Benzofuran derivatives differentially modulate oxidative stress and increase cellular homeostasis in response to radiation and modeled microgravity stresses.


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Microgravity and radiation are profound stressors on the immune system. The purpose of this study is to determine the efficacy of benzofuran derivatives (known for anti-inflammatory effects) as possible immunological countermeasures, in-flight using the ISS platform. We determined the effects of benzofuran-2-carboxylic acid derivatives (KMEG and KM12) on normal human lymphocytes and lymphoblastoid TK6 on cell proliferation, survival, and apoptosis. We also determined the effects of proton irradiation on both cells. Experiments to assess the effects of Space related radiation in 1’g’ and modeled microgravity (mmg) on human lymphocytes and TK6 cells were conducted under different scenarios (0.1Gy-4Gy), with and without the compounds at Loma Linda University in August 2013. Radiation dosimetry was carried on in parallel for all doses. The cells were divided for RNA and proteomics. Samples were analyzed via proteomics (iTRAQ), PCRsuperarrays (RT Profiler) and western blotting. The panel and genes were compared across groups for significant protein and gene alterations in oxidative stress response, proliferation and apoptosis. Preliminary findings in KMEG treated normal human lymphocytes showed that KMEG possibly decreases oxidative stress by up-regulation of peroxiredoxin6 and increases maintenance of cellular homeostasis by up-regulation of regucalcin. In 1’g’ and modeled microgravity (mmg) again KMEG up regulates peroxiredoxin and regucalcin decreasing oxidative stress and maintaining calcium homeostasis. Preliminary results in KM 12 treated TK6 cells indicate that the genes involved in oxidation such as EPX, GPX3, and PRDX5 were over-expressed and the genes involved with antioxidants such as SOD3, ALB, and SRXN1 were down regulated in proton irradiated cells.