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Modeled Microgravity Induces Neutrophil Extracellular Trap (NET)osis Formation and Reduced Phagocytosis of Polymorphonuclear Neutrophils

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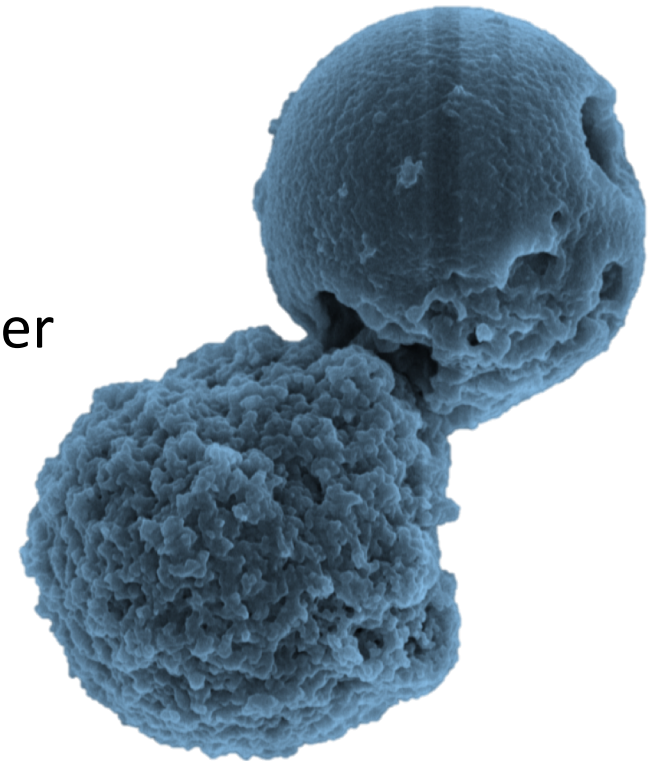
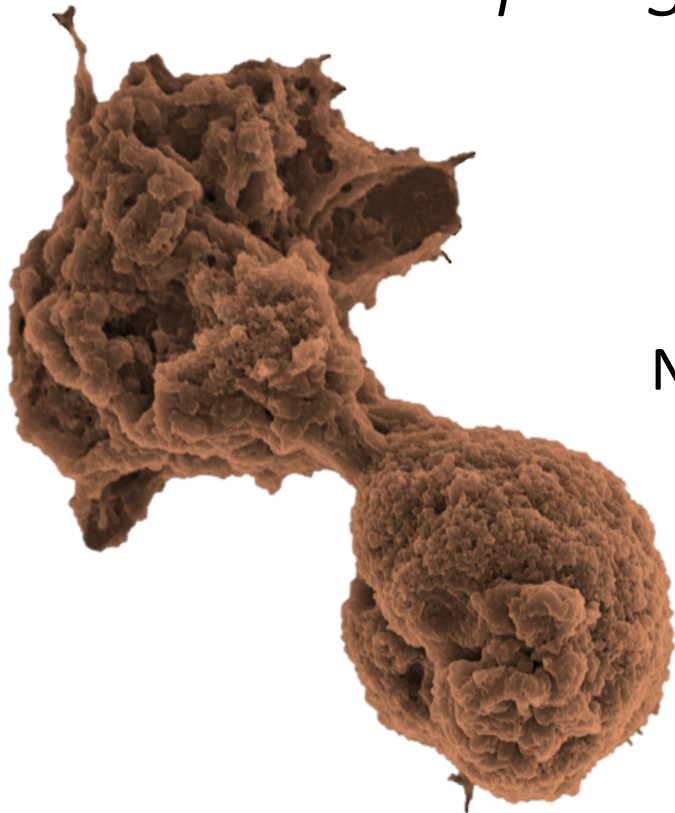
*Modeled microgravity induces neutrophil
extracellular trap (NET)osis formation and
reduced phagocytosis of polymorphonuclear
neutrophils*

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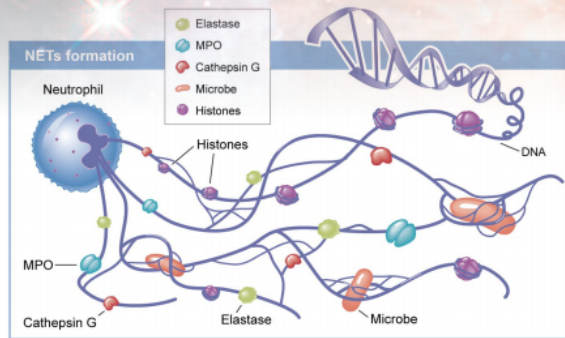
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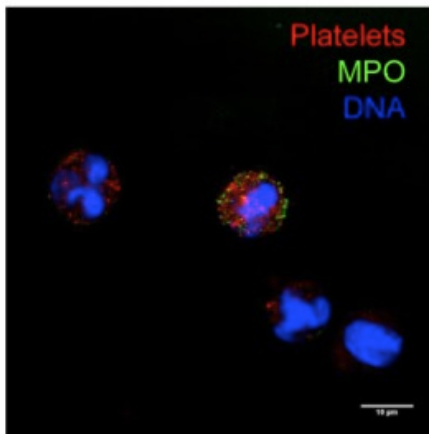
Spaceflight and Immunity

- Elevated granulocytes inflight (Crucian et al., 2015) → granulocytes innate, inflammatory cells with impaired function (cite)
- Impaired Lymphocyte function, elevated senescence
- Inflammaging --> chronic low-grade inflammation occurs in spaceflight (cite 2018 group)
- Post-flight studies have indicated elevated ROS (Pecaut et al., 2018, Mao et al., 2018).
- Elevated DNA molecules in plasma indicator of inflammation, may be elevated NETs?

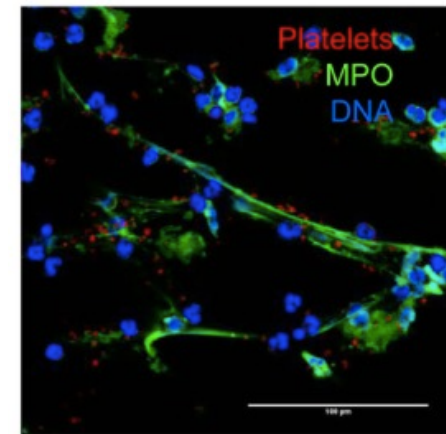
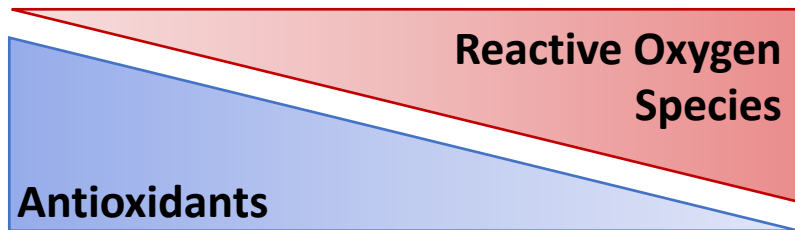
Neutrophil Extracellular Traps (NETs)



DNA strands containing MPO/Elastase that are released into the extracellular environment to survey and capture foreign or self challenges.



REDOX Balance



PMNs under non-inflammatory environment undergo apoptosis (controlled/non-inflammatory) cell death vs under inflammatory conditions (NETosis predominates) → controlled by a gradient of inflammation

Hypothesis & Specific Aims

Since Spaceflight elevates inflammation, and elevated ROS can trigger NETosis,

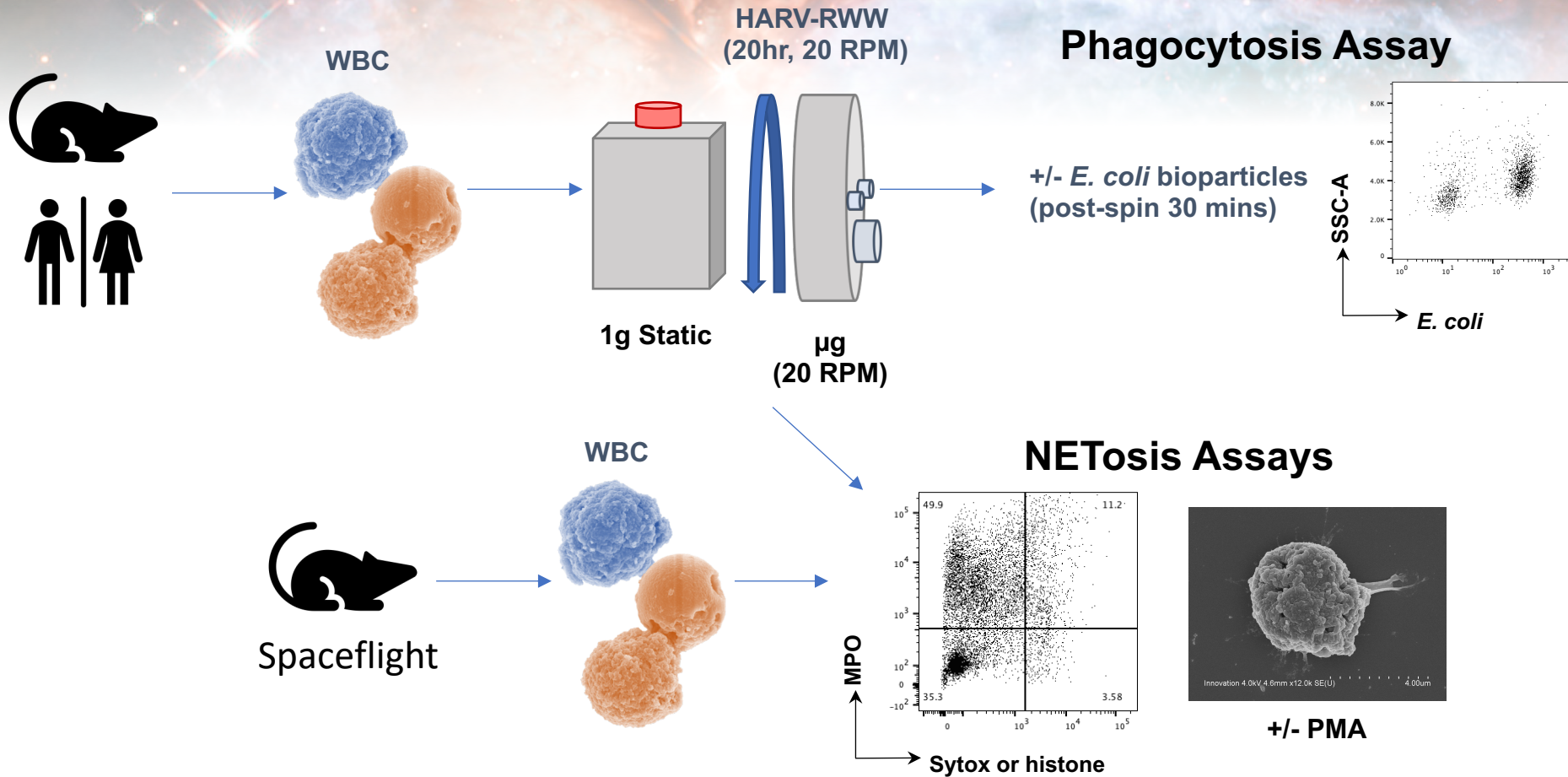
NETosis may be used as a biomarker of inflammation during spaceflight.

Aim 1: Confirm reduced phagocytosis in reduced gravity

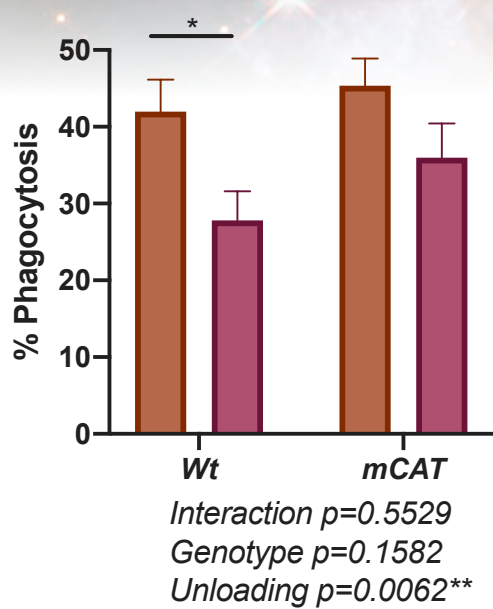
Aim 2: Determine if elevated NETosis occurred modeled microgravity and compare to spaceflight-return samples

Aim 3: Confirm elevated ROS contributes to elevated NETosis and reduced phagocytosis

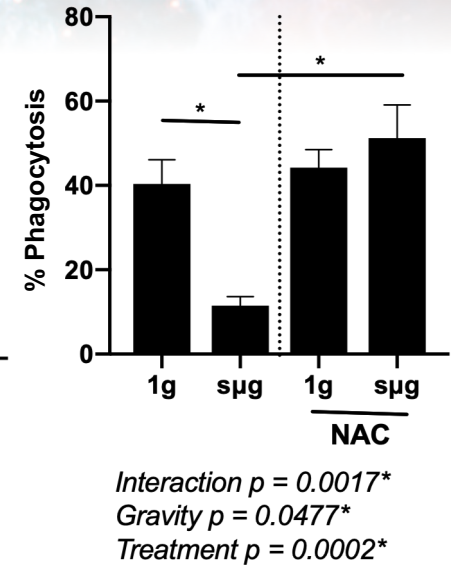
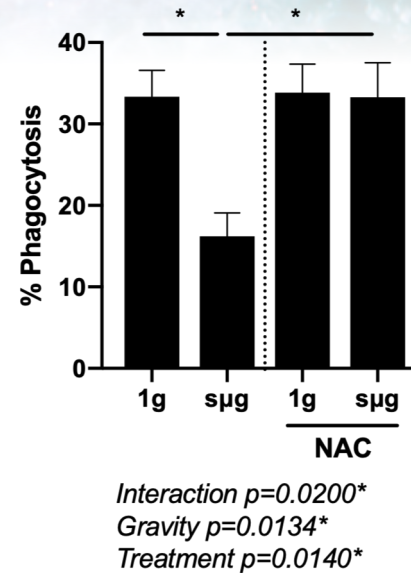
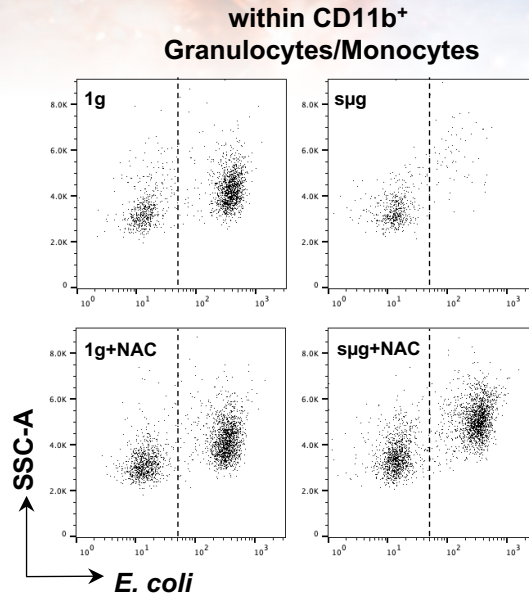
Methods



Phagocytosis is impaired in simulated microgravity



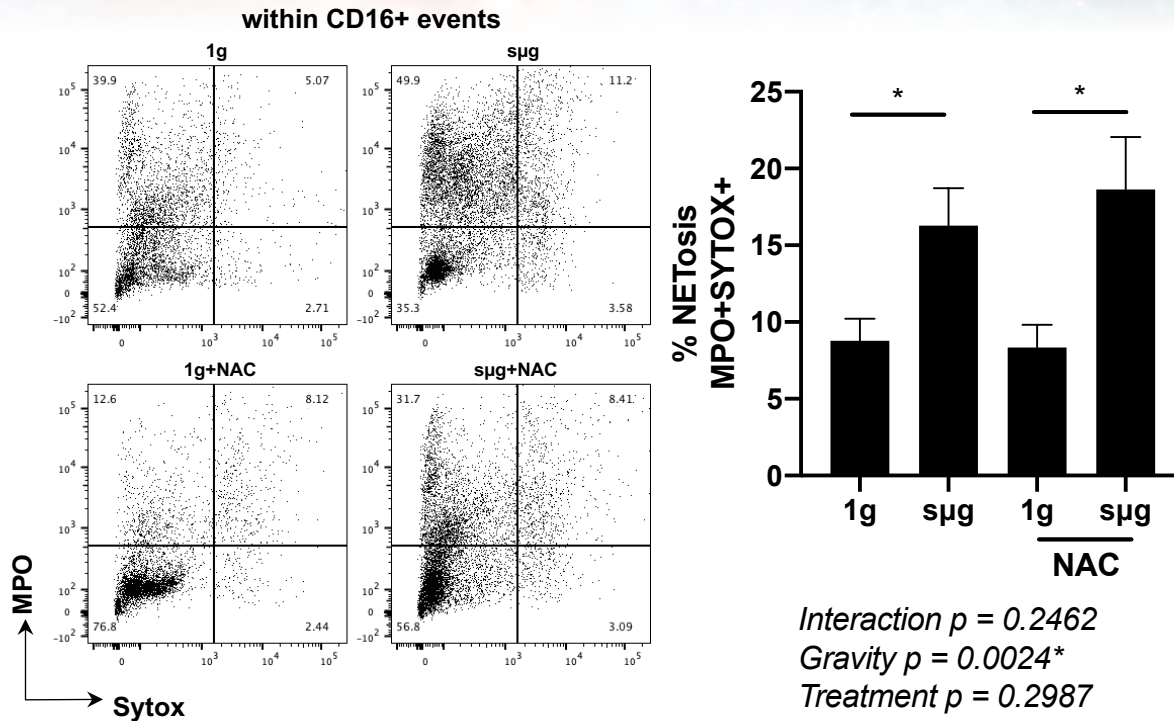
■ 1g
■ μg



Antigen presentation potentially impaired, which can impair in T cell function

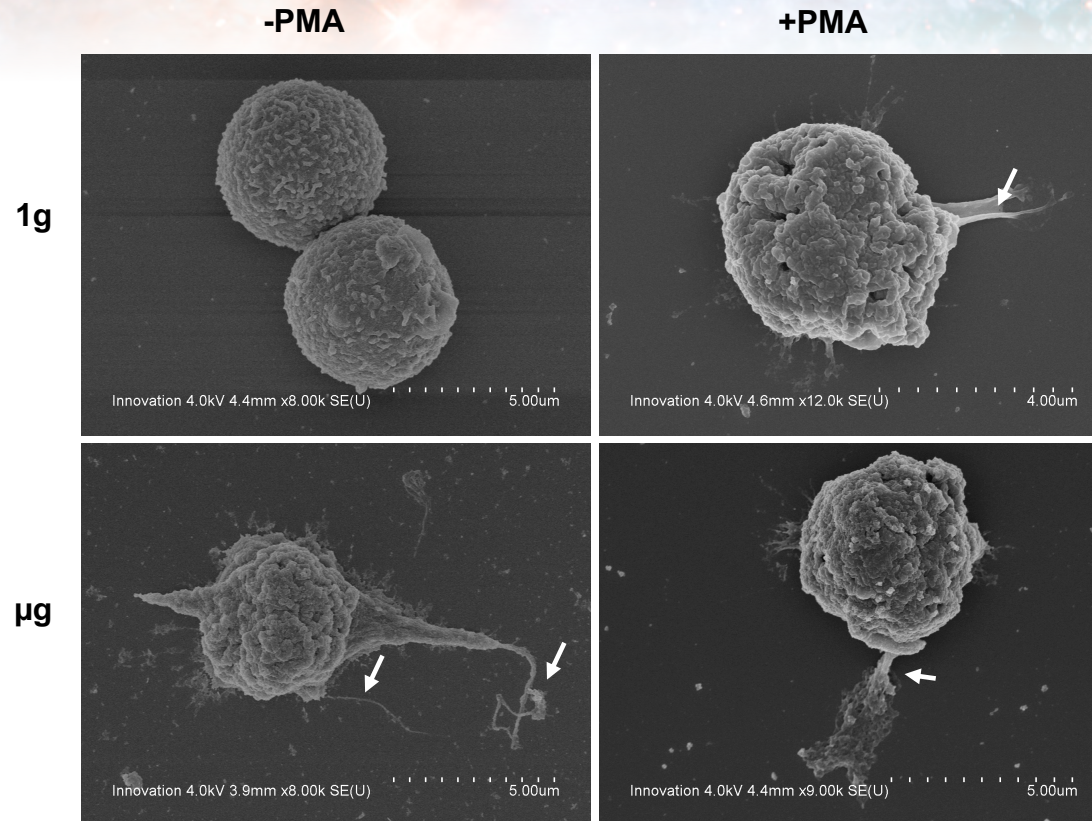
mCAT – Transgenic mice expressing human catalase

Simulated microgravity elevates NETosis



Can contribute to unchecked inflammation (extracellular DNA → DAMPs), therefore an inflammatory biomarker

Simulated microgravity elevates NETosis



Elevated NETosis with ROS and in μg \rightarrow ROS levels define PMN function

Summary

Simulated Microgravity

Impaired phagocytosis and elevated NETosis

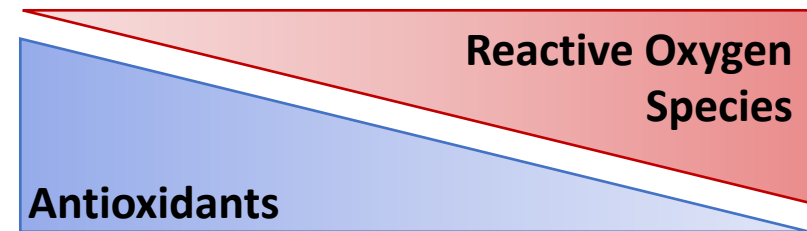
Elevated antioxidant (NAC) and *mCAT* resulted in partial or complete rescue of phagocytosis impairment, but did not restore NETosis

→ Irreversible commitment of PMN to NETosis

NETosis observed in spaceflight-returned samples → elevated NETosis during spaceflight

NETosis as an inflammatory biomarker → can be sensed by the immune system as a danger signal → inflammatory cascade

REDOX Balance



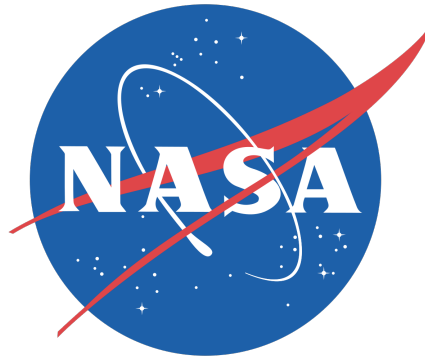
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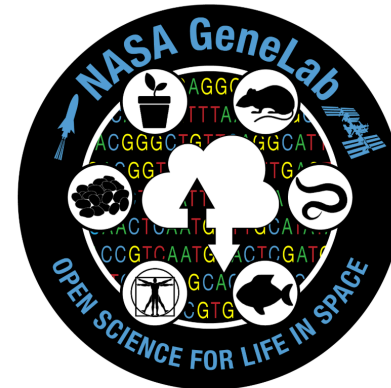
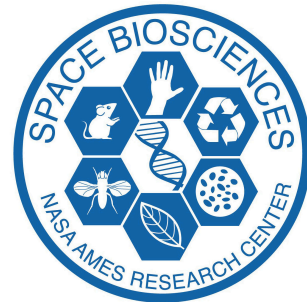
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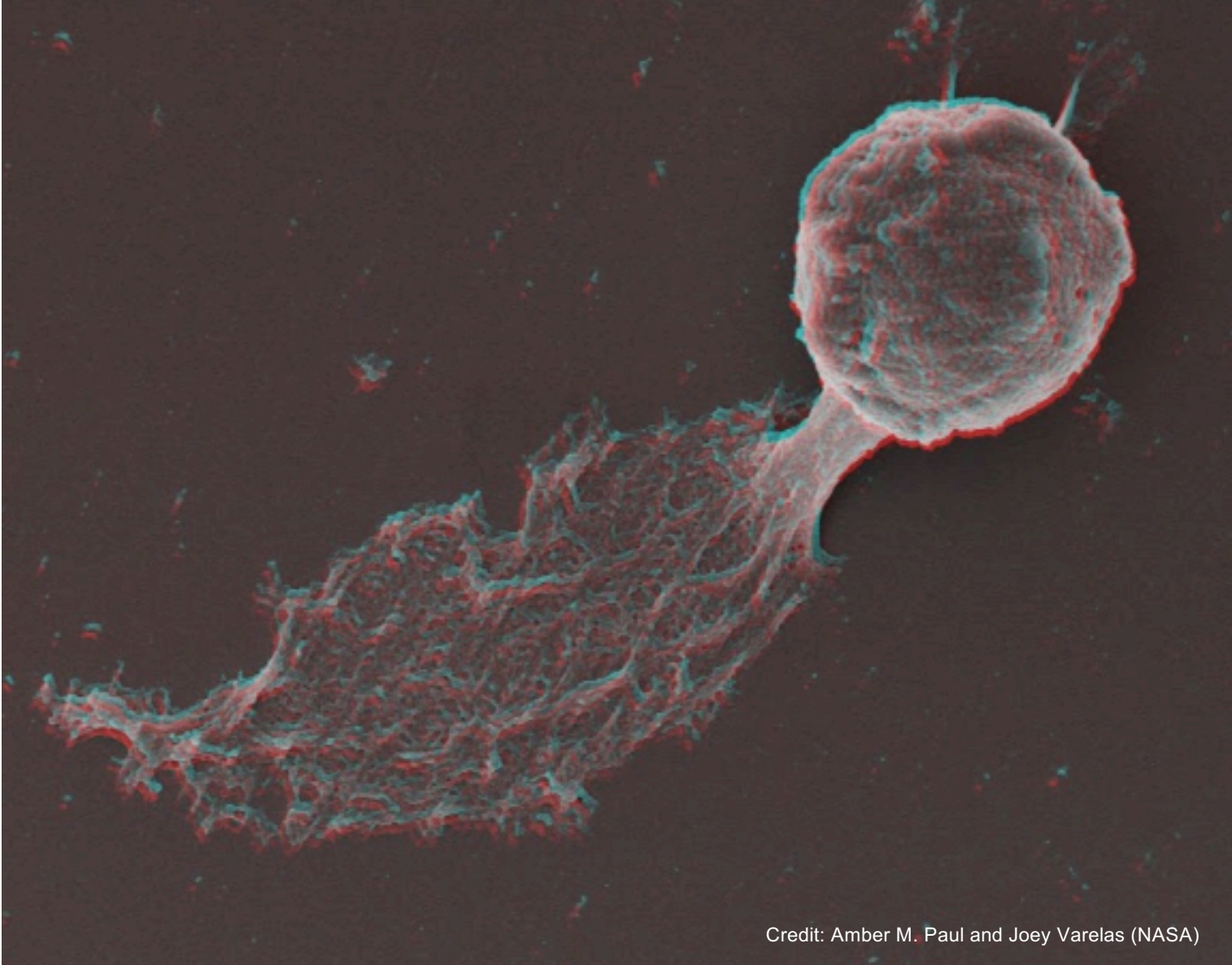
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