

## Observations on “Journey to Mars: A Biomedical Challenge. Perspective on future human space flight”

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Dear Editor,

We have read with enthusiasm the article by Bizzarri et al. entitled “Journey to Mars: A Biomedical Challenge. Perspective on future human space flight” that’s recently published in the latest issue of *Organisms. Journal of Biological Sciences* (Bizzarri et al., 2017). These researchers have tried to address the microgravity and cosmic radiation effect as the main health risk for space crew. Despite its strengths, the paper authored by Bizzarri et al. has a major shortcoming. This shortcoming is due to ignoring the key point of radio-adaptation in long-term manned space missions. Interestingly, the authors have discussed the issue of adaptive physiological changes to microgravity “*Adaptive physiological changes to microgravity in space can alter the pathophysiology of diseases, the clinical manifestation of illness and injury, as well as the pharmacokinetics and the pharmacodynamics of drugs*”. However, the significant importance of radio-adaptive response in deep space missions that is addressed in the recent report of NASA is entirely ignored by the authors. “*There have been several studies performed that indicate an adaptive response to low-dose ionizing radiation can provide a level of protection against future exposures* (Bhattacharjee and Ito, 2001; Mortazavi et al. 2003; Elmore et al., 2008; Rithidech et al. 2012). *This may be particularly important for understanding risks in the space environment....*” (Huff et al., 2016). In this light, pre-exposure to protons can

increase the resistance of cells through an adaptive response phenomenon. It is worth noting that introducing the key role of pre-exposures and induction of adaptive response phenomena in decreasing the risk of radiation in deep space missions dates back to 2003 (Mortazavi et al., 2003, Mortazavi et al., 2005, Mortazavi, 2013, Mortazavi and Mozdarani, 2013). Recently, more supporting evidence has been provided showing that exposure to low dose radiation can lead to activation of DNA repair and triggered apoptosis of damaged cells. Therefore, ground-based in vitro pre-exposure of lymphocytes of peripheral blood to low dose radiation can be performed to determine individual radio sensitivity of each candidate for a deep space mission. This pre-exposure triggers the nonspecific defensive mechanisms that can make living organisms resistant to high dose radiation or any other detrimental agents. As proposed by Mortazavi et al., the adaptive response of all candidates should be measured by routine cytogenetic tests before any long-term space mission. In these tests, after *in vitro* exposure of blood lymphocytes to an adapting low dose and later to a challenging high dose, the magnitude of the observed adaptive response will be evaluated and only those candidates with the highest levels of induced adaptive response should be chosen for long-term missions. During the mission, as indicated by Bizzarri et al. astronauts will be exposed to two different type of

radiation “Astronauts in outer space are exposed to two forms of radiation: the first one is due to a chronic low-dose exposure to galactic cosmic rays (GCRs), the other one is due to a short-term exposures to the solar energetic particles (SEPs)”. Thus, chronic low-dose exposure to GCRs can considerably decrease radiation susceptibility of the selected candidates and better protect them against the unpredictable short-term exposures to intense SEPs (Bevelacqua *et al.*, Bevelacqua and Mortazavi, 2018).

It can be concluded that although as stated in the paper authored by Bizzarri *et al.* “galactic cosmic ray radiation remains a significant and worsening factor that limits mission”, adaptive response can significantly reduce the risk of all four major challenges of a long-term space mission; carcinogenesis, central nervous system damage, tissue degeneration, and acute radiation disease “Radiation hazard is indeed known to exert radiobiological consequences at all levels of the organism. Four major challenges can be recognized: 1) carcinogenesis, 2) central nervous system damage, 3) tissue degeneration, and 4) acute radiation disease (Sihver 2008)”.

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## Editor’s reply

Dear Dr Mortazavi,

Thank you so much for your interest in ORGANISMS. Your letter adds precious information on a very controversial field. Popular journals and newspaper are currently addressing the perspective of space travels in a very embarrassing way, given that specific and threatening challenges are usually dismissed. I was aware of your priceless contribution, and precisely for this reason, I think that the only ‘true’ radiation risk is constituted by cosmic rays. Therefore, I agree that adaptive response (belonging to the hormesis class of response in biology) (Vaiserman, 2010) can (paradoxically) reduce the risk of all four major challenges of a long-term space mission.

Mariano Bizzarri  
Editor in Chief

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