Synopsis of Original Research Paper

Regulation by dendritic cell SHPS-1 of skin immunity and its therapeutic application for skin allergy

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SHPS-1 is a transmembrane protein that binds the protein tyrosine phosphatases SHP-1 and SHP-2 and is abundant on the surface of $CD11c^+$ dendritic cells (DCs). We recently showed that SHPS-1 is essential for priming by DCs of $CD4^+$ T cells and for development of Th17 cell-mediated experimental autoimmunity. We have now further evaluated the importance of SHPS-1 and that of its ligand CD47 in contact hypersensitivity (CHS) to 2,4-dinitro-1-fluorobenzene (DNFB). Whereas the DNFB-induced CHS response was impaired in mice that express a mutant form of SHPS-1 lacking most of the cytoplasmic region, it was unaffected in CD47-deficient mice. Moreover, treatment of wild-type mice with mAbs to SHPS-1 that either block or do not block the binding of SHPS-1 to CD47 inhibited the CHS response, whereas that with a mAb to CD47 had no such effect. The 2,4-dinitro-benzenesulfonic acid-induced proliferation of, and production of IFN-γ or IL-17 by, T cells from DNFB-sensitized wild-type mice were inhibited by either mAb to SHPS-1 but not by that to CD47. In contrast, the blocking mAbs to SHPS-1, but not that to CD47, inhibited an allogenic mixed leukocyte reaction. These results suggest that SHPS-1 is essential for development of CHS, likely as a result of its positive regulation of the priming by DCs of $CD4^+$ T cells. However, such regulation by SHPS-1 does not appear to require its interaction with CD47.