IDENTIFICATION AND CHARACTERIZATION OF HDAC1 AND HDAC2 INTERACTION NETWORKS IN TH17 CELLS

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The differentiation and function of $CD4^+$ T helper (Th) subsets has to be tightly regulated, since their dysregulation is linked with immune-mediated diseases. Th cell differentiation is accompanied by reversible changes in histone acetylation, mediated by the opposing activity of histone acetyltransferases (HATs) and histone deacetylases (HDACs), however many non-histone targets are emerging, indicating that HAT/HDACs act beyond the regulation of chromatin. Results of my laboratory demonstrate an essential role for HDAC1 but not for HDAC2 in regulating Th17 cell effector function and that loss of HDAC1, but not of HDAC2, in T cells protects mice from the development of experimental autoimmune encephalitis. This clearly indicates unique Th subset-specific functions for HDAC1 in the control of T cell-mediated autoimmunity in comparison to HDAC2. Since HDAC1 and HDAC2 are part of larger multiprotein complexes we hypothesized that the crucial role of HDAC1 in Th17 cells is mediated by factors that interact with HDAC1 but not with HDAC2.
Following pull-down of HDAC1/HDAC2 complexes and subsequent mass spectrometry analysis, we identified several factors that preferentially interact with HDAC1. One of those factors and a potential implication in immune-mediated diseases will be described in my talk.

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