

Innate Immune Responses of *Drosophila melanogaster* are Altered by Spaceflight

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Abstract

Alterations and impairment of immune responses in humans present a health risk for space exploration missions. The molecular mechanisms underpinning innate immune defense can be confounded by the complexity of the acquired immune system of humans. *Drosophila* (fruit fly) innate immunity is simpler, and shares many similarities with human innate immunity at the level of molecular and genetic pathways. The goals of this study were to elucidate fundamental immune processes in *Drosophila* affected by spaceflight and to measure host-pathogen responses post-flight. Five containers, each containing ten female and five male fruit flies, were housed and bred on the space shuttle (average orbit altitude of 330.35 km) for 12 days and 18.5 hours. A new generation of flies was reared in microgravity. In larvae, the immune system was examined by analyzing plasmacyte number and activity in culture. In adults, the induced immune responses were analyzed by bacterial clearance and quantitative real-time polymerase chain reaction (qPCR) of selected genes following infection with *E. coli*. The RNA levels of relevant immune pathway genes were determined in both larvae and adults by microarray analysis. The ability of larval plasmacytes to phagocytose *E. coli* in culture was attenuated following spaceflight, and in parallel, the expression of genes involved in cell maturation was downregulated. In addition, the level of constitutive expression of pattern recognition receptors and opsonins that specifically recognize bacteria, and of lysozymes, antimicrobial peptide (AMP) pathway and immune stress genes, hallmarks of humoral immunity, were also reduced in larvae. In adults, the efficiency of bacterial clearance measured *in vivo* following a systemic infection with *E. coli* post-flight, remained robust. We show that spaceflight altered both cellular and humoral immune responses in *Drosophila* and that the disruption occurs at multiple interacting pathways.