# SLAMF7 (CD319) is a key regulator of CD4 T-Cell differentiation


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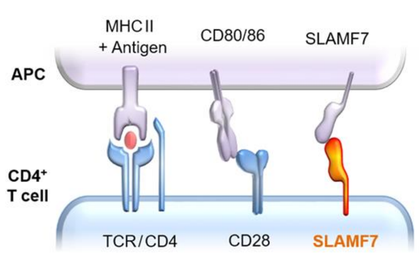
## INTRODUCTION

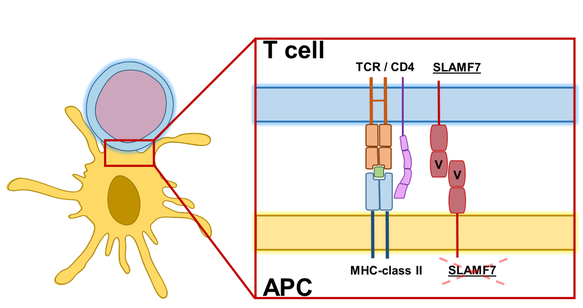



- SLAMF7 is a self-adhesion receptor and was initially identified on NK cells.
- SLAMF7 expression is linked to the cytolytic CD8 T-cell response program (Lingel et al. 2024).
- SLAMF7 promotes coordinated CD8 T-cell response (Lingel et al. 2024).

## AIM OF THE STUDY

Investigate the expression, signalling and role of SLAMF7 during the CD4 T-cell differentiation.

## METHODS




1. CD4 T cells with TCRtg + OVA-peptide presented by WT APC or SLAMF7 KO APC
2. WT CD4 T cells + αCD3/αSLAMF7 coupled microspheres
3. SLAMF7 KO CD4 T cell + αCD3/αSLAMF7 coupled microspheres

## RESULTS

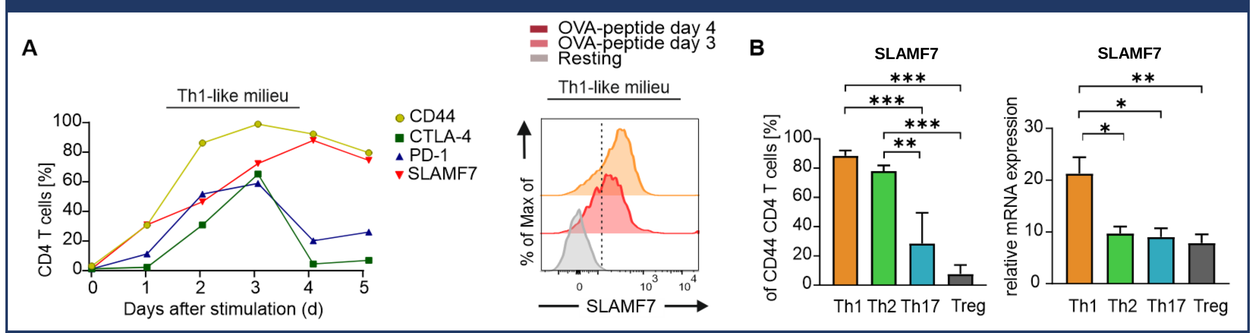



**Figure 1. SLAMF7 expression on the surface of CD4 T cells**

(A) Kinetics of SLAMF7 surface expression on CD4 T cells upon activation. OVA-specific, naive CD4 T cells were enriched via MACS and stimulated with congenic APCs and OVA-peptide in the presence of Th1 polarizing cytokines. (B) Surface expression of SLAMF7 in different Th subsets (left). Relative mRNA expression of SLAMF7 in different Th subsets (right). CD4 T cells were enriched by MACS and stimulated with microspheres coupled to αCD3/αCD28.

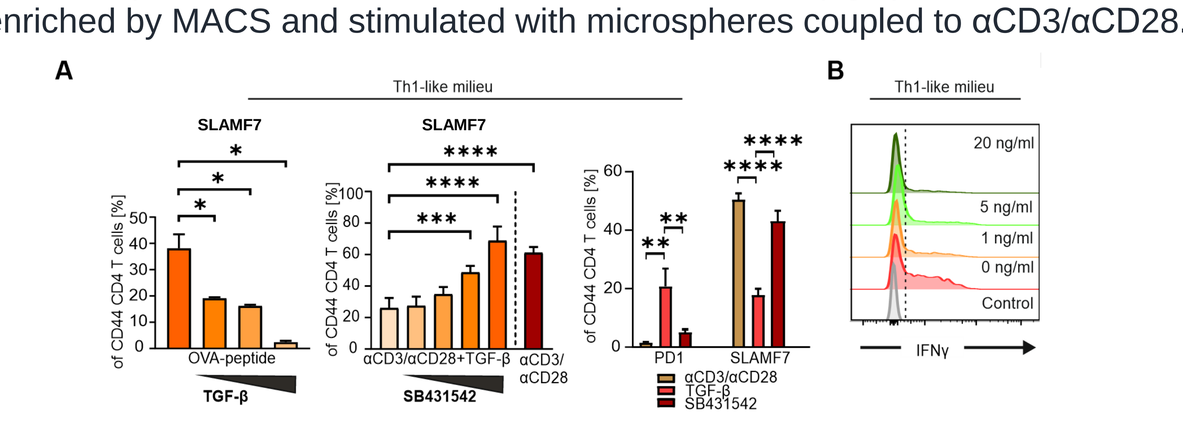



**Figure 2. TGF-β and IFNs regulate SLAMF7 expression in CD4 T cells.**

(A) TGF-β inhibits SLAMF7 surface expression in a dose-dependent manner (left). Blocking the TGF-β pathway prevents TGF-β-induced downregulation of SLAMF7 (middle). TGF-β signalling plays an opposite role in the regulation of SLAMF7 surface expression compared to PD-1 (right). CD4 T cells were stimulated as in Figure 1A. (B) Intracellular IFNγ expression in CD4 T cells stimulated with microspheres coupled to αCD3/αCD28 with and without addition of TGF-β. (C) SLAMF7 expression on CD4 T cells in the Th17-like milieu dependent on IFNγ but not IL-12 in cell culture. (D) IFN type 1 increase SLAMF7 expression in Th17 cells. (E) Enhanced SLAMF7 expression in IL-17 producers after addition of IFN type 1 in cell culture.

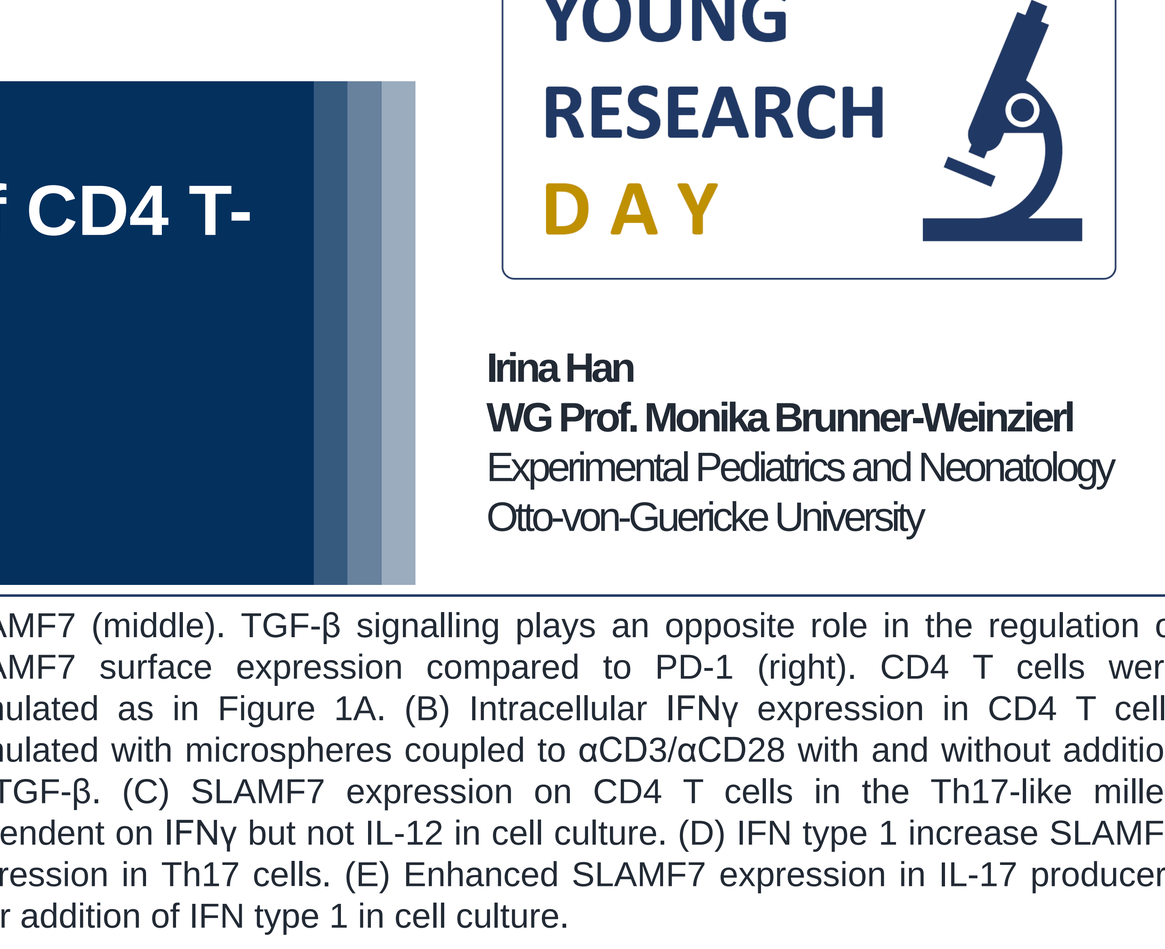



**Figure 3. SLAMF7 doesn‘t require completion of cell cycle and promotes T-cell proliferation**

(A) Proliferation and SLAMF7 expression were analysed by flow cytometry in CD4 T cells stimulated as in Figure 1A. (B) Proliferation and SLAMF7 expression were analysed in CD4 T cells stimulated as in Figure 1B after G1/G2 cell cycle arrest. (C) Proliferation in CD4 T cells from C57Bl/6 mice after stimulation with microspheres coupled to αCD3/αSLAMF7 or to αCD3/Isotype as control. (D) Proliferation in CD4 T cells from SLAMF7 KO mouse after stimulation with microspheres coupled to αCD3/αCD28/αSLAMF7 or to αCD3/αSLAMF7.

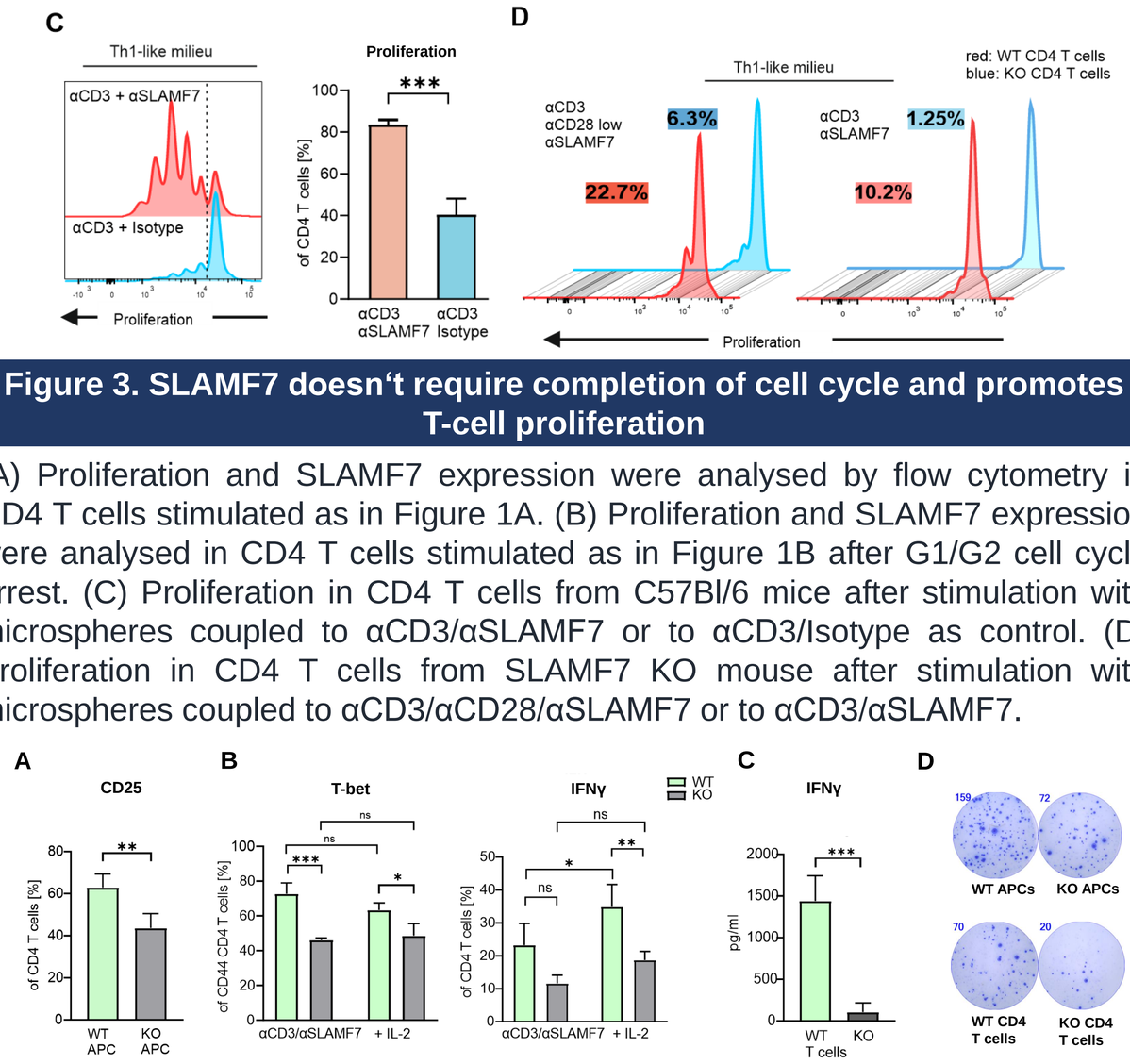



**Figure 4. SLAMF7 promotes T-cell activation and Th1-cell polarization.**

(A) CD25 expression on activated CD4 T cells. CD4 T cells were isolated from OT-II mice and stimulated with OVA peptide presented by either WT APCs or SLAMF7 KO APCs (B) Expression of T-bet and IFNγ in CD4 T cells from WT or SLAMF7 KO mice as measured by flow cytometry. Cells were stimulated with αCD3/αSLAMF7 coupled microspheres with or without IL-2 in cell culture. (C) IFNγ in supernatants of CD4 T cells stimulated with αCD3/αSLAMF7 coupled microspheres. (D) IFNγ producers detected by EliSpot. CD4 T cells were stimulated as in A (top row). CD4 T cells were stimulated as in C (bottom row).

## CONCLUSIONS

- SLAMF7 expression is dependent on T cell activation, but not on cell cycle completion.
- TGF-β prevents SLAMF7 expression, whereas IFNs type 1 enhance it.
- CD4 T cells genetically lacking SLAMF7 show reduced proliferation, downregulated T-bet expression and reduced IFNγ production.

These findings identify a target molecule on the surface of T helper cells that may play a key role in regulating CD4 T-cell differentiation and responses.