ISEI Abstract – 10 Exercise prescriptions for our ageing populations

CMV-specific T-cells mobilized with exercise have broad epitope specificity and a high-differentiated effector memory phenotype

SPIELMANN G[1], BOLLARD CM[2], BIGLEY AB[1], HANLEY PJ[2], BLANEY JW[2], LAVOY ECP[1], PIRCHER H[3], and SIMPSON RJ[1] .

[1]Laboratory of Integrated Physiology, University of Houston; Houston, TX, USA.
[2]Center for Cell and Gene Therapy, Baylor College of Medicine; Houston, TX, USA.
[3]Institute for Medical Microbiology, University of Freiburg; Freiburg, Germany.

ABSTRACT

Introduction: Dynamic exercise evokes a rapid redeployment of cytotoxic T-cell subsets with high surface expression of β_2 adrenergic receptors, presumably to enhance immunosurveillance during acute stress. As this response is affected by age and infection history, the main aim of this study was to examine latent CMV infection as a potential confounder to age-related differences in blood CD8+ T-cell responses to exercise. The second aim of this study was to examine the impact of acute exercise on the mobilization of CMV-specific T-cells in the peripheral blood compartment. **Methods:** Healthy young (n=16) and older (n=16) humans counterbalanced by CMV IgG serostatus (positive or negative) exercised for 30-minutes at ~80% peak cycling power. Isolated blood lymphocytes phenotypes were assessed by flow cytometry and Enzyme-linked immunospot (ELISPOT) analysis was used to determine the frequency and function of T-cells secreting IFN-γ in response to CMV antigens. Maximum likelihood linear mixed models (LMM) were used to determine main effects of exercise (pre, post and 1h post-exercise), age (young or old) and CMV status (positive or negative) on total numbers of blood lymphocytes and their subsets. **Results:** Those with CMV redeployed ~2 times more CD8+ T-cells and ~6-times more KLRG1+/CD28- and CD45RA+/CCR7- CD8+ subsets than non-infected exercisers. Seronegative older exercisers had an impaired redeployment of total CD8+ T-cells, CD45RA+/CCR7+ and (KLRG1-/CD28+) CD8+ subsets. Redeployed CD8+ T-cell numbers were similar between infected young and old. CMVpp65 specific CD8+ cells in HLA/A2* subjects increased ~2.7 fold after exercise, a response that was driven by the KLRG1+/CD28-/CD8+ subset. Stimulating PBMCs before and after exercise with CMVpp65 and CMV IE-1 antigens and overlapping peptide pools revealed a 2.1 and 4.4 fold increases in CMVpp65 and CMV IE-1 IFN-γ secreting cells respectively. The breadth of the T cell response was maintained after exercise with the magnitude of the response being amplified across the entire epitope repertoire. **Conclusion:** We conclude that latent CMV infection overrides age-related impairments in CD8+ T-cell redeployment with exercise. We also show for the first time that many T-cells redeployed with exercise are specific to CMVpp65 and CMV IE-1 antigens, have broad epitope specificity, and are mostly of a high-differentiated effector memory phenotype. We anticipate that these findings may have clinical implications, with acute exercise serving as a simple strategy to increase numbers of available antigen-specific cells in blood that can be harvested for expansion and adoptive T-cell transfer in HSCT recipients.