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Macro meets T: Signaling Lymphocyte Activation Molecule Family Member 1 (SLAMF1) promotes protective immunity against *Mtb* through macrophage-T cell interaction

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In an RNA-seq screen, we found that SLAMF1 was highly induced in infected murine bone marrow-derived MΦs (BMDM) and CD4 T cells when they were co-cultured. SLAMF1 is a homophilic receptor. In T-cells, engagement of SLAMF1 triggers T-cell proliferation and IFNγ production. In MΦs, upon recognizing bacterial antigens, SLAMF1 induces autophagy, phagosome formation/maturation, ROS generation, and bacterial killing. Here, we hypothesize that SLAMF1 is vital in mediating MΦ-T cell interaction and controlling Mtb. We found that antigen-specific CD4 T cells promoted SLAMF1 surface expression in MΦs if the MΦs were infected with Mtb. Additionally, we found that SLAMF1 induction in infected MΦs depended on direct contact with T-cells. We assessed if T-cells are required for SLAMF1 induction in MΦs in vivo by infecting Tcra-/- and Rag-/- mice. We found that SLAMF1 expression was reduced in Mtb-infected monocytes and monocyte-derived cells (MDCs). Adoptive transfer of naïve CD4 T cells to Mtb-infected Tcra-/- mice, restored SLAMF1 expression in monocytes and MDCs. We further examined if SLAMF1 contributes to controlling Mtb infection in mice. Analysis of bacterial burden in the lungs of WT and Slamf1-/- KO (SKO) mice at 4 wpi showed higher bacterial load in SKO than WT mice. Lung cell immunophenotyping showed that SLAMF1 expression increased in both CD4 and CD8 T cells and infected myeloid cells of WT mice upon infection. Moreover, infected SKO mice had more T cells, myeloid cells, and dysregulated inflammatory cytokine production than WT. Also, SKO mice succumbed earlier to Mtb infection than the WT mice. Furthermore, we examined whether SLAMF1 contributes to ROS generation in macrophages by infecting BMDMs with redox-sensitive reporter Mtb strain. We found that Mtb encountered lesser oxidative stress in SKO MΦs than WT MΦs, suggesting that SKO MΦs are defective in producing ROS. SLAMF1 engagement on MΦs and T-cells mediates protective immune responses against Mtb infection.

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Conflicts of Interest

None