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Titel des Beitrags: Expression of miRNAs miR-133b and miR-206 in the Il17a/f Locus Is Co-Regulated with IL-17 Production in ?? and ?? T Cells.

Abstract: Differentiation of T helper 17 cells (Th17) is a multistep process that involves the cytokines IL-6, TGF-?, and IL-23 as well as IL-1?, IL-21, and TNF-?. Thereby, robust induction of the capacity to produce IL-17 involves epigenetic modifications of the syntenic Il17a/f locus. Using inbred mouse strains, we identified co-regulation of gene transcription at the Il17a/f locus with the nearby microRNAs miR-133b and miR-206 that are clustered approximately 45 kb upstream of Il17a/f. Expression of these microRNAs was specific for Th17 as compared to other CD4(+) T cell subsets and this was equally valid for in vitro polarized and ex vivo derived cells. From all factors analyzed, IL-23 was the most important cytokine for the in vitro induction of miR-133b and miR-206 in naïve CD4(+) T cells of wild type mice. However, analysis of IL-23R deficient mice revealed that IL-23R signaling was not essential for the induction of miR-133b and miR-206. Importantly, we found a similar co-regulation in CCR6(+) and other ?? T cell subsets that are predisposed to production of IL-17. Taken together, we discovered a novel feature of T cell differentiation towards an IL-17-producing phenotype that is shared between ?? and ?? T cells. Notably, the specific co-regulation of miR-133b and miR-206 with the Il17a/f locus also extended to human Th17 cells. This
qualifies expression of miR-133b and miR-206 in T cells as novel biomarkers for Th17-type immune reactions.