Epigenetic signature in T helper 17 and regulatory T cells in multiple sclerosis patients during pregnancy

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Poster Title: Epigenetic signature in T helper 17 and regulatory T cells in multiple sclerosis patients during pregnancy

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Abstract:
Relapsing Remitting Multiple Sclerosis (RRMS) shows a protective effect of pregnancy in relapse rates. Immune tolerance associated with pregnancy correlates with high levels of circulating estrogens. Therefore, estrogens may act on CD4+ T lymphocytes dynamics by remodeling chromatin hubs. Here we performed an integrative analysis of human CD4+ epigenomic and transcriptomic data. We identified cell type-specific regulatory regions (CSR) by combining super enhancers' prediction using H3K27ac ChIP-Seq data with a genome-wide chromatin states analysis. Selected CSRs, associated to a set of transcription factors, defined a core regulatory network in Th17 and Treg cells. Thus, estrogen response element found in CSRs, revealed potentially ERα-modulated core genomic regions in these cells. 17β-estradiol induced active histone marks enrichment at FOXP3- CSRs and repressive histone marks enrichment at RORC-CSRs in in vitro polarized Th17 cells. We validated this epigenetic profile in peripheral blood mononuclear cells of RRMS patients, suggesting a FOXP3 positive regulation in third trimester of pregnancy while RORC is positively regulated in the postpartum. Altogether, these data indicate that estrogens act as immunomodulatory factors on the epigenomes of CD4+ T cells in RRMS; the identified CSRs may represent potential biomarkers for monitoring disease progression or new potential therapeutic target.