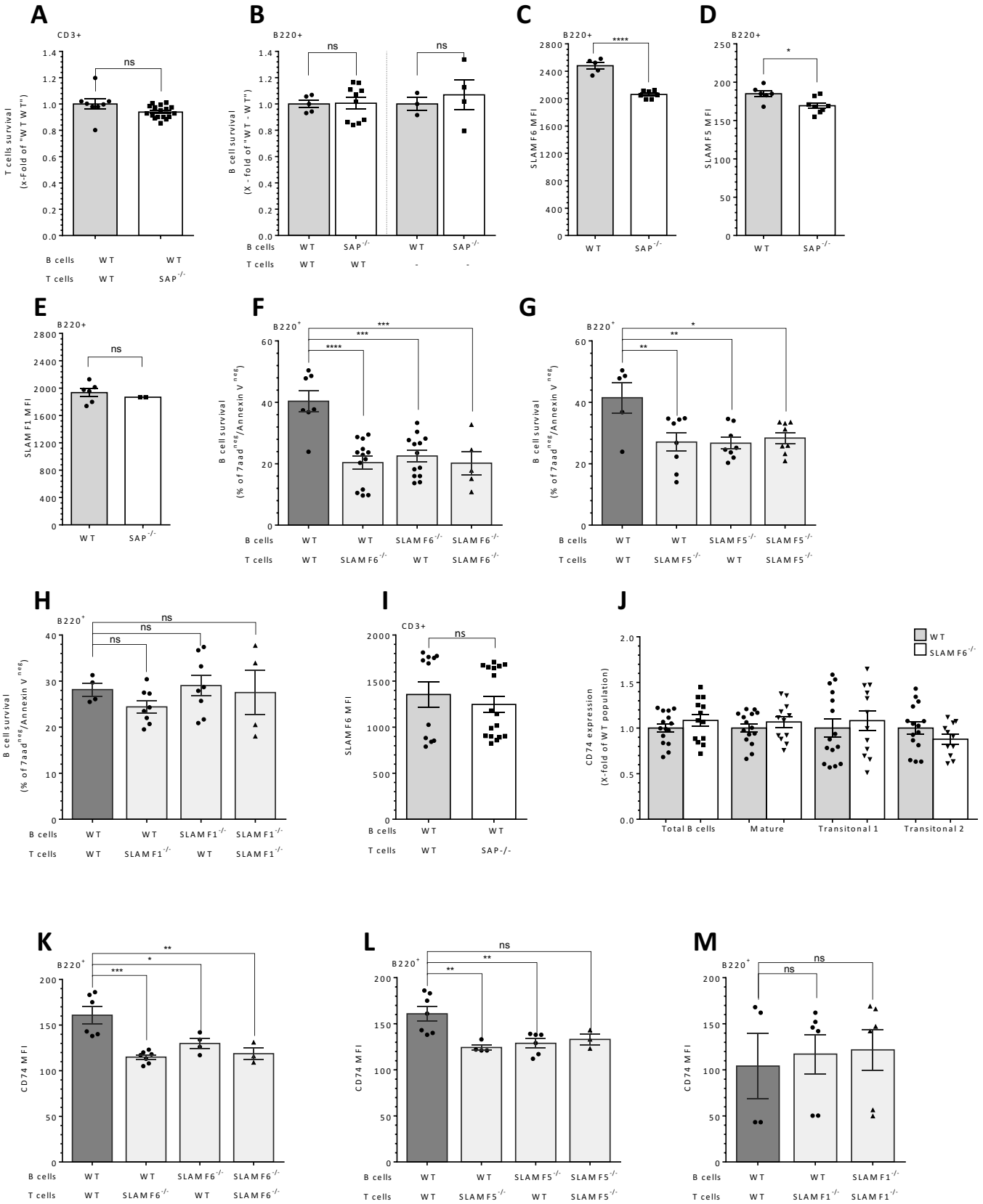
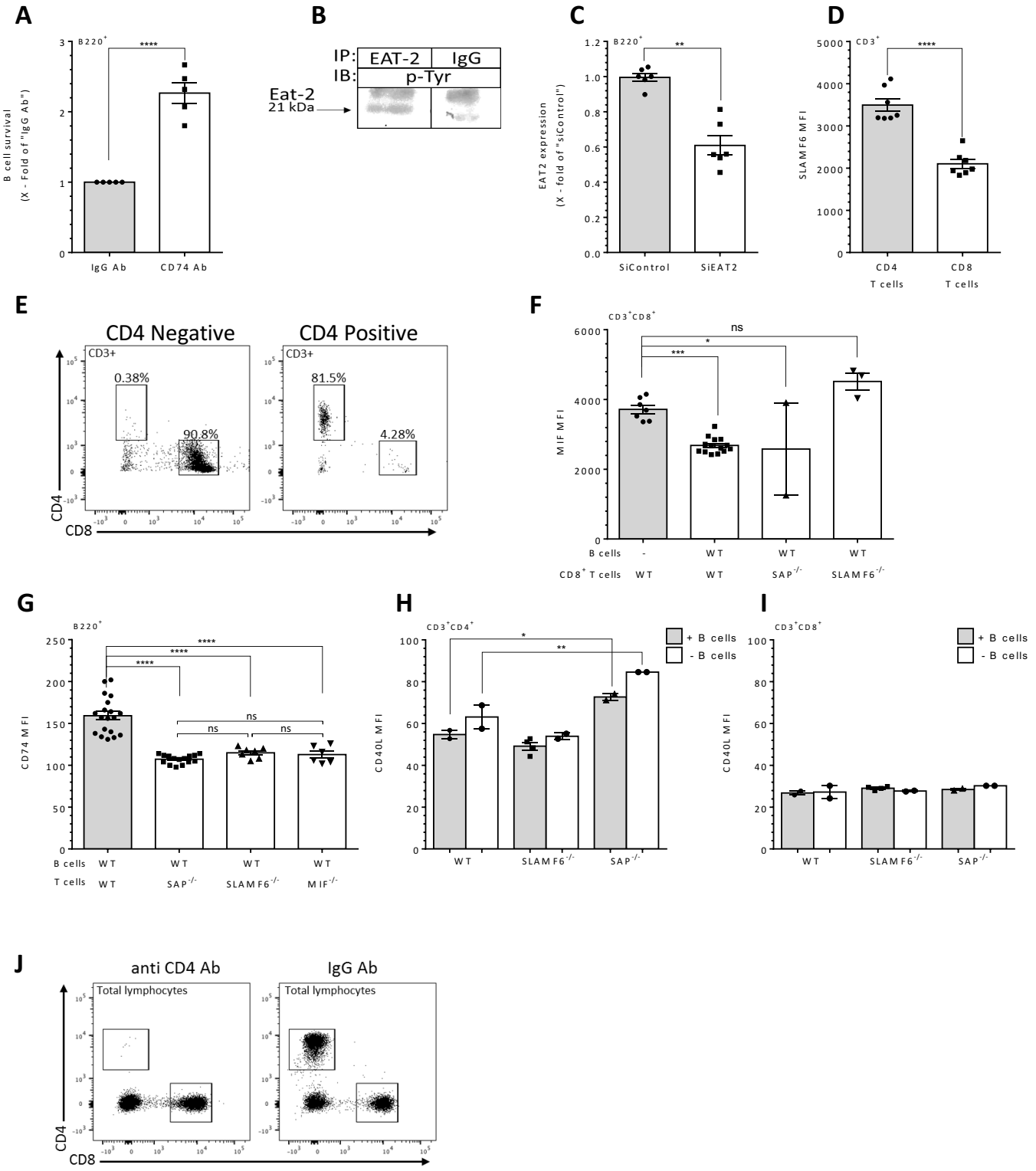


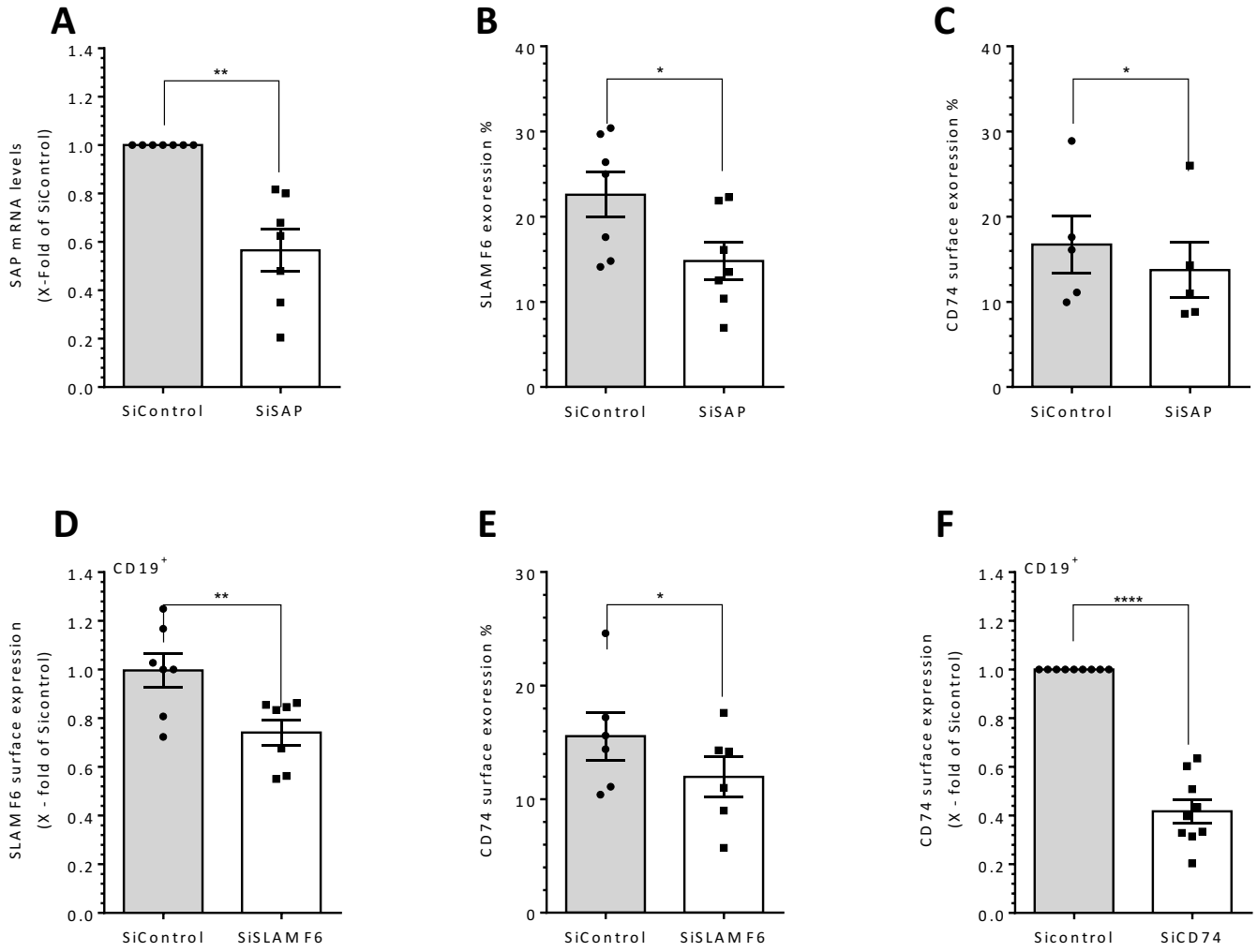
Supplementary Figure 1- SAP and SLAMs in B cell maintenance

(A) Purified naïve wt B cells were cultured at 1:1 ratio with $5x10^6$ wt or SAP$^{-/-}$ T cells. After 24 hours, the T cells were analyzed by flow cytometry for T cell survival. Results are shown as fold of change compared to "wt B cells and wt T cells" culture. N=7 **(B)** Purified wt or SAP$^{-/-}$ derived B cells were cultured alone or at 1:1 ratio with $5x10^6$ wt T cells. After 24 hours, the B cells were analyzed by flow cytometry for cell survival. Results are shown as fold of change compared to "w B cells and wt T cells" (left) or compared to wt B cells alone (left). N=3. **(C-E)** Fresh wt and SAP$^{-/-}$ derived mature naïve B cells were analyzed by flow cytometry for **(C)** SLAMF6 N=3 , **(D)** SLAMF5 N=3 and **(E)** SLAMF1 N=1 surface expression. Results are shown as the SLAMs MFI. Purified naïve wt or SLAMF6$^{-/-}$ N=4. **(F)** or SLAMF5$^{-/-}$ N=3. **(G)** or SLAMF1$^{-/-}$ N=2. **(H)** B cells were cultured at 1:1 ratio with $5x10^6$ wt or SLAMF6$^{-/-}$ / SLAMF5$^{-/-}$ or SLAMF1$^{-/-}$ T cells. After 24 hours, the B cells were analyzed by flow cytometry for B cell survival (Results are shown as the percentage of live B cells (double negative to Annexin V/7AAD). **(I)** Naïve wt B cells and wt or SAP$^{-/-}$ T splenocytes were cultured alone or at a 1:1 ratio with $5x10^6$ wt or SAP$^{-/-}$ T cells. After 24 hours, cells were analyzed by flow cytometry for SLAMF6 expression on T cells (CD3$^+$ gate). Results shown as SLAMF6 MFI. N=4 **(J)** Wt and SLAMF6$^{-/-}$ splenocytes were analyzed by flow cytometry for surface CD74 expression on B cell populations; Total B cells (B220$^+$); mature population (B220$^+$, CD21^{int}CD24^{low}), Transitional 1 (B220$^+$, CD21^{low}CD24^{high}) and Transitional 2 (B220$^+$, CD21^{high}CD24$^+$CD23$^+$), results are shown as CD74 surface expression as X-fold of WT populations. N=4. **(K-M)** Purified naïve wt or SLAMF6$^{-/-}$ (N=6) **(K)**, SLAMF5$^{-/-}$ (N=3) **(L)** or SLAMF1$^{-/-}$ (N=2). **(M)** B cells were cultured at 1:1 ratio with $5x10^6$ wt or the respective knock out T cells. After 24 hours, the B cells were analyzed by flow cytometry for CD74 expression (results are shown as CD74 MFI).



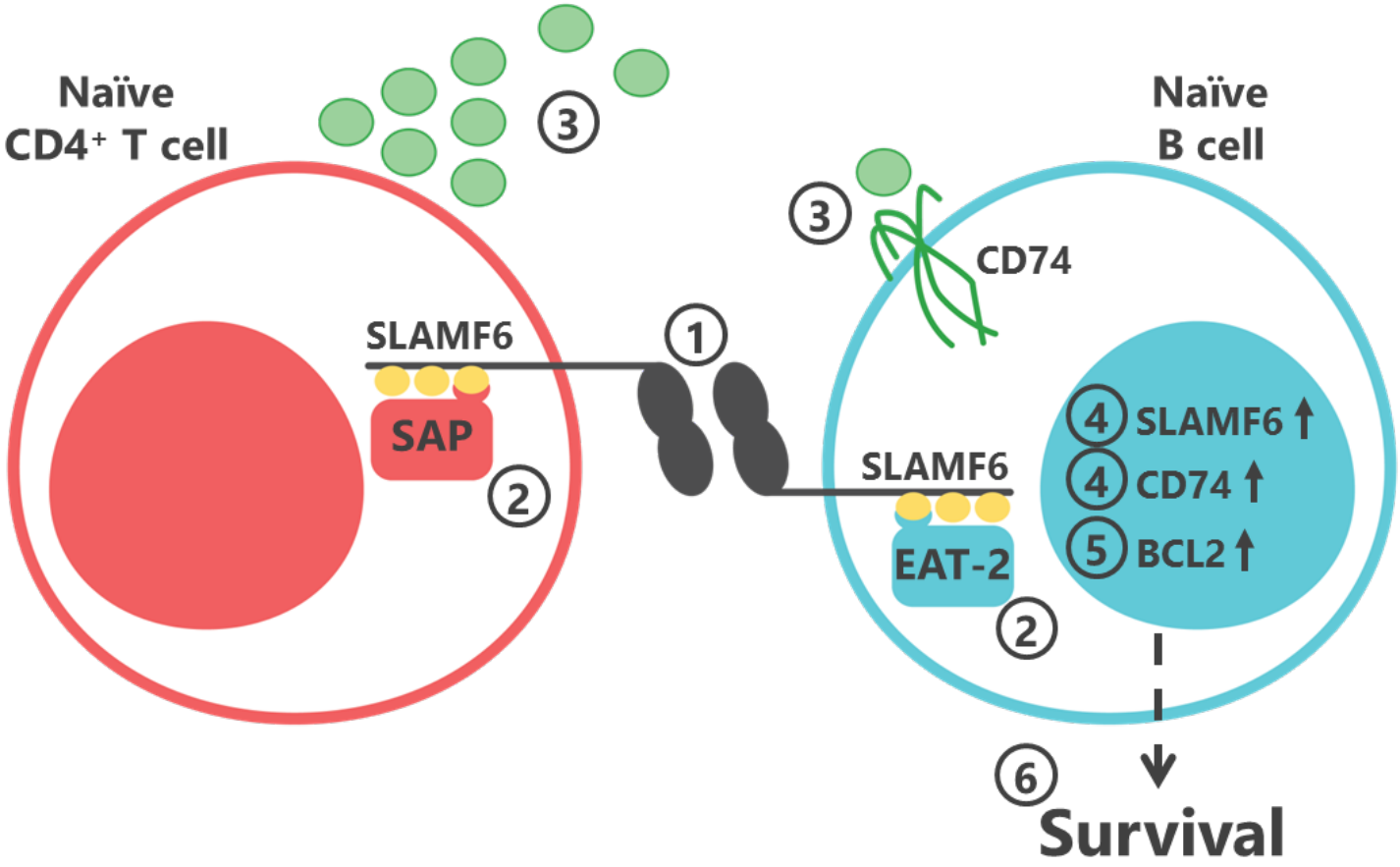
Supplementary Fig 2- Characterization of CD74 and SLAMF6 in T cell function

(A) Naïve mature wt B cells were activated with anti-CD74 or IgG control antibodies for 18 hours. Cells were then analyzed for B cell survival by Annexin V/7AAD staining on the $B220^+$ gate. N=2 **(B)** Purified wt B splenocytes were lysed, and EAT-2 was immunoprecipitated. Proteins were separated by 12% SDS-PAGE and analyzed for p-Tyr expression n=2 . **(C)** Naive B cells were treated with siRNA EAT2 or si control and were co-cultured with untreated naive T cells. After 48 hrs, the cells were stained for EAT2. N=2 **(D)** Splenocytes were stained for CD3, CD4, CD8 or SLAMF6. Graph shows SLAMF6 expression on T cells (MFI). **(E)** Naïve or $SAP^{-/-}$ splenocytes were harvested and enriched first for $B220^+$ by BD bioscience magnetic beads. The negative fraction was further enriched for $CD4^+$ by anti-CD4 magnetic beads. Following the separation the cells were stained for $CD3^+$, $CD4^+$ and $CD8^+$. Representative dot plots of $CD3^+$ cells: left; CD4 beads negative fraction, right; CD4 beads positive fraction. **(F)** Naïve wt / $SAP^{-/-}$ /$SLAMF6^{-/-}$ T splenocytes were cultured alone or at a 1:1 ratio with $5x10^6$ wt B cells. After 24 hours expression of MIF in $CD3^+CD4^+$ was analyzed by flow cytometry. N=2 **(G)** Purified naïve wt B cells were cultured at 1:1 ratio with $5x10^6$ wt / $SAP^{-/-}$ / $SLAMF6^{-/-}$ or $MIF^{-/-}$ T cells. After 24 hours B cells were analyzed by Flow cytometry for CD74 cell surface expression. Graph shows CD74 MFI levels. N=8 **(H-I)** Purified naïve $5x10^6$ wt / $SAP^{-/-}$ or $SLAMF6^{-/-}$ $CD4^+$ T cells, **(H)** or $CD8^+$ T cells **(I)** cells were cultured alone or with WT B cells. Following 24 hours, CD40L expression was analyzed on the T cells by flow cytometry. **(J)** Wt mice were i.v. injected with 150 µg/ml anti-CD4 or IgG control Abs diluted in sterile PBS to a final volume of 200 µl. Mice were bled and stained for $CD8^+CD4^+$ cells to verify CD4 depletion. A representative dot plot is shownIn all graphs, each dot represents a biological repeat. N represents the number of experiments. Bars showing SEM. ns $p \geq 0.05$, * $p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$



Supplementary Figure 3-siRNA in human PB B cells

(A-F) Healthy human PB B cells were co-cultured with healthy human (from the same donor) PB T cells that were treated with control scrambled (siControl) or SAP (siSAP) **(A-C)** SLAMF6 (siSLAMF6) **(D,E)**, or CD74 (siCD74) **(F)** siRNA. (A)Following 24 hours of incubation RNA was purified and SAP mRNA levels were analyzed by qRT-PCR. Following 48 hr cell surface expression of SLAMF6 (B,D) or CD74 (C,E,F) on B cells. Results are shown as fold change relative to the siControl; bars indicate SEM, Each dot represents a biological repeat. **p<0.01, ****p<0.0001. N=3



Supplementary figure 4 – Visual Abstract
(1) SLAMF6 receptors mediate the interaction of naïve B and CD4+ T cells. **(2)** SLAMF6 in B cells recruits EAT-2 while SLAMF6 in T cells recruits SAP. This interaction induces a signaling cascade in **(3)** T cells leading to mif secretion. Mif then binds CD74 receptor on B cells leading to a downstream positive feedback loop **(4)** of SLAMF6 and CD74 elevation. This consequently **(5)** leads to an increase in BCL-2 and to **(6)** B cell survival.