ABSTRACT: Microgravity has been shown to negatively affect biological processes by causing changes in the transcriptome, leading to bone loss, muscle atrophy, and immune system impairment, to name a few examples. We are interested in identifying a “gravitome”, which we define here as gene networks responsive to changes in the gravitational field. In particular, we performed simulated microgravity experiments on C. elegans (F1 generation) and followed the evolution of the gravitome throughout four generations after return to ground control conditions. Our results showed that the majority (78.5%) of the upregulated genes in F1 compared to P0 (ground) maintained their increased levels for more than one generation (78.5%, 45.7%, and 16.3% for F2, F3, and F4, respectively). Similarly, up to 75.5% of the downregulated genes in F1 compared to P0 maintained their lower expression in the following generations (75.5%, 59.1%, and 0.1% for F2, F3, and F4, respectively). F2 and F3 generations display additional upregulated genes which play a putative role in re-adaptation to the ground conditions, and all the upregulated genes in F4 (n=72) were retained from F1. Our results indicate that the Neuropeptide Signaling Pathway was downregulated only for the generation exposed to microgravity. The most enriched gene ontology terms for the downregulated genes for the microgravity-exposed and two ground-reverted generations were: Defense Response to Other Organism, Locomotion, Body Morphogenesis, and Collagen and Cuticulin-based Cuticle. These results suggest that certain previously observed phenotypes, such as immune-deficiency and anatomical changes in astronauts, potentially maintain their impact for two more generations. Others have found abnormal reproductive development under microgravity with different species including mice and plants. Similarly, we have observed upregulation of the genes involved in reproduction and hermaphrodite genitalia development and the increased level of these genes were sustained for three and two generations, respectively. By further investigating the epigenome and regulatory non-coding RNA elements, we also identified the controlling switches of the gravitome. Our approach, besides correlating with the previous findings, displays the additional gene regulatory mechanisms, the sustained multigenerational effect, and the required time for recovery from exposure to microgravity.