TACSM Abstract

Short-Term CD8+ T Cell Depletion Results in Blunted Liver Inflammation in Old Mice

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ABSTRACT

Advanced age is associated with an increase in basal inflammation of the organs. Previously we have found that T cells accumulate in the liver of old animals. A large proportion of these cells are CD8+ and produce inflammatory cytokines. We have previously demonstrated that CD8+ T cell depletion results in improved glucose tolerance in old mice. However, the mechanisms by which CD8+ depletion improves glucose tolerance is unclear. Therefore, we sought to determine whether pharmacologic CD8+ depletion would result in decreased liver specific inflammation in old mice compared to their old CD8+ intact counterparts. **PURPOSE**: To test the hypothesis that old CD8+ T cell depleted mice would exhibit blunted histopathological inflammation and lower inflammatory gene expression compared to old CD8+ T cell intact mice. **METHODS**: Old (22-24mo) mice (n=5-13) were injected every 5 days with anti-CD8+ or Isotype (control) antibodies for 28 days. A lobe of the liver was saved for histology, and the remaining liver was saved for qPCR analysis. Livers were embedded, sectioned, and stained using Hematoxylin and Eosin and scored to assess histopathological inflammation. Liver inflammatory gene expression was assessed by qPCR. Group differences were assessed by independent samples T-test. Data is presented as mean ± SEM (qPCR data normalized to old Isotype; Units Arbitrary (AU)). **RESULTS**: Old CD8+ depleted mice tended to have lower gene expression of the cytokine *Il6* (Control: 1.00±0.24 AU, Anti-CD8 0.5±0.2 AU; p=0.06), while the cytokine *Tnfa* (Control: 0.90±0.21 AU, Anti-CD8: 0.92±0.25 AU; p=0.4) was not different. In addition, the inflammatory chemokines *Ccl2* (Control: 1.00±0.27 AU, Anti:CD8: 0.58±0.17 AU; p=0.1) and *Ccl5* (Control: 1.00±0.43 AU, Anti-CD8: 0.38±0.11 AU; p=0.06) tended to be lower in the depleted mice compared to controls. Histopathological analysis of the liver revealed that CD8+ depleted mice tended to have lower inflammation scores (Control: 2.4±0.40 AU, Anti-CD8: 1.6±0.24 AU; p=0.06) compared to CD8+ intact controls. **CONCLUSION**: Short-term manipulation of CD8+ T cells may result in decreased liver inflammation compared to old controls. The specific mechanisms in which old CD8+ T cells influence liver inflammation are unknown.