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FCγRIIIA IS A DISTINCT ACTIVATING COSIGNAL IN CD4+ T CELLS THAT SYNERGIZE WITH TLR9

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We have been exploring the mechanistic insight of the stimulatory effects of FcγRIIIa cosignaling in human $CD4^+$ T-cells. $CD4^+$ T cells also express FcγRIIa and these cells accumulate HIV provirus. We have previously shown that FcγRIIIa cosignal participate in relocating endosomal NA-TLRs to the cell surface, where they can recognize modified self-nucleic acid. Joint signaling from FcγRIIIa and TLR9 (CpG ODN 2006) enhances IL-17A, IL-21 production. Now, we show that FcγRIIIa cosignaling generate a new subset that show Syk phosphorylation and express TFH markers i.e. Bcl6, CXCR5, ICOS and PD1. In HIV infection, blood TFH cells do not express Bcl6+, contrary to this finding we observed Bcl6 in blood pSyk+ T cells *in vivo* in systemic lupus erythematosus (SLE) and in *in vitro*. Bcl6+ cells in blood produce IFN-γ, IL-17A and IL-21. The Syk inhibitor block IL-21 production. pSyk+ cells show moderate PD1 expression compared to a second population that express high PD1. Our RNA-seq data show differential expression of lincRNA and microRNA from FcγRIIIa cosignaling that contribute to T cell differentiation. A key finding was upregulation of *mir*1307, a recognized risk allele for SLE in GWAS studies. We propose that FcγRIIIa drives epigenetic changes in CD4+ T cells. Transcription factors c-Maf, FOXO were upregulated. FcγRIIIa cosignal modulated ubiquitination, HSPs, proteasome assembly, and GPCR signaling. Our data provide new insight into the FcR biology in adaptive responses and raises several interesting questions. Does FcRs bearing effector CD4+ T cells superior helper, for the development of autoreactive B cells?