Effect of deep space-related conditions on central nervous system performance in multicellular organisms as a function of their genetic background

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In light of future human exploration of deep space, a fundamental need is to understand how terrestrial organisms may be affected by the peculiar conditions that characterize this extreme environment. Moreover, it will be crucial to dissect how the individual genetic structure may facilitate or jeopardize the adaptation to deep space, with specific regards to normal functioning of the central nervous system.

Compared to terrestrial surface, deep space is characterized by combination of microgravity and peculiar radiative environment, dominated by particle shots and galactic cosmic rays. Terrestrial organisms have adapted to maintain their genomic stability in presence of completely different threats, such as gamma rays from natural radioactivity. However, it is essentially unknown how deep space conditions, characterized by high energy charged particles and secondaries produced by their interactions with surrounding materials, may affect genome stability, especially in complex organisms. Modern genomic studies have revealed that all phenotypically 'normal' humans may carry a high number of mutations, which reduce the function of specific genes but do not produce overt phenotypes under standard environmental conditions. It is possible that some of these defects would become significant vulnerability factors upon exposure to deep space environment.

Since the nervous system is particularly sensitive to radiation, a fundamental and particularly challenging question is to predict how deep space conditions may influence the function and plasticity of neural networks controlling the behaviour of multicellular organisms. An even more challenging question would be to establish whether specific genetic variants or variant combinations would make individuals more sensitive to deep space conditions, and which could exert protective effects. In particular, it would be critical to assess which genetic factors may facilitate or prevent neurodegenerative phenomena under deep space conditions.

The main goal of our group would be to analyze the impact of deep space conditions on different aspects of multicellular organisms' biology, including genome stability, behaviour and neurodegeneration, using both terrestial irradiations with radiation fields mimicking the conditions expected in deep space and experiments performed in actual conditions using Cube-Sats platforms.

We aim at implementing a setup capable of hosting the growth of model organism Caenorhabditis elegans in terrestrial simulators and Cube-Sats. The choice of this model organism is justified by the following elements:

- short life cycle (3 days from eggs to adult - 3 weeks from conception to death);
- high resistance to extreme conditions;
- possibility of hibernation;
- small size and ease analysis of neuromuscular phenotypes;
- great adaptability to growth in microfluidic devices;
- great availability of genetically modified strains, allowing to assess the functional relevance of specific genetic alterations and to test sophisticated genetic hypotheses;
- great similarity of proteome with the human proteome.

Using standard and genetically modified strains, together with dynamic microscopy, the following quantities will be measured and correlated with the radiation dose: viability, rate of reproduction, movement, expression of fluorescent markers of stress and damage. Moreover, the degeneration of specific neuronal populations, labeled by expression of fluorescent proteins, will be analyzed [1].

A more sophisticated setup could also include the capability of performing gene sequencing and gene expression analysis, through adaptation of the minION technology.

The final goal will be to validate the most important findings on simplified human models, such as mini-brain cultures, kept under simulated conditions.

[1] I. de Carlos Cáceres, D.A. Porto, I. Gallotta, P Santonicola, J. Rodríguez-Cordero, E. Di Schiavi, H. Lu. Automated screening of C. elegans neurodegeneration mutants enabled by microfluidics and image analysis algorithms. Integr Biol (Camb). 2018 Sep 17;10(9):539-548. doi: 10.1039/c8ib00091c