Chromatin remodeling in Th17 and Treg plasticity induced by E2 immunomodulation

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Poster Title: Chromatin remodeling in Th17 and Treg plasticity induced by E2 immunomodulation

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Abstract:
Immune cell plasticity makes its dynamic on genomic regulatory regions, key points for cues from environment. In Multiple Sclerosis (MS), T cell plasticity mirrors Th17 and Treg cells balance. Estrogens represent one of extracellular cues that may influence T cell plasticity and relapse rate reduction in MS patients during third trimester of pregnancy support hypothesis of estrogens as immune response regulators. Therefore, the shifting from normal to pathological states changes genomic regulatory regions core controlling immune plasticity and estrogens may act on lymphocytes dynamics by remodeling these chromatin hubs. Using integrative data approach, we selected cell-type specific regulatory regions that may control Th17 and Treg cells plasticity. In the first step, we identified super-enhancers focusing chromatin states associated with active enhancers for each cell types. Then, we selected cell-type specific genomic regions associated with transcription factors expressed in cell type subsets. In the second step, computational reconstruction of core regulatory network identified a set of transcription factors putative target of Estrogen Receptor alpha (ERα). In vitro treatment with 17β-Estradiol (E2) induces epigenetic modifications at specific cell-type genomic regulatory regions associated with FOXP3 and RORC, master regulators for Treg and Th17 cells. Epigenetic dynamics at these regulatory regions have been observed also in peripheral blood mononuclear cells of SM patients during third trimester and post-partum. Altogether these data indicate that E2 may act as immunomodulatory factor on the epigenomes of T cells.