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NMR-spectrocopic assessment of interactions between contact sensitizers and proteins of the skin

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The skin, as a barrier, is daily exposed to chemicals, drugs, cosmetics, etc. It is also a metabolically competent organ involved in activation/detoxification of chemicals anda major actor of the immune system.Therefore, skin exposure to chemicals can lead to adverse toxic reactions likeallergic contact dermatitis (ACD).

It is now well recognized that the first key step for induction of an ACD is the chemical interaction between the allergen or hapten and nucleophilic residues onepidermal proteins. In some cases chemicals have no obvious protein reactivity but will become reactive through a metabolic transformation/activation and will be regarded as prohaptens.

For many years such interactions/activations have been studied using simple models such as amino acids or peptides in solution. If theses experiments allowed gainingvaluable knowledge on the chemical reactivity of skin sensitizers, they are very far from conditions present in a complex and organized 3D living epidermis.

In the recent years we have been developing the use of the High Resolution at Magic Angle Spinning (HRMAS) Nuclear Magnetic Resonance (NMR) technique to follow the behavior (reactivity/metabolism) of chemicals in 3D-Reconstructed Human Epidermis (RHE). This NMR technique, first developed to study soft solids, has been shown to be very well adapted to the in situobservation of the epidermis.

In addition to the observation of the epidermis metabolome, we have been showing that it was possible, using carbon-13 substituted molecules, to follow the reaction of haptens with nucleophilic residues and therefore characterize structures of the formed adducts as well as the nature of amino acids modified. This approach can be extended to the metabolic activation/ transformations of prohaptens with the ability to follow in situ how chemicals are modified and how they subsequently react with nucleophiles.

HRMAS NMR/RHE association allows investigating, in a living epidermis, chemical activations and interactions taking place between chemicals and amino acids. This technique can be a valuable tool to study the activation and behavior of prohaptens and opens perspectives for the molecular understanding of ACD.