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INFLAMMATORY DISEASES

# Anti-CD1a antibody reduces inflammation in psoriasis

> In a well-established mouse model of psoriasis... CD1a-tg mice had more ear swelling and cellular infiltration than wild-type mice, and anti-CD1a antibodies blocked this response

Inflammation of the skin can be triggered by lipids such as urushiol, which is found in various plants, including poison ivy. Now, the surface molecule CD1a has been found to have a role in inflammation by presenting urushiol and other lipid antigens to T cells. Anti-CD1a antibodies were shown to alleviate skin inflammation, both in response to urushiol and in a mouse model of psoriasis.

CD1a is abundantly expressed on human Langerhans cells — skin-specific dendritic cells — but understanding of this molecule has been hampered by its absence in mice. Therefore, to investigate the role of CD1a in urushiol-mediated inflammation, the authors applied urushiol to the ear of mice transgenically engineered to express human CD1a (CD1a-tg mice). Urushiol increased ear thickness and the number of $CD4^+$ T helper ($T_H$) cells producing interleukin-17 (IL-17) and IL-22 ($T_H17$ cells) to a greater degree in CD1a-tg mice than in wild-type mice. Systemic treatment of CD1a-tg mice with CD1a-blocking antibodies prevented this hyper-response. $CD4^+$ T cells from urushiol-treated CD1a-tg mice, but not wild-type mice, responded to plate-immobilized CD1a that had been pre-incubated with urushiol, suggesting that CD1a-mediated presentation of urushiol to T cells causes inflammation.

Consistent with these findings in mice, T cells isolated from people who had experienced a moderate-to-severe poison ivy rash in the past 6 months produced more IL-17 and IL-22 than control cells did upon stimulation with urushiol-pulsed antigen-presenting cells (APCs). This phenomenon was dependent on the presence of CD1a on the APCs.

In a well-established mouse model of psoriasis, in which imiquimod is administered to the skin, CD1a-tg mice had more ear swelling and cellular infiltration than wild-type mice, and anti-CD1a antibodies blocked this response. Although these mice were not challenged with lipid, $CD4^+$ T cells from imiquimod-treated CD1a-tg mice responded to immobilized CD1a loaded with self-lipid, whereas $CD4^+$ T cells from wild-type mice did not. These results suggest that self-lipids, released by imiquimod-mediated damage, are presented to T cells by CD1a on Langerhans cells, thereby promoting inflammation.

Furthermore, in patients with psoriasis, isolated memory T cells produced more IL-17 and IL-22 in response to autologous dendritic cells than did cells from healthy donors. Notably, this response was blocked with an anti-CD1a antibody.

These results indicate that lipid antigens presented by CD1a could have an important role in psoriasis and the response to urushiol. Therapies that block the interaction of CD1a with receptors on T cells could be a skin-specific treatment for these conditions.

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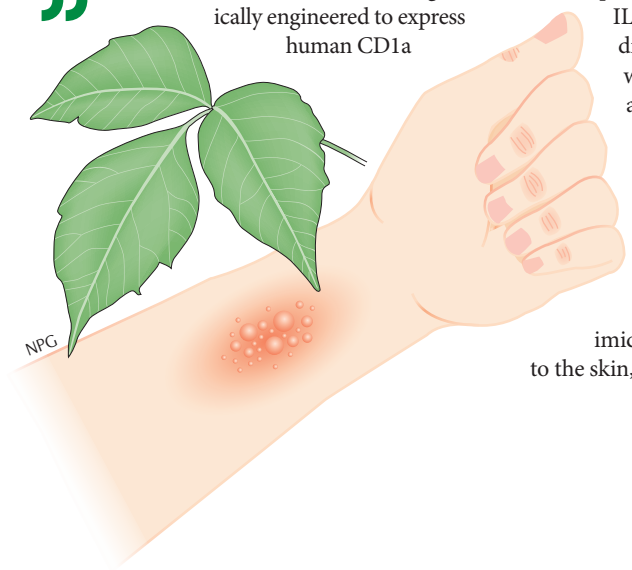


**ORIGINAL ARTICLE** Kim, J. H. *et al.* CD1a on Langerhans cells controls inflammatory skin disease. *Nat. Immunol.* http://dx.doi.org/10.1038/ni.3523 (2016)