

# **THREE-DIMENSIONAL NORMAL HUMAN NEURAL PROGENITOR TISSUE-LIKE ASSEMBLIES: A MODEL FOR PERSISTENT VARICELLA-ZOSTER VIRUS INFECTION AND PLATFORM TO STUDY VIRAL INFECTIVITY AND OXIDATIVE STRESS AND DAMAGE**

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The environment of space results in a multitude of challenges to the human physiology that present barriers to extended habitation and exploration. Over 40 years of investigation to define countermeasures to address space flight adaptation has left gaps in our knowledge regarding mitigation strategies partly due to the lack of investigative tools, monitoring strategies, and real time diagnostics to understand the central causative agent(s) responsible for physiologic adaptation and maintaining homeostasis. Spaceflight-adaptation syndrome is the combination of space environmental conditions and the synergistic reaction of the human physiology. Our work addresses the role of oxidative stress and damage (OSaD) as a negative and contributing Risk Factor (RF) in the following areas of combined spaceflight related dysregulation: i) radiation induced cellular damage [1], [2] ii) immune impacts and the inflammatory response [3], [4] and iii) varicella zoster virus (VZV) reactivation [5]. Varicella-zoster (VZV)/Chicken Pox virus is a neurotropic human alphaherpesvirus resulting in varicella upon primary infection, suppressed by the immune system becomes latent in ganglionic neurons, and reactivates under stress events to re-express in zoster and possibly shingles. Our laboratory has developed a complex three-dimensional (3D) normal human neural tissue model that emulates several characteristics of the human trigeminal ganglia (TG) and allows the study of combinatorial experimentation which addresses, simultaneously, OSaD associated with Spaceflight adaptation and habitation [6].

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- 2) Blakely, E.A. (2000). Biological effects of cosmic radiation: Deterministic and stochastic. *Health Physics* 79:495-506
- 3) Crucian BE, Stowe RP, Mehta s, Uchakin P et al., (2013) Immune System Dysregulation Occurs During Short Duration Spaceflight On Board the Space Shuttle, *J. Clin. Immunol*, 2013, Volume 33, 456-465
- 4) Crucian BE, Stowe RP, Pierson DL, Sams CF, (2008) “Immune system dysregulation following short- vs long-duration spaceflight”, *Aviat Space Environ Med*, Sep;79(9):835-43
- 5) Cohrs RJ, and Gildea DH (2007) Prevalence and abundance of latently transcribed varicella-zoster virus genes in human ganglia. *J Virol* 81: 2950–2956
- 6) Goodwin TJ, McCarthy M, Osterrieder N, Cohrs RJ, et al., (2013) “Three-Dimensional Normal Human Neural Progenitor Tissue-Like Assemblies: A Model of Persistent Varicella-Zoster Virus Infection”. *PloS Pathog* 9(8): e1003512. doi:10.1371/journal.ppat.1003512.