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From molecular processes to adverse outcome pathways of sensitization induction in humans exposed to xenobiotics and proteins

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Novel methods for assessing the sensitizing potential of substances have improved the molecular understanding of the mechanisms behind sensitization induction. There are animal free approaches emerging which are more accurate in predicting a sensitization potential than animal models, and which, in contrast to the *in vivo* studies, distinguish e.g., between skin and respiratory sensitizers. Evaluation of the potency of chemical sensitizers with *in vitro* methods may become reality in the near future. While the understanding of the molecular mechanisms driving skin sensitization is substantial, the mechanisms driving respiratory sensitization and oral sensitization are less well understood. For xenobiotics, the understanding of the relation between reactivity rates, mechanism of haptentation, protein target selection, pathway activation and T-cell skewing is still not sufficient to profile chemicals using animal-free testing methods. For proteins, the molecular initiation effect is often not known. More efforts should focus on refining existing methods and further developing new methods that lead to an improved awareness of the real mechanisms of a substance in triggering a sensitization reaction in exposed human beings.

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Immunotherapy for atopic dermatitis as the causative treatment

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Atopic dermatitis is the eczematous skin allergic disease which is currently the issue to be solved. Until now, the nature of atopic dermatitis is not completely understood concerning the pathogenesis and the cause. Accordingly, the effective treatment for atopic dermatitis has not done. More than 10 years ago, food allergy is reported to be the important cause of atopic dermatitis. Interestingly, the nature of food allergy in atopic dermatitis is non-IgE mediated allergy in which skin prick test and specific IgE for the causative food allergens were negative. From this report, the nature of atopic dermatitis became unveiled. The nature of atopic dermatitis is non-IgE mediated allergy to food and inhalant allergens. Tolerance induction for food allergy of non-IgE mediated type in atopic dermatitis was successful using IFN-gamma. Also, desensitization for inhalant allergens also was succeeded using IFN-gamma. From both treatments, the concept of the causative diagnosis and treatment for atopic dermatitis become the real. With the success of tolerance induction for food allergy of non-IgE-mediated type and desensitization for inhalant allergens using IFN-gamma, the pathogenesis and nature of atopic dermatitis become clearer. Moreover, the pathogenesis of allergy becomes more clarified. Most of all, the difference of food and inhalant allergens in the role and the pathogenesis in atopic dermatitis become suspected. The architecture of the pathogenesis of atopic dermatitis is reconstructed on the base of clinical and immunological study.

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