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Author: Mr. Elvis Okoro
Texas Southern University, United States

ALLEVIATION OF INFLAMMATION AND STIMULATION OF THE IMMUNE RESPONSE BY DIETARY SUPPLEMENT,ACTIVE HEXOSE CORRELATED COMPOUND (AHCC) IN STRESSFUL PHYSIOLOGICAL ENVIRONMENTS.

Abstract

High altitude, aging, microgravity and inflammation cause long-term physiological stress. Microgravity as physiological stressor model has been described as being similar to ageing (Di Giulio, 2013). AHCC has been shown to alleviate inflammation and immune dysfunction in in vitro and in vivo in conditions of physiological stress (cancer, inflammation and immune suppression) in humans. In a separate set of in vitro experiments, we isolated Peripheral Blood Mononuclear cells (PBMCs) from buffy coat and treated the cells with different concentrations of AHCC – 0 g/ml, 50 g/ml, 100 g/ml, 250 g/ml, 500 g/ml and 1000 g/ml. After a time lag, clumping and aggregation of the cells were seen between 24 to about 72 hours of incubation, after which cells become adherent and phenotypical changes were observed i.e. macrophage like, spindle shaped, elongated, fibroblast like up until 264 hours and beyond. These changes were irreversible and manifested even after AHCC was removed from the media and was donor independent. This could result in a quicker and enhanced immune response. AHCC promotes activation, proliferation and differentiation of leukocytes (multipotent stem cells), as was seen in the genes responsible for these such as LAT (Linker for activated T cells), FLRT2, GIT-1, which were upregulated with very high significance. The LAT signalosome propagates signal branching to three major signaling pathways, the Ca2+, the mitogen-activated protein kinase (MAPK) kinase and the nuclear factor-B (NF-B), leading to the mobilization of transcription factors that are critical for gene expression and essential for T cell growth and differentiation. We also observed actin up-regulation and reorganization indicating that there were T lymphocyte specific gene expression changes in AHCC treated PBMCs (transcription factors such as NFat and NFk) downstream of LAT leading to overexpression of actin. We stained the cells by immunofluorescence for both and found that both translocated to the nucleus. We thus postulate that AHCC augments the immune response via promoting lymphocyte proliferation and actin reorganization via upstream activation of LAT. It is now in human use to augment the immune response. We propose that AHCC could be used in physiologically stressed environments as a countermeasure to boost the immune system.