Mathematical modelling of Skin Sensitisation

Gavin Maxwell
SEAC, Unilever, Colworth Science Park, Sharnbrook, Bedford MK44 1LQ, UK

Despite our understanding of the key events that drive skin sensitisation, our ability to combine non-animal hazard data with exposure information to establish whether inclusion of a sensitising chemical at a particular level within a home or personal care product will be safe for the consumer population remains a key gap. Consequently, our aim is to apply mechanistic understanding of skin sensitisation to improve our ability to make risk assessment decisions. Central to our approach is a mathematical model of the induction of skin sensitisation, that predicts the probability of an individual becoming allergic for a given skin exposure to sensitiser [1].

Chemical-specific model parameters are derived from bespoke in vitro experiments designed to measure reactivity rate and skin bioavailability. Biological parameters are taken from the immunological literature. The model has been used to simulate data from the study of Friedmann et al. [2] in which 132 healthy volunteers were exposed to one of five doses of the contact allergen 2,4-dinitrochlorobenzene (DNCB). These data provide an opportunity to compare clinical sensitisation with model predictions of naïve CD8+ T cell activation. To do so, the model was parameterised for DNCB and a prediction made for the extent of naïve CD8+ T cell activation occurring across doses. Reverse dosimetry analysis was then performed to calculate the minimum sensitising dose to DNCB and the probability of the average individual acquiring contact allergy at any given dose. Characterisation of sensitiser-specific T cell responses in allergic contact dermatitis patients [3] and alopecia areata patients undergoing Diphenylcyclopropenone (DPCP) treatment is underway to extend the model such that it captures the T cell dynamics of sensitiser-induced responses.

References
1. MacKay, C., M. Davies, V. Summerfield and G. Maxwell. From Pathways to People: Applying the Adverse Outcome Pathway (AOP) for Skin Sensitization to Risk Assessment. ALTEX. 2013. 30. 473-486