Synopsis of Original Research Paper

Development of a Therapy for Psoriasis Targeting Stemness of T-helper 17

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IL-17-producing helper T (Th17) cells are long-lived and serve as central effector cells in chronic autoimmune diseases. The underlying mechanisms of Th17 persistence remain unclear. We demonstrated that abatacept, a CD28 antagonist, effectively prevented the development of skin disease in a Th17-dependent experimental autoimmune dermatitis model. Abatacept selectively inhibited the emergence of IL-7R-negative effector-phenotype T cells while allowing the survival and proliferation of IL-7R+ memory-phenotype cells. The surviving IL-7R+ Th17 cells expressed genes associated with alcohol/aldehyde detoxification and showed potential to transdifferentiate into IL-7R-negative effector cells. Inhibiting aldehyde dehydrogenase reduced IL-7R+ Th17 cells in vivo, independently of CD28, and exhibited additive effects when combined with abatacept. Our findings suggest that CD28 blockade prevents inflammation without eliminating persistent memory cells. These remaining memory cells can be targeted by other drugs, such as aldehyde dehydrogenase inhibitors, to limit their survival, thereby facilitating the treatment of chronic autoimmune diseases.