Nanomedicine in space: Models and countermeasures

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Human space exploration is progressively extending toward long-duration missions on the Moon and Mars. However, exposure to the combined stressors of microgravity and cosmic radiation deeply affects astronaut health. Micro- (or reduced) gravity induces musculoskeletal atrophy, impaired postural control, and altered immune responses, while radiation accelerates oxidative damage and degenerative processes. A common denominator of these conditions is the excessive generation of reactive oxygen species (ROS), which leads to cellular injury, mitochondrial dysfunction, and increased susceptibility to neurocognitive decline. Current antioxidant countermeasures, typically administered as dietary supplements, are short-lived in their effects and require repeated dosing, limiting their effectiveness for long-term missions. Novel strategies with sustained protective capacity are therefore urgently needed.

Our group develops nanotechnology-based countermeasures designed to overcome these limitations. Inorganic nanoceria, with intrinsic catalytic antioxidant properties, and organic polydopamine nanoparticles have been engineered to provide persistent ROS scavenging activity and to modulate key cellular pathways involved in oxidative stress and inflammation. Using advanced *in vitro* microphysiological models, including human endothelial and astrocytic co-cultures mimicking the blood–brain barrier, as well as immune-relevant microglia, we demonstrated that microgravity alters barrier permeability, inflammatory marker expression (CD40, CD14, CD11b), and oxidative stress levels. Treatment with smart nanomaterials may mitigate these alterations, by preserving barrier function and reducing pro-inflammatory activation.

Beyond ground-based models, our team has participated in several spaceflight campaigns (Figure 1). In the NANOROS and NOEMI missions, skeletal muscle and neuronal cells were exposed to real microgravity aboard the International Space Station (ISS), with and without nanoparticle treatment. Transcriptomic analyses revealed gravity- and radiation-dependent modulation of gene clusters associated with oxidative stress, mitochondrial regulation, and synaptic signaling. Hierarchical clustering confirmed that antioxidant nanomaterials reshaped cellular transcriptional profiles toward a protective phenotype, counteracting the deleterious effects of microgravity and cosmic radiation [1, 2]. In the ongoing PROMETEO mission, polydopamine nanoparticles and nanoceria are being tested in neuronal models to further explore their neuroprotective potential in spaceflight.

These findings advance the understanding of how space environments perturb molecular and cellular homeostasis, while simultaneously validating nanotechnology-based countermeasures for astronaut health. Importantly, the translational potential of these strategies extends well beyond space medicine. Oxidative stress is a major driver of neurodegenerative diseases such as Parkinson's and Alzheimer's, and preliminary data suggest that the same nanomaterials may mitigate neuronal damage in terrestrial disease models. By bridging aerospace research and biomedicine, our work paves the way for dual-use antioxidant nanotherapies, capable of safeguarding both astronauts in orbit and patients on Earth.

Keywords: microgravity, cosmic radiation, oxidative stress, nanoceria, polydopamine nanoparticles, space medicine.

References

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Figures

Figure 1. Space missions accomplished by the IIT Smart Bio-Interfaces Research Unit.