Epicutaneous immunotherapy to a specific allergen prevents from sensitisation and anaphylaxis to further allergens: the role of regulatory T cells

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Background: A model of mice sensitized to a definite allergen showed that early epicutaneous immunotherapy (EPIT) against this definite allergen prevents from further sensitizations to other allergens (Mondoulet et al. EAACI, 2014). This study aims to better understand the mechanism involved by evaluating the protection induced by early EPIT against anaphylaxis and by depicting the role of regulatory T cells (Tregs).

Method: BALB/c mice were orally sensitized to milk, then treated by milk-EPIT or Sham before being sensitized to peanut 2 weeks later. Mice were then intravenously (IV)-challenged with peanut. In a second experiment, CD4+CD25+regulatory T cells (Tregs) were isolated from spleen of milk-sensitized mice after EPIT or Sham, and transferred into naive or milk-sensitized mice (recipient). Recipient mice were then sensitized to peanut and IV-challenged to peanut. Also, Foxp3+ Tregs were adoptively transferred to recipient mice which were then submitted to peanut sensitization and to peanut IV-challenge. Outcome tools were body temperature, hypersensitivity reactions and plasma mast cell protease-1 (mMCP1).

Results: After sensitization to peanut, the milk-EPIT group, as opposed to sham, showed no induction of peanut-specific IgE and a significant increase of peanut-specific IgG2a. Sham mice submitted to peanut sensitization exhibited after peanut IV-challenge a significant drop in temperature (p< 0.001), severe systemic score (grades 2 to 4), and a significant increase in plasma mMCP1. As opposed, milk-EPIT mice did not exhibit any drop in temperature following peanut IV-challenge and their plasma mMCP1 was decreased compared to Sham (p< 0.05). The adoptive transfer of milk EPIT-induced Tregs protected recipient mice from sensitization to peanut and from peanut IV-challenge anaphylaxis whatever the initial immune status (naive or milk-sensitized) (p< 0.05). Similar protection was achieved with the adoptive transfer of Foxp3+ Tregs.

Conclusion: In a model of iterative sensitizations mimicking the allergic march, early EPIT prevented from sensitisation and anaphylaxis to further allergens, via a Tregs mechanism, with a core role of Foxp3+ Tregs.
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