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RELATIONSHIPS BETWEEN CARDIORESPIRATORY FITNESS AND MARKERS OF SENESENCE AND EXHAUSTION IN PERIPHERAL BLOOD CD8+ T-CELLS AND NK-CELLS

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Relationships between cardiorespiratory fitness and markers of senescence and exhaustion in peripheral blood CD8+ T-cells and NK-cells in the context of latent cytomegalovirus infection: preliminary findings from the Texas City Stress and Health Study

Lifelong infection with the beta-herpesvirus, cytomegalovirus (CMV), may contribute to immune cell exhaustion and the premature acquisition of a senescent phenotype. Regular exercise is considered a viable behavioral intervention to improve latent viral control and prevent the early onset of immunosenescence. We examined relationships between cardiorespiratory fitness (VO_{2max}) and markers of exhaustion (PD-1) and senescence ($p16_{INK4a}$) in peripheral blood T-cells and NK-cells obtained from 317 respondents of the Texas City Stress and Health Study; a large ($n = 1,455$, 58.4 percent female; age 25-91 years) tri-ethnic community located on the southwest shoreline of Galveston Bay, Texas. VO_{2max} was estimated using non-exercise equations that incorporate physical activity rating, body-mass index, age and sex. PD-1 and $p16_{INK4a}$ were measured in cryopreserved CD8+ T-cells and NK-cells by 8-color flow cytometry as part of an ongoing comprehensive immunophenotyping panel. CMV serostatus and optical density (surrogate measure of viral load) was determined by ELISA. The expression of $p16_{INK4a}$ in both CD8+ T-cells and NK-cells was inversely associated with VO_{2max} . Moreover, those with higher VO_{2max} had a lower expression of PD-1 on CD8+ T-cells but not NK-cells. These findings were independent of both CMV serostatus and CMV viral load. However, CMV viral load was positively associated with PD-1 expression on both CD8+ T-cells and NK-cells, and also with $p16_{INK4a}$ in CD8+ T-cells. The relationships between

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CMV viral load and PD-1 expression was strongest in those aged 45-64 years, whereas the relationship with p16_{INK4a} was strongest in those older than 65 years. In conclusion, these preliminary findings have revealed associations between VO_{2max} and the composition of exhausted and senescent CD8+ T-cells and NK-cells, thus advocating exercise as a viable behavioral intervention to offset age-related declines in immune function. Further analysis of this data set will provide important information on the possible protective effects of cardiorespiratory fitness on the premature acquisition of a senescent phenotype in the context of latent herpesvirus infections, low-grade inflammation and a host of psychosocial factors.