Skin Dendritic Cells Progressively Subvert The Activation Of Pathogenic Type-2 Immunity Upon Epicutaneous Allergen Immunotherapy

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Epicutaneous specific-immunotherapy (EPIT) is a promising treatment that hinders IgE-mediated symptoms and food allergy, leading to a higher tolerance threshold. The mechanisms by which EPIT inhibits mast cell/basophil degranulation and tissue inflammation include Tregs stimulation and profound immune deviation of allergen-specific T and B cell responses. To date, little is known about the contribution of skin dendritic cells to EPIT efficacy.
To address this question, we used a preclinical mouse model of allergy to ovalbumin (OVA), in which sensitized or naive C57BL/6 mice were treated once a week with OVA-containing patches for 48h over an 8 weeks period. Dynamics and phenotype of skin dendritic cell (skDC) subsets were assessed by flow cytometry. DC function was further characterized using in vitro T-cell assays.
Our results demonstrated that repeated patch applications prompted a type-2 response (IL-4, IgE), that is progressively balanced by an accumulation of Tregs and the production of counter-regulatory cytokines (IL-10, IL-17) and specific IgG1/IgG2a. Alternatively, we observed that skDC subsets (Langerhans cells, dermal conventional DC1 and DC2) retain their capacity to capture OVA in the skin and to migrate towards draining lymph nodes during EPIT. However, their activation status and stimulatory properties were progressively hampered, as shown by (i) weaker CD86 or CD40 expression in OVA+ DC subsets and (ii) the significant drop of OVA-specific T cells priming after 8 weeks of EPIT. Interestingly, we recorded that OVA+ LCs progressively lost their capacity to prime CD4+ T effector cells (Teff) upon EPIT, but gained Treg stimulatory properties. We are currently investigating the mechanisms by which each skin DC subset subverts the contribution of pathogenic type-2 immunity to prevent the development of allergic symptoms.
Taken together, our results open new avenues to better understand the complex mechanisms that lead to the efficacy of EPIT.

Keywords : allergy , dendritic cell, epicutaneous specific immunotherapy
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