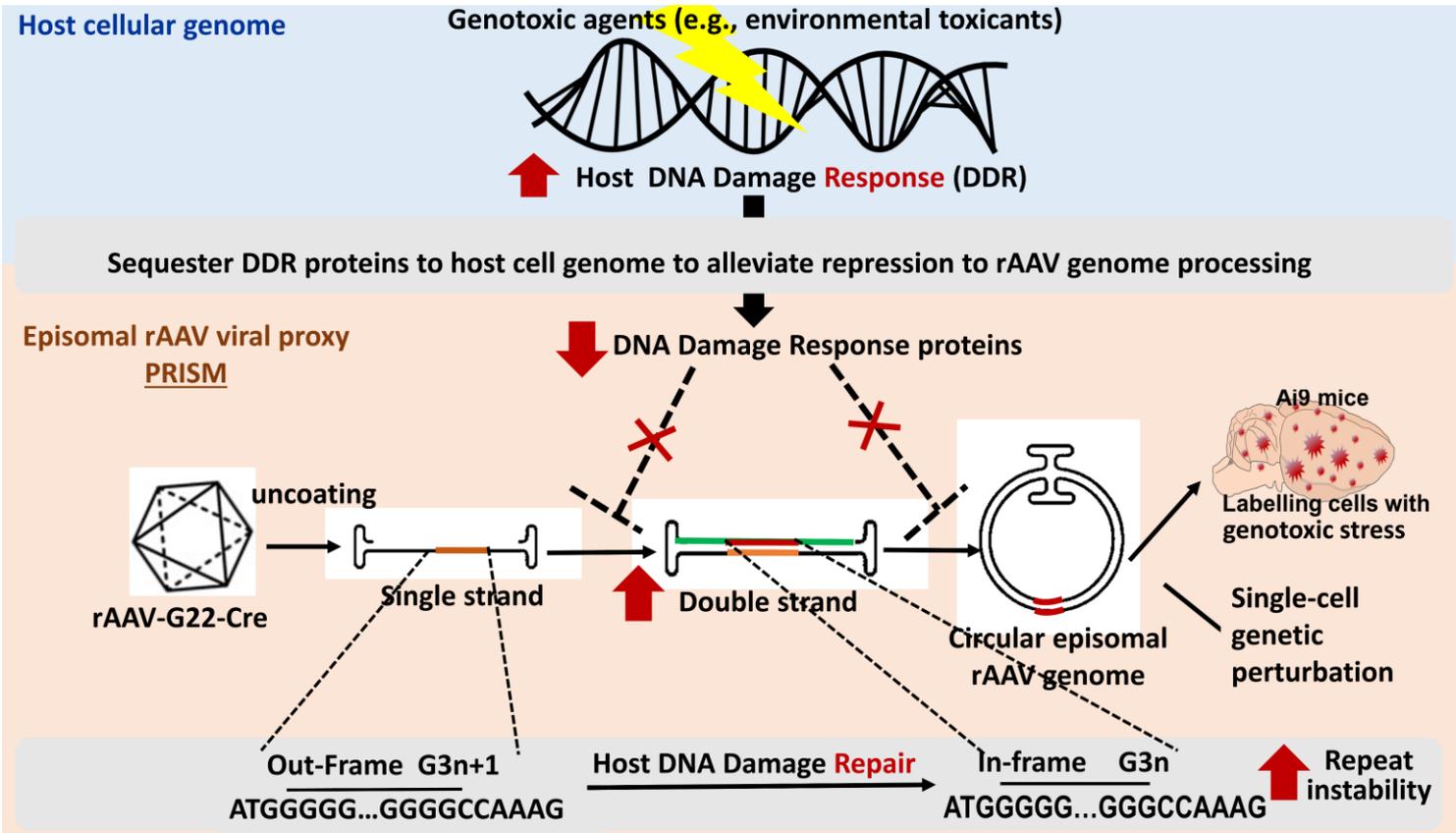
Ion	Energy (MeV/n)	Fraction
H	1000	35%
Si	600	1%
He	250	18%
O	350	6%
Fe	600	1%
H	250	39%



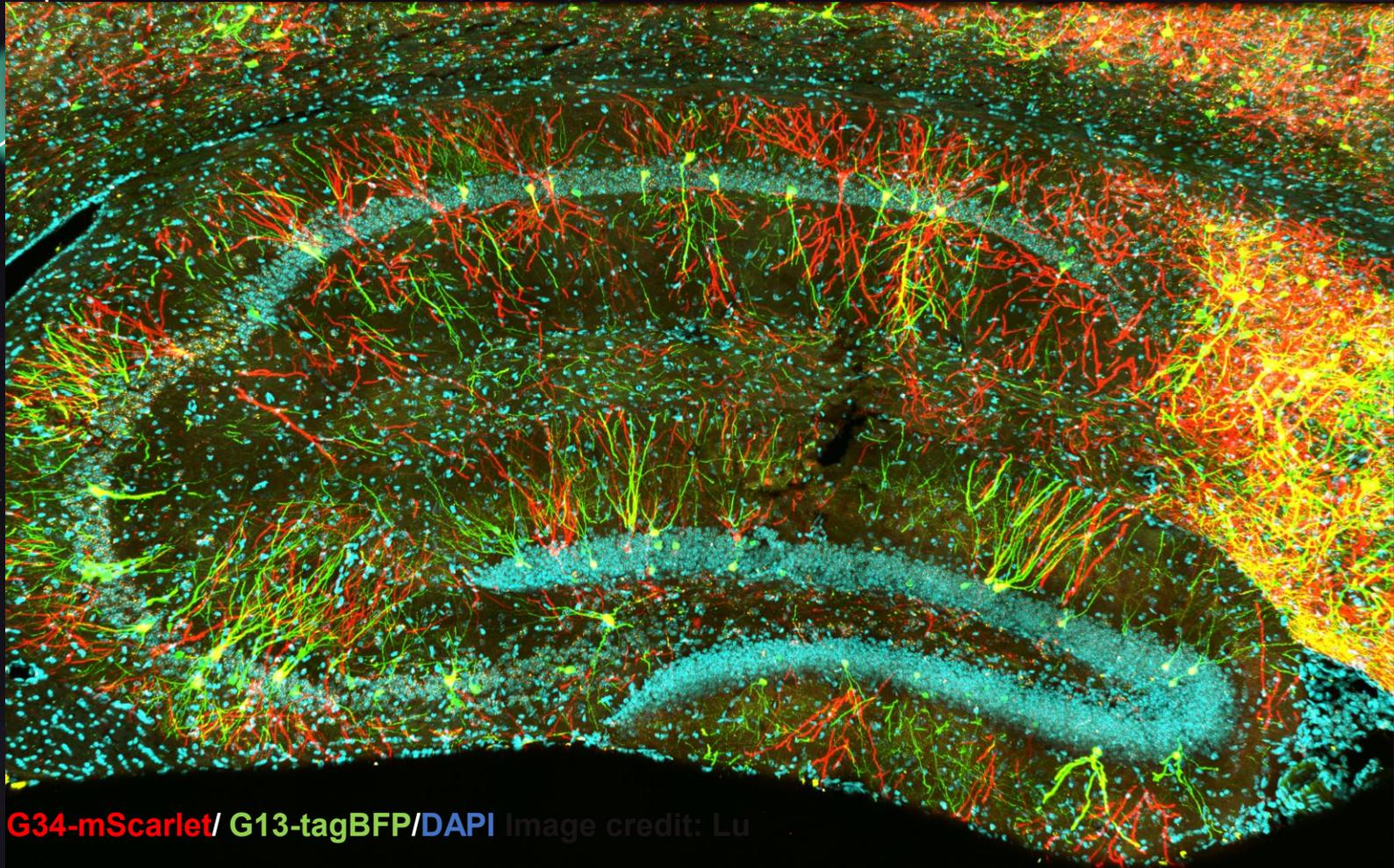
Exploration Mission	Mission Duration	Dose Equivalent (mSv) ^b	
ISS in LEO	6 months	50–100	
ISS in LEO	1 year	100–200	
Sortie to Gateway (free space)	30 days	55	
Lunar Surface Mission (2 weeks on surface)	42 days	70	
Sustained Lunar Operations	1 year	300–400	Low
Deep-Space Habitat	1 year	500–650	Medium
Mars Mission	650 to 920 days	870–1,200	High

NASA's first ground-based Galactic Cosmic Ray Simulator: Enabling a new era in space radiobiology research, PLoS Biol 18(5): e3000669. 2020

PRISM (Probe with a viral proxy for Instability of DNA Surveillance/repair in somatic brain Mosaicism)



PRISM sensor in neuron



G34-mScarlet/ G13-tagBFP/DAPI Image credit: Lu

100 μm

Novel PRISM sensor in brain endothelia cell

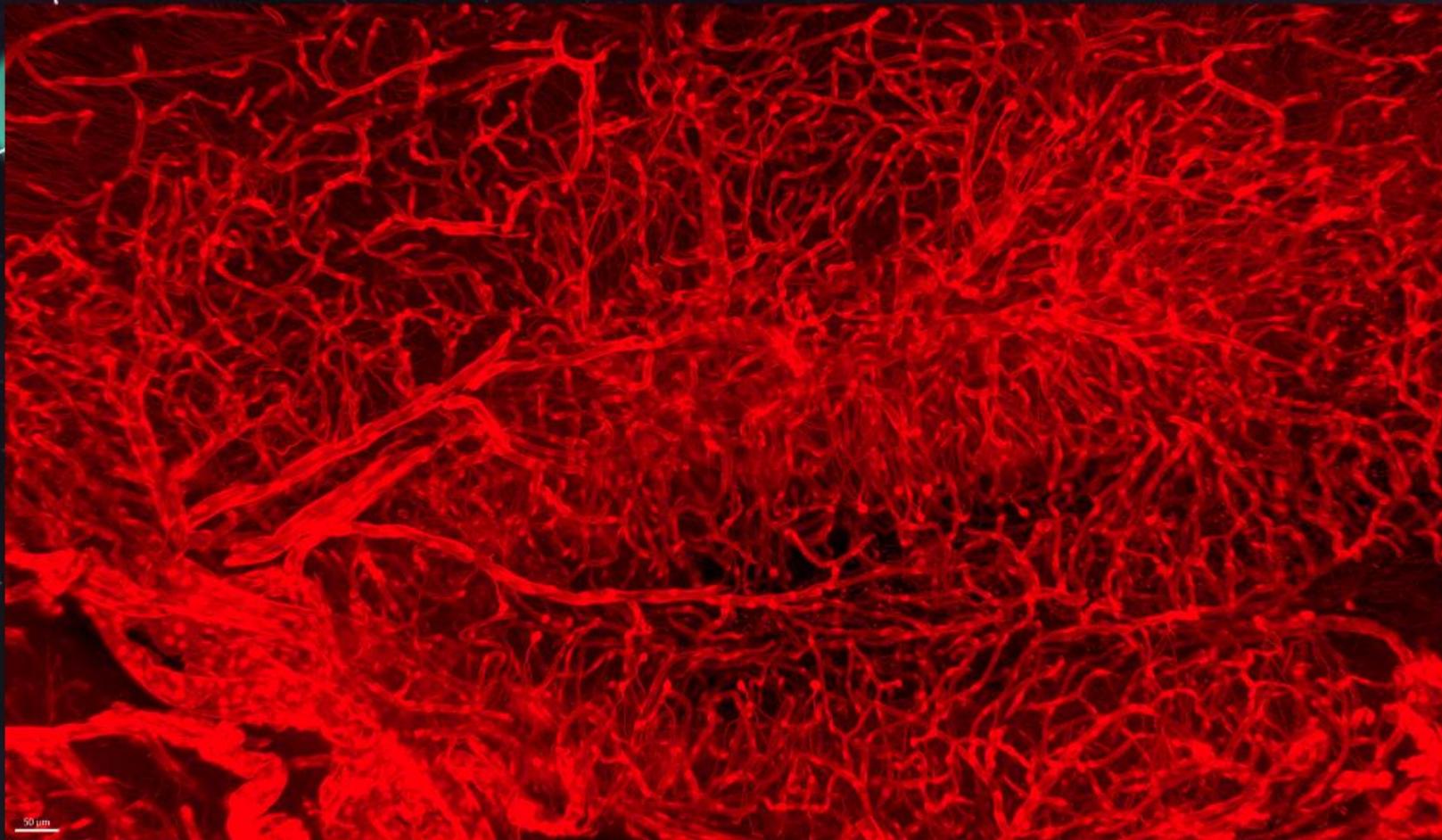


Image credit: Jessie Li and X. Lu

Novel PRISM sensor for all cell types in hippocampus

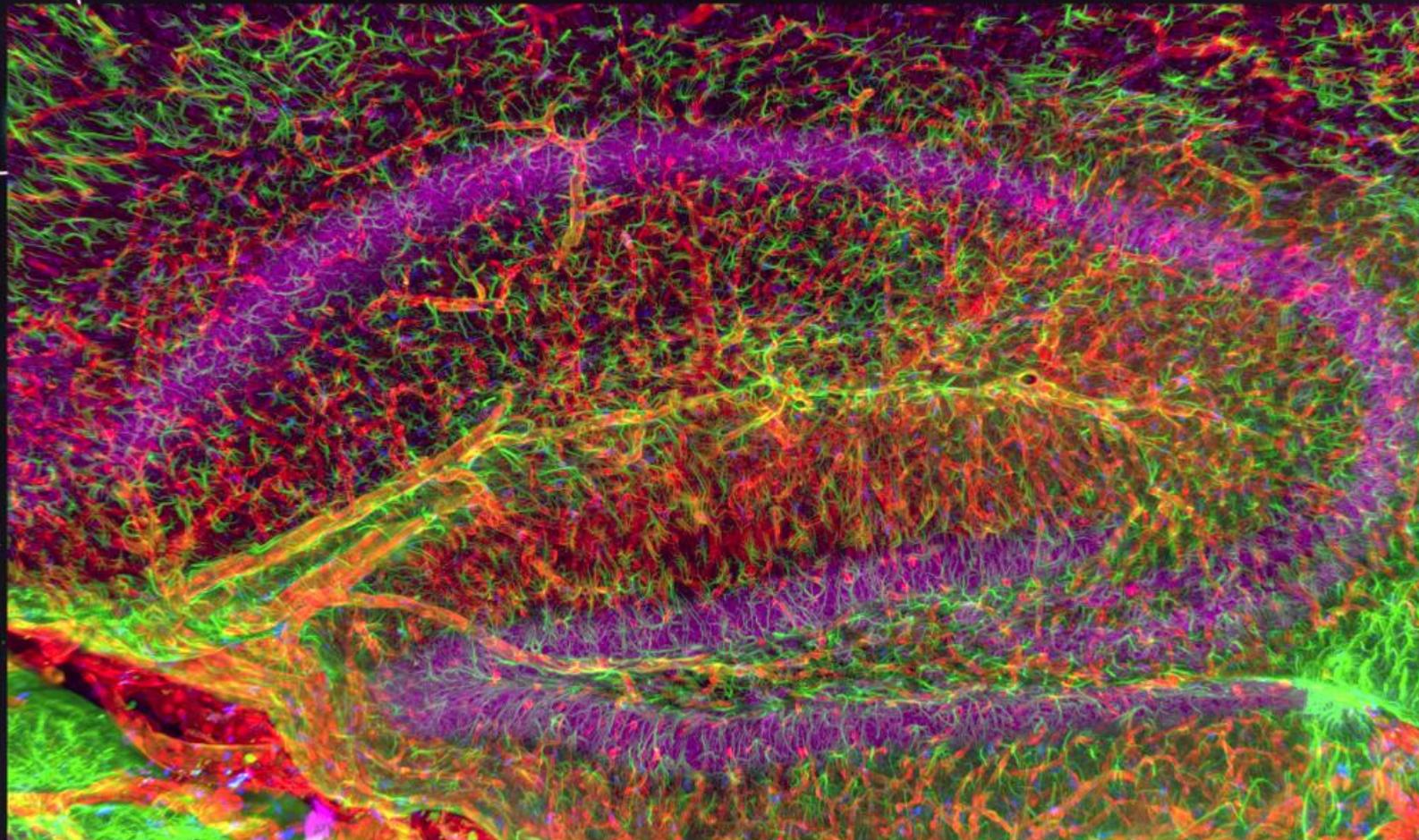
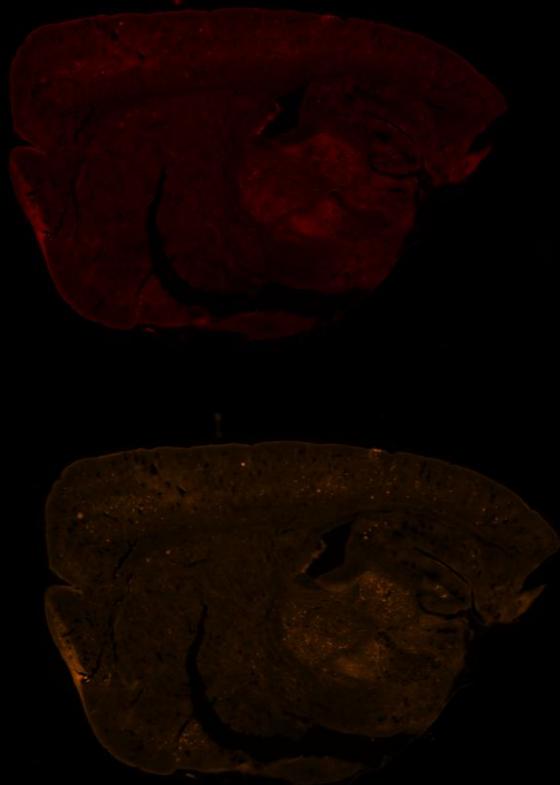


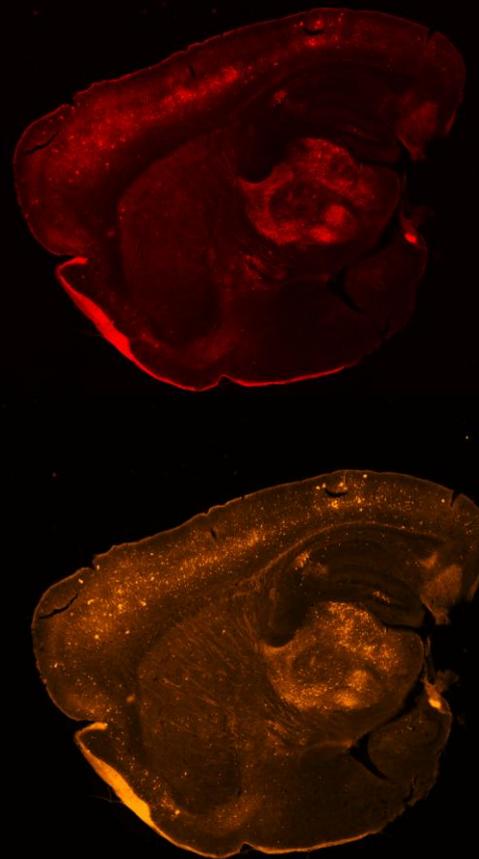
Image credit: Jessie Li, X. Tian, and X. Lu

Control (no irradiation)

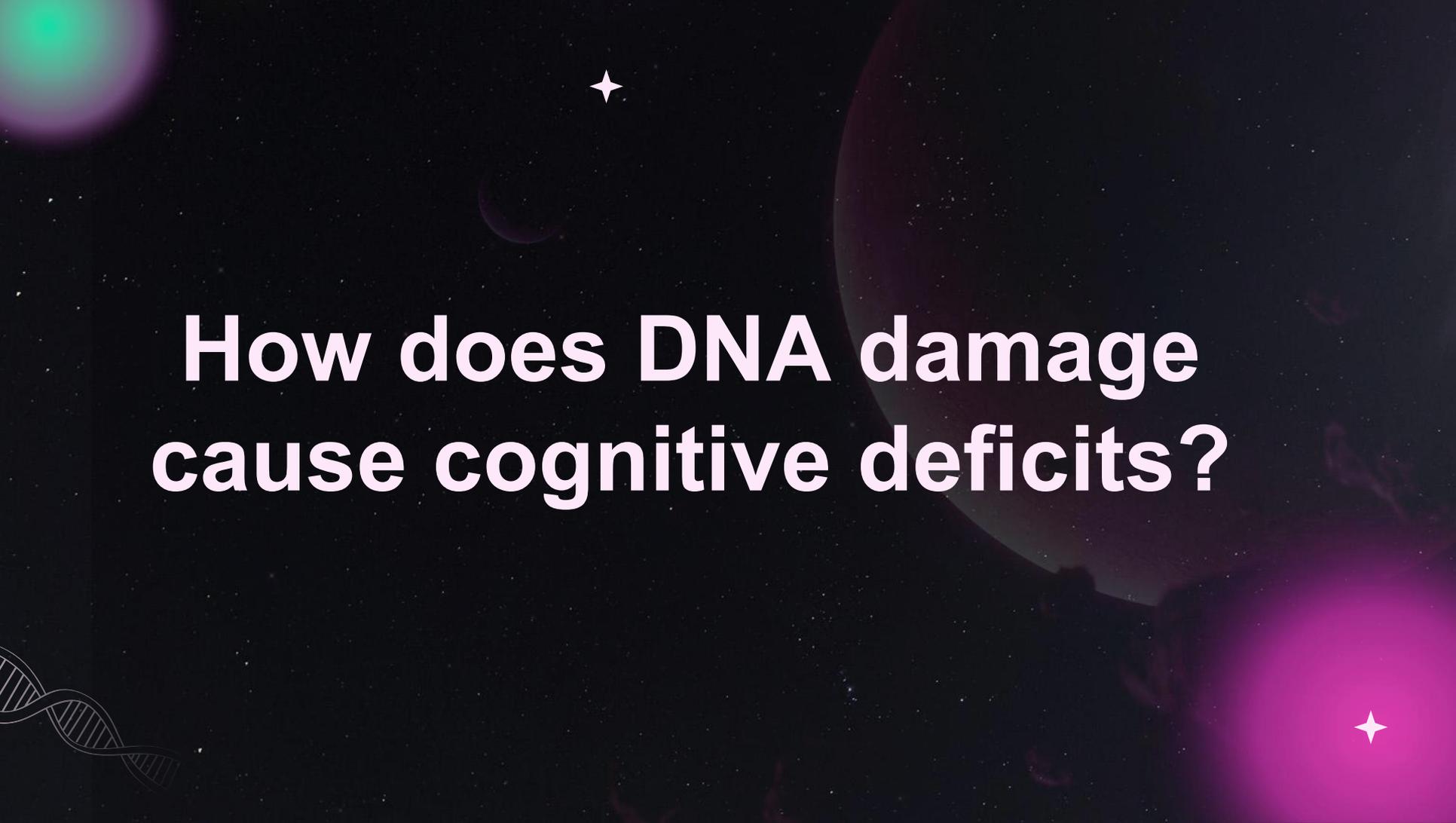


G34-mScarlet / G13-BFP / DAPI

High dose (80 cGy irradiation)

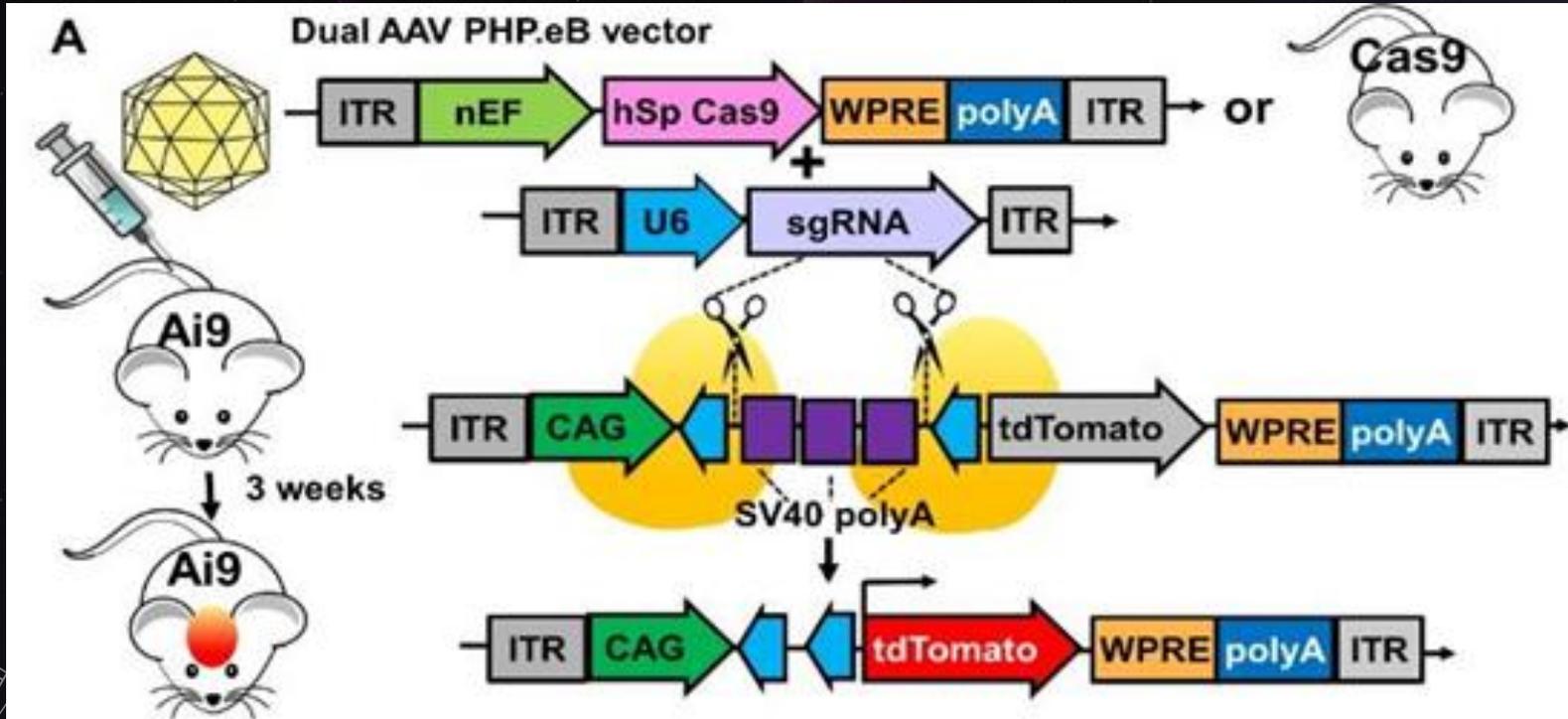


G34-mScarlet / G13-BFP / DAPI

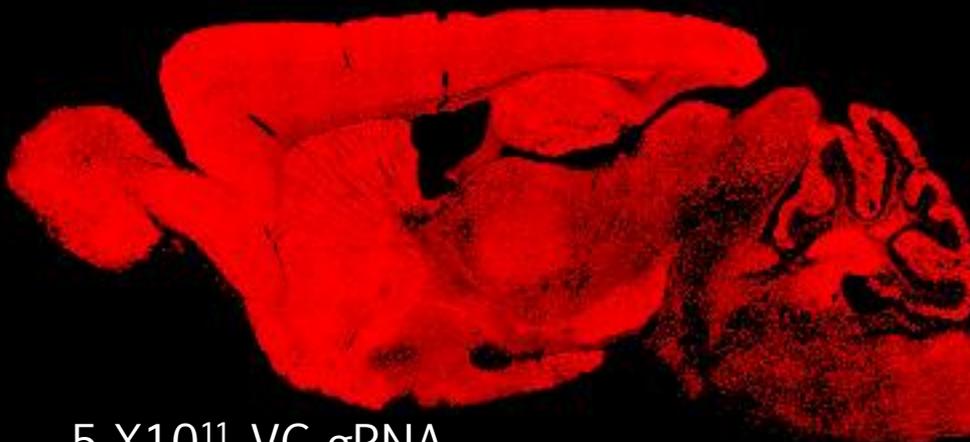
The background is a dark space scene with a large, dimly lit planet on the right side. There are several bright stars, including a prominent four-pointed star in the upper center and another in the lower right. A faint DNA double helix is visible in the bottom left corner.

**How does DNA damage
cause cognitive deficits?**

Using CRISPR-Cas9 to Replicate Radiation Damage



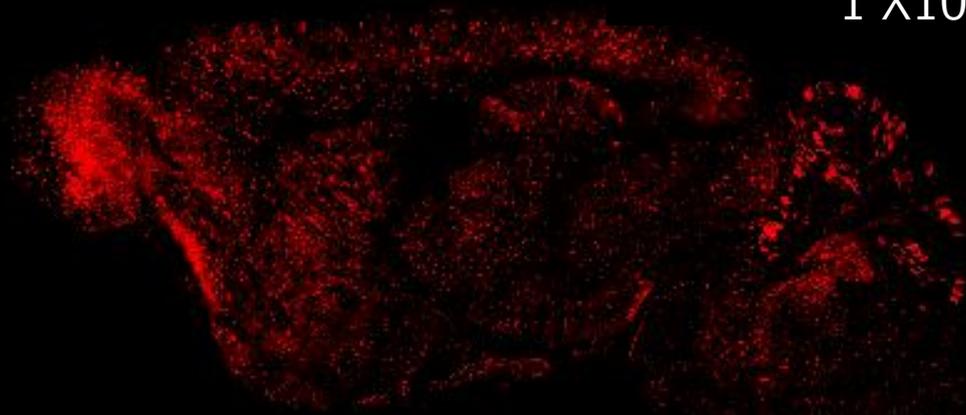
Non-invasive and expansive CRISPR/Cas9 mediated DSB in CNS



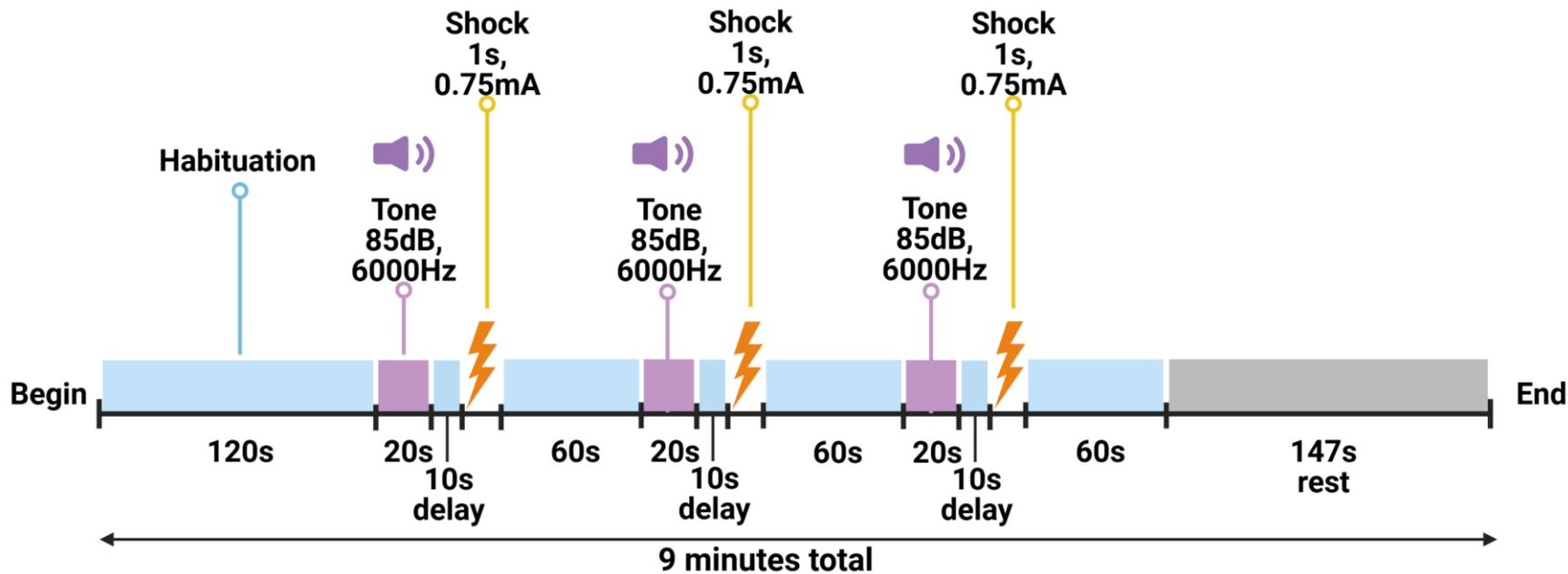
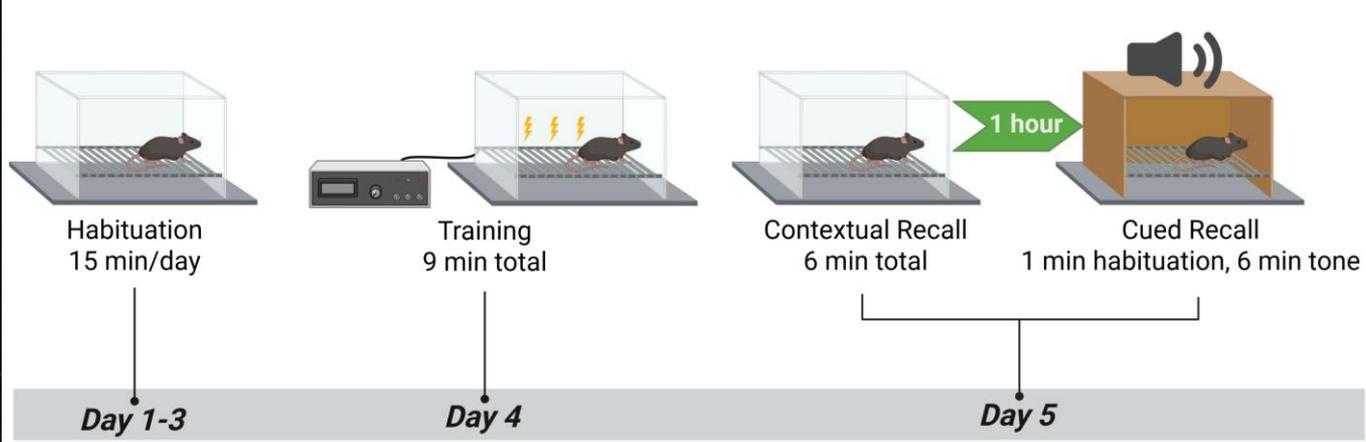
5×10^{11} VG gRNA



1×10^{11} VG gRNA

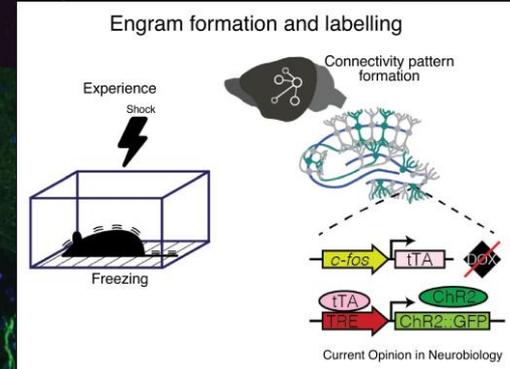


0.5×10^{11} VG gRNA

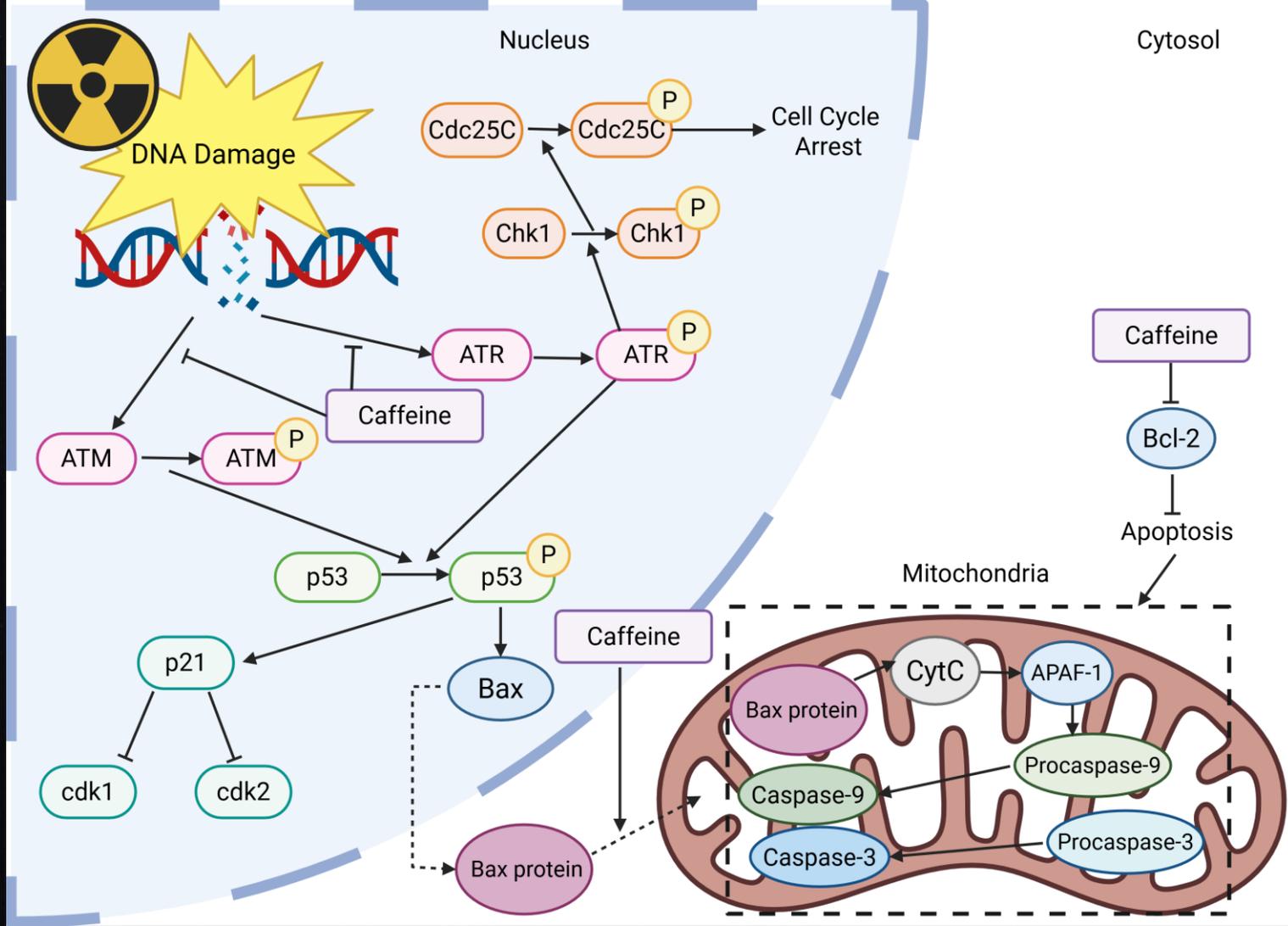


Memory Engrams

Engrams: A window into the memory trace



Investigating the relationship between DNA damage and memory engrams





Ongoing Study: Evaluate caffeine as a potential therapy for spaceflight

