IL-2 as a Therapeutic Target for Treatment of Autoimmune Alopecia Areata

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Alopecia areata (AA) is a prevalent autoimmune disease caused by T cell mediated destruction of hair follicles. Immune pathways involved in AA are not well understood, restricting development of targeted treatments. Recent genetic studies in AA performed in our lab have identified mutations in genomic regions of interleukin 2 receptor A (IL-2RA), implicating IL-2 signaling in AA pathogenesis. Last year, it was shown that alopecic T effector cells had increased response to IL-2 upon stimulation ($p<0.05$). In this study, IL-2 was used as a therapeutic target for AA treatment. Interestingly, opposing approaches to IL-2 manipulation - inhibition of IL-2 signaling via Jakinibs and administration of IL-2 via low dose IL-2 therapy – suggested positive treatment of AA. AA patients who received treatment with FDA approved drug Ruxolitinib, a JAK1/2 inhibitor, demonstrated near full hair regrowth after three months and decreased T effector cell response to IL-2 upon stimulation. When low dose IL-2 therapy was administered in a mouse model of AA (C3H/HeJ), reduced severity during the onset of the disease was observed. Among PBMCs of low dose IL-2 treated mice, there was a decrease in CD8 and CD4 T cell numbers and an increase in T regulatory cells (Tregs) compared to PBS controls. Taken together, it was concluded that IL-2 plays a crucial role in autoimmunity and is an attractive therapeutic target due to its dichotomous role that can induce both immune activation and tolerance. This study highlights the pleiotropic nature of cytokines that allows them to be versatile therapeutic targets. Findings from this study may also be applicable to other autoimmune diseases such as Type 1 diabetes, Celiac disease, rheumatoid arthritis, and psoriasis, which also harbor an IL2RA mutation.