

PERSONALIZED RISK ASSESMENT FOR ADVERSE DRUG REACTIONS AND TREATMENT FAILURES

[E. Peletskaya](#)¹ and Y.V. Griko²

¹ *DiaCarta Inc. Richmond, CA, USA*, ² *NASA, Ames Research Center, Moffett Field, CA 94035, USA*

As NASA and other space agencies prepare for future long-term space missions beyond the LEO, the cumulative impact of risk factors encountered in space increases substantially rising concerns about astronauts health. Application of on-board medications to mitigate clinical symptoms associated with certain medical conditions and illnesses is the first line of response to ensure sustainable health and performance of crew. Unfortunately, very limited research has been conducted to determine efficacy of the earth-based pharmaceuticals in a microgravity environment. In some instances, orally administered medications taken during flight were reported to be less effective than expected.

Evaluation of series of experiments involving astronauts from shuttle flights shows notable individual variability to several pharmaceuticals during flight. These data provide reasonable assumption of perturbation in CYP450 enzymes during spaceflight, which contribute to the hepatic metabolism of the majority of drugs and therefore may have significant effects on therapeutic efficacy and increase treatment-related toxicity. The genes encoding the CYP450 enzymes are highly variable in humans. Inheritable variations of CYP450 hepatic metabolizer enzymes and transport proteins play a crucial role in the inter-individual variability of drug efficiency and risks of adverse drug reactions. Additionally, there are some reports that document changes in the levels of production of drug-metabolizing enzymes in microgravity. Therefore, in order to provide a safe and effective pharmaceutical treatment in space, medications selection should be based not only on the specific efficacy of medications but also on the individual drug sensitivity and flight-induced changes in metabolism of astronauts chosen for a particular mission. To our knowledge, there was no pre-flight drug sensitivity testing on a genetic level for any of the previous manned NASA space missions. Therefore, technologies capable of predicting and managing medication efficacy, side effects, and toxicity of drugs based on individual genetic variability of crew members are increasingly needed. In this report, we present results of testing the market available Personalized Prescribing System (PPS), a comprehensive, non-invasive solution for safer, targeted medication management for every crew member. Statistical accuracy and simplicity of non-invasive sample analysis demonstrate the feasibility of drug sensitivity assessment and record-keeping tool for flight surgeons and astronauts in applying the recommended medications for situations arising in flight. The information on individual drug sensitivity will translate into personalized risk assessment for adverse drug reactions and treatment failures for each drug from the medication kit as well as predefined outcome. This will address the HHC's raised "Concern of Clinically Relevant Unpredicted Effects of Medication" as recently updated.