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# Understanding natural genetic networks and engineering artificial gene circuits in microgravity

Sayak Mukhopadhyay\*<sup>1</sup> and Sangram Bagh<sup>†1</sup>

<sup>1</sup>Saha Institute of Nuclear Physics, HBNI. – Sector 1, AF Block, Bidhan Nagar, Bidhannagar, Kolkata, West Bengal 700064, India

## Abstract

Microgravity is known to negatively affect human health in long-term space missions. Humans originated in 1G environment and are well adapted to it, with long term habitation in microgravity many physiological changes emerges as an adaptive response. These physiological responses have been well studied and are well explained. It has been found that single cell organisms are also affected from microgravity, similarly many studies showed changes in gene expression in human cells but the underlying mechanism is still not clear. Thus for long term manned mission a thorough understanding about the effect of microgravity at cellular and molecular level is required. To gather deeper insights into the molecular mechanism we employed a set of systems-biology tools to analyze the effect of microgravity on more than 8000 molecular pathways of various functional categories in published global gene expression datasets of human cells exposed to microgravity. Our pipeline revealed hundreds of novel statistically significant altered pathways from individual dataset. Despite diverse experimental and genetic background of cells, comparative analysis of altered pathways between each datasets revealed hundreds of common pathways. Pathways related to reduced inflammation, autoimmunity, diabetes and asthma were identified. We identified Notch1 mediated downregulation of Nf-B pathway as a plausible mechanism for reduced immunity in microgravity. Cancer related signature including liver cancer and leukemia and increased drug response to cancer in microgravity were also identified. Enhancement of olfactory signal transduction pathway in response to microgravity was observed. Next, we identified and clustered leading genes of the common pathways based on their expression pattern using a machine-learning algorithm. The clustered genes revealed plausible regulatory and functional connections within genetic networks. This pipeline provides an integrated systems level insight into microgravity-induced alterations of molecular pathways and networks and generates few testable hypotheses, and may help in estimating risk and developing medicine for space missions. Next, we examined the effect of simulated microgravity on synthetic genetic circuit. We designed an N-IMPLY synthetic genetic gate in *E.coli*, which is externally controllable using two chemical signals and we found a significant behavioural change between microgravity and earth gravity.

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\*Speaker

<sup>†</sup>Corresponding author: sangram.bagh@saha.ac.in