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Abstract

Cutaneous innate immunity activation in response to xenobiotics: how do contact allergens manage this activation ?

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Abstract

The skin provides a first line of defense against microbial pathogens, physical and chemical insults. It displays a protective function but may induce or inhibit the quality of immune response. Immune function of the skin is crucial since its dysfunction is implicated in a variety of inflammatory skin disorders, including allergic contact dermatitis, atopic dermatitis. The cutaneous innate immune system, localized in epidermis and dermis, consists of keratinocytes, dendritic cells, macrophages and mast cells. Many other cells can be mobilized such as neutrophils, inflammatory dendritic cells. Epithelial and resident innate immune cells in the skin express Pattern Recognition Receptor (PRR) such as TLRs, NLRs. It has been shown that xenobiotics such as chemical allergens control, directly or indirectly, PRR's activation contributing to the development of cutaneous inflammation as well as immune tolerance of the skin. They cause sterile inflammation by activating mechanisms of innate immune system. The mechanistic insights into innate immune system activation by contact allergens demonstrate the role of DAMPs and other endogenous danger signals in the activation of TLR2 and TLR4 and of the NLRP3 inflammasome in allergic contact dermatitis.

Moreover, Nrf2 as received attention, due to its critical role in the regulation of defensive machinery. In fact, Nrf2 activation induces innate immune response to suppress or eliminate bacterial and viral pathogens. In response to chemical sensitizers Nrf2 is induced in the skin and controls inflammation via innate immune response. Therefore, xenobiotics mimic viral or bacterial antigens and their chemical reactivity participates in the activation of the Nrf2 pathway by also playing a role in innate immunity.

Finally, innate immunity is induced by xenobiotics similarly to viral or bacterial antigens. Using common signaling pathways, xenobiotics activate and orchestrate the response via numerous innate immunity cells, resulting in adverse reactions.

Keywords—innate immunity, skin, Nrf2, xenobiotics, contact allergens

Professional Biography

Saadia Kerdine-Römer has her expertise in Immunotoxicology, in the field of Skin Allergy. She has been working for many years in the activation of dendritic cells by allergenic molecules. She demonstrated with her group that haptens can be real danger signals. Her work is part of the identification of new signaling pathways in immunity cells in response to haptens. She is also working on the transcription factor Nrf2 and its link in the inflammatory response of skin allergic origin.

Recent Publications (up to 5)

1. Raffalli C, Clouet E, Kuresepi S, Damiens MH, Lepoittevin JP, Pallardy M, Ferret PJ, Giménez-Arnau E, Kerdine-Römer S. Editor's Highlight: Fragrance Allergens Linalool and Limonene Allylic Hydroperoxides in Skin Allergy: Mechanisms of Action Focusing on Transcription Factor Nrf2. Toxicol Sci. 2018 Jan1;161(1):139-148. doi: 10.1093/toxsci/kfx207. PubMed PMID: 29029310.

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