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Cutaneous exposure to clinically-relevant pigeon pea (*Cajanus cajan*) proteins promote TH2-dependent sensitization and IgE-mediated anaphylaxis in BALB/c mice
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Introduction
Epicutaneous (EC) sensitization to food allergens may occur when the skin has been lightly damaged. The study here tested whether cutaneous exposure to pigeon pea protein(s) may cause allergic sensitization. BALB/c mice were either orally gavaged or epicutaneously sensitized by repeated application of pigeon pea crude protein extract (CPE) on undamaged areas of skin without any adjuvant; afterwards, both groups were orally challenged with the pigeon pea CPE. The experimental results support the hypothesis that in addition to oral exposure, skin exposure to food allergens can promote Th2-dependent sensitization, IgE-mediated anaphylaxis and intestinal changes after oral challenge. Based on this, an avoidance of cutaneous exposures to allergens might prevent development of food anaphylaxis.

Methods
1. Epicutaneous and oral treatment
2. Analysis of signs and symptoms of anaphylaxis
3. Type 1 skin test
4. Measures of specific IgE and IgG1 and of MCPT-1 and TSLP
5. Histopathology of skin and intestine
6. Expression of cytokines and TFs
7. Isolation of skin and intestinal proteins and Western blotting
8. Mast cell staining

Results
In the epicutaneously-sensitized mice, elevated levels of specific IgE and IgG1, as well as of MCPT-1, TSLP, TH2 cytokines and TFs, higher anaphylactic scores and histological changes in the skin and intestine were indicative of sensitization ability via both routes in the pigeon pea CPE-treated hosts. Elevated levels of mast cells were observed in both the skin and intestine. Decreased levels of filaggrin in skin may have played a key role in the skin barrier dysfunction, increasing the chances of sensitization.

Conclusions
Little is known regarding the prevention of food allergy development via the EC exposure. The current study identified an IgE-mediated anaphylaxis following oral challenge and induction of TH2-biased adaptive immune responses when mice were exposed to pigeon pea proteins on their healthy intact skin. An additional interesting finding was that EC sensitization also yielded intestinal changes with reference to mast cells. The immune response caused by IL-4 and IL-13 contributes to the impairment in filaggrin, therefore neutralization of IL-4 and IL-13 that may improve skin barrier dysfunction. These findings support the hypothesis that cutaneous exposure to food allergens may be a risk factor for the allergic sensitization and development of food allergy.

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