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Title: T CELL SUBSETS ALTERED IN A MURINE ALZHEIMER'S MODEL SUPERIMPOSED WITH LATENT U94A

Abstract: Alzheimer's disease (AD) is a complex disease with a wide range of contributing factors. Recently, both human herpesviruses (HHV6) and the peripheral immune system has been implicated in AD but the individual role of viruses and its interaction with the immune system has not been studied extensively. U94A, the HHV6 latency associated viral gene, is constitutively expressed during latency. Using a U94A transgenic mouse model, which only expresses U94A and no other viral products, we have shown that U94A exacerbates AD pathology by both accelerating amyloid plaque formation and behavioral decline. However, while this work focuses on neurological aspects of AD, immune subsets, particularly those influencing inflammation, were not studied. Various T cell subsets, such as cytotoxic CD8⁺ T cells, can promote inflammation while other subsets, such as Tregs, can modulate/suppress inflammation through secretion of anti-inflammatory IL-10. To address whether the peripheral immune system is also affected, we interrogate the peritoneal cavity, spleen, and peripheral blood in APPNL-G-F (APPKI), APPKI/U94, and wild-type C57/BL6 mice using high-dimensional flow cytometry which allows us to isolate multiple T cell subsets. Here we observe differences in T cell subsets which correlate with our histological and behavioral data. Our results provide both a potential for both immune-targeted therapeutics for AD and early-detection screening in the context of latent viral infections which has not been studied previously.