Lymph node-ﬁbroblastic reticular cells regulate differentiation of T CD4 cells through CD25

Methotrexate (MTX), a ﬁrst-line systemic agent for the therapy of psoriasis, is often associated with adverse effects. Localized transdermal delivery of MTX using dissolving microneedles (MN) was demonstrated to be both more efﬁcacious and better tolerated than oral administration in our previous work. This study aims to elucidate the detailed therapeutic mechanisms of MTX-loaded MNs and to explore whether topical MTX treatment can affect the skin of mice by topical IMQ application. Histological and immunohistochemical (Ki67, CD25) analyses showed that CD25 treatment regulated CD4 T cell differentiation. CD25-deﬁcient MNs promoted Th? cell differentiation and induced expression of genes involved in Th17-mediated inﬂammation. Hence, Th17 cell-mediated inﬂammatory skin disease was markedly enhanced in mice lacking CD25 on FRCs. Therefore, our results suggest that CD25 expression on FRCs regulates CD4 T cell differentiation by modulating early IL-2-mediated signaling of neighboring, naive CD4 T cells, and thus inﬂuences the overall character of the immune response.

Localized administration of methotrexate regulates psoriasis-like skin inﬂammation and protects from secondary sensitization at a distant site

Indoleamine 2,3-dioxygenase 2 knockout exacerbates imiquimod-induced psoriasis-like skin inﬂammation

Acitretin (Act) is one of the ﬁrst-line treatments for moderate to severe psoriasis, while the systemic side effects caused by Act greatly restrict its clinical application. Herein, we developed the Dextran-based Act nanoparticles (DANPs) and proved their enhanced therapeutic efﬁcacy and reduced side effects in imiquimod-induced psoriasis-like mouse models. Acitretin (Act)-loaded nanoparticles (DANPs) showed the highest anti-psoriatic eVect against recurrent immune disorders at a distant site, emerging as a potential alternative treatment for psoriasis.