

Interleukin-4 Inhibition in Recalcitrant Dermatitis

To the Editor:

We commend Hoot et al¹ for reporting observed effects of the novel IL-4 receptor inhibitor (IL-4R α -Inh), dupilumab, on patch testing and the differences between T_H1- and T_H2-mediated allergens. Hoot et al¹ described a case of a 26-year-old woman with atopic dermatitis (AD), asthma, and environmental allergies that developed progressive recalcitrant eyelid dermatitis despite treatment with dupilumab. In this context, it is unclear whether the rebound dermatitis in the patient described was a compensatory T_H2 response or a flare of an emerging contact dermatitis, which warranted a patch test evaluation. Although we concur with the authors that dupilumab treatment has been associated with transient dermatitis flares, we believe that the “contraindicatory effect [dupilumab has] on concomitant allergens” warrants further exploration considering that (1) the etiology of the patient's flare was not classified and (2) predupilumab treatment patch test was unavailable.

Atopic dermatitis is primarily a T_H2 disease at its initiation, and importantly, established lesions of AD express the T_H1 cytokines that are classically associated with allergic contact dermatitis, which may predispose to the concurrent development of allergic contact dermatitis.¹ Furthermore, certain allergens elicit through T_H2-driven pathways. One of the most clear-cut contact T_H2-driven responses is to house dust mite extract.² Along these same lines, molecular profiling of contact dermatitis lesions has been performed to identify allergen-dependent differences in immune responses. For example, Dhingra et al³ reported that nickel had a relatively higher induction of the innate immune system, T_H1/T_H17, and T_H22, although a T_H2 component was still present, whereas fragrances and rubber clearly demonstrated a stronger T_H2 axis bias based on gene expression and cell studies using immunohistochemistry, polymerase chain reaction genetic profiling, and gene array analysis.³ Of interest, dupilumab was recently reported to alleviate recalcitrant dermatitis in patients with contact allergies to both nickel and fragrances, primarily in patients with a history of AD, further suggesting that these select contact allergens may engage in the T_H2 axes.⁴

Inhibition of the T_H2 axis through blocking the downstream effect of IL-4R α -Inh on both IL-4 and IL-13 would theoretically shift the immune arm towards an amplified T_H1 axis response

with an enhanced response to “strong” contact allergens.^{1,3} Hoot et al's patient had relevant ($\pm$) reaction to carba mix and lanolin, (1+) triethanolamine and black rubber, and (3+) bacitracin and neomycin.¹ Of interest, carba and black rubber mix allergens have been reported as T_H2-based haptens.³ Likewise, Puza and Atwater⁵ reported a 63-year-old patient with chronic recalcitrant AD who patch tested positive to (+1) methylisothiazolinone (a strong allergen known to provoke more robust reactions) and ($\pm$) dimethylaminopropylamine after dupilumab initiation. Immunologically, this supports the notion that the IL-4R α -Inh could have an inhibitory effect against “weaker” T_H2-mediated contact allergens by improving the cutaneous molecular T_H2 signature, while maintaining an attenuated response to “strong” T_H1/interferon- γ allergens.⁶ Thus, although patch testing patients on IL-4R α -Inh can be of diagnostic value, we assert that patch testing on dupilumab should be interpreted with care.

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The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000427

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