Depletion of syndecan-4+ T lymphocytes by saporin-conjugated DC-HIL alleviates T cell-mediated inflammatory disease

Contributed by Kiyoshi Ariizumi, Hideo Akiyoshi, Jin-Sung Chung, Mizuki Tomiharu, Ponciano D. Cruz Jr.
Department of Dermatology, The University of Texas Southwestern Medical Center and Dermatology Section (Medical Service), Dallas Veterans Affairs Medical Center, Dallas, TX

T lymphocyte activation is regulated by stimulatory and inhibitory signals transduced by binding of T cell receptors to corresponding ligands on antigen-presenting cells (APC). Stimulatory receptors tend to be present constitutively even on resting T cells, whereas many inhibitory receptors require activation for expression. Thus, inhibitory receptors may serve as a marker for the functional state of T cells.

We discovered a novel inhibitory pathway composed of the APC receptor DC-HIL and its exclusive T cell ligand, syndecan-4 (SD-4). DC-HIL specifically recognizes particular structures of heparan sulfate on SD-4 peculiar to T cells. SD-4 is expressed by activated (but not resting) T cells, including effector/memory CD4+ and CD8+ T cells. Infusion of soluble DC-HIL into mice inhibits the DC-HIL/SD-4 pathway, and results in enhanced immune responses. The current report addresses the hypothesis that depleting SD-4+ T lymphocytes using DC-HIL conjugated to a toxin will suppress elicitation of a T cell-mediated inflammatory response.

We biotinylated and conjugated soluble DC-HIL receptor or control Fc alone (IgG-SAP) to Streptavidin-ZAP (streptavidin conjugated to saporin; Cat. #IT-27), and showed that DC-HIL-SAP selectively kills SD-4+ activated T cells.

We next examined the effect of DC-HIL-SAP on an ongoing contact hypersensitivity (CH) response, which is an established model of a delayed T cell-mediated response. Mice were sensitized to a contact allergen oxazolone (Ox) on abdominal skin (day 0), then challenged with Ox on ear skin (day 6). Mice were injected i.v. with DC-HIL-SAP, IgG-SAP (control conjugate), or PBS 3 h prior to challenge (Fig. 1). PBS-injected