

## **Exercise Mobilizes Early and Late Differentiated CD8 T cells Expressing a Marker of Exhaustion**

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### ABSTRACT

T cell differentiation occurs following activation of key functions, such as proliferation and cytokine production. Naïve (NA) and central memory (CM) T cells are early differentiated, whereas effector memory (EM) and RA+ effector memory cells (EMRA) are later differentiated. CD57 expression, a putative marker of exhaustion, has also been used to identify later differentiated cells, although recent data indicate CD57 can also be expressed by NA and CM. Exercise mobilizes EM and EMRA to a greater extent than NA and CM. Separately, exercise has been shown to preferentially mobilize CD57+ cells. Whether these exercise responsive CD57+ cells arise from highly differentiated T cells or from across T cell subsets is not known. **PURPOSE:** Determine whether CD57+ cells within NA, CM, EM, and EMRA T cell subsets are mobilized to a greater extent than CD57- cells within the same subsets. **METHODS:** Seventeen participants (7 female; aged 18-40 years) cycled 30 minutes at 80% of their estimated heart rate max. Venous blood obtained pre, post, and 1-hour post-exercise was analyzed by flow cytometry. CD45RA and CCR7 expression within CD8+ T cells identified NA, CM, EM, and EMRA subsets, and CD57 expression within each was quantified. The fold change (FC) in cell frequency was calculated post exercise (post/pre) and 1h post-exercise (1h-post/post). Data were natural log transformed and paired-samples t-tests used to compare CD57+ and CD57- FC within each subset. Separate models compared post-exercise and 1h post-exercise FC. **RESULTS:** Within NA, CD57+ cells were mobilized to a greater extent post exercise than CD57- (FC = 0.92 vs 0.10;  $t = 4.96$ ,  $p < 0.001$ ,  $d = 0.68$ ), as well as 1-hour post-exercise (FC = -0.98 vs -0.20;  $t = -3.91$ ,  $p = 0.001$ ,  $d = 0.82$ ). While CM CD57+ and CD57- cells did not differ in post-exercise FC, CD57+ CM exhibited a greater relative decline 1h-post exercise than CD57- (FC = -0.65 vs -0.20;  $t = -4.55$ ,  $p < 0.001$ ,  $d = 0.41$ ). Within EM, CD57+ cells were mobilized to a greater extent post exercise than CD57- (FC = 0.66 vs 0.35;  $t = 3.77$ ,  $p = 0.002$ ,  $d = 0.35$ ), as well as 1-hour post-exercise (FC = -0.82 vs -0.37;  $t = -4.17$ ,  $p < 0.001$ ,  $d = 0.45$ ). Within EMRA cell subsets, CD57+ cells were also mobilized to a greater extent immediately post-exercise than CD57- (FC = 0.84 vs 0.51;  $t = 4.69$ ,  $p < 0.001$ ,  $d = 0.29$ ) as well as 1-hour post-exercise (FC = -1.06 vs -0.64;  $t = 4.69$ ,  $p < 0.001$ ,  $d = 0.37$ ). **CONCLUSION:** Relative to CD57- cells, CD57+ cells within NA, CM, EM, and EMRA CD8 T-cells subsets exhibit a greater mobilization both into and out of the bloodstream after exercise. These results indicate that CD57 expression associates with greater exercise-response in CD8 T cells, even amongst early differentiated subsets. These results could help to shed light on the denotation of CD57 expression.