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# Expression of *Sirpα* Tailless Mutant in Mice Impairs Naïve CD4+ T Cell Adhesion to Immobilized ICAM-1 and TCR Induced Proliferation.

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Signal Regulatory Protein alpha (SIRPα) interaction with its ligand CD47 plays an important role in immune cell homeostasis. CD47 is expressed by essentially all cell types, and acts as a "don't eat me signal" and a marker of self. We previously demonstrated that CD47 on both endothelium and T cells plays an important role in T cell adhesion and diapedesis *in vivo* and *in vitro,* and that $CD47^{-/-}$ $CD4^{+}$ T cells had impaired antigen mediated proliferation in a model of Experimental Autoimmune Encephalomyelitis (EAE). In contrast to CD47, SIRPα has been reported as selectively expressed in the Central Nervous System (CNS), in most myeloid cells and at very low levels-to-absent in lymphoid cells in humans. To gain insight into the function of SIRPα in leukocyte recruitment, *Sirpα* truncated cytoplasmic, non-signaling mutant *(Sirpatm1Nog)* transgenic mice and WT mice were studied in TNFα-induced dermal air pouch model of inflammation. Unexpectedly, $CD4^{+}$ T cells in *Sirpatm1Nog* mice, compared to WT mice, had significantly decreased recruitment into the air pouch (WT, $11.9 \pm 2.9 \times 10^3$ vs *Sirpatm1Nog,* $7.8 \pm 2.6 \times 10^3$, $p<0.05$), whereas no differences in $CD8^{+}$ T cell or myeloid cell recruitment were observed. Interestingly, flow cytometric analysis using P84 monoclonal antibody showed that a low but significant fraction of $CD4^{+}$ T cells in both WT and *Sirpatm1Nog* mice expressed SIRPα. Expression of Very Late Antigen-4 (VLA-4) and Lymphocyte Function Associated Antigen-1 (LFA-1) integrins, which are ligands of Vascular Cell Adhesion Molecule-1 (VCAM-1) and Intercellular Adhesion Molecule-1 (ICAM-1), respectively, were similar in T cells from WT and *Sirpatm1Nog* mice. Additional studies showed naïve $CD4^{+}$ isolated from *Sirpatm1Nog,* compared to WT mice, had significantly blunted proliferation 48 hrs after T cell receptor crosslinking (TCR-XL), and that CD4 T cells had impaired SDF-1α induced arrest on immobilized ICAM-1 under shear flow conditions. In summary, these studies demonstrate that SIRPα plays an unexpected and important role in T cell recruitment *in vivo* and *in vitro* and in TCR-XL induced proliferation *in vitro.* These data suggest that loss of SIRPα signaling in SIRPα+ T cells leads to impaired LFA-1 activation.

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