Synopsis of Original Research Paper

Establishment of a Foundational Risk Assessment Model for HLA-Associated Allergic Contact Dermatitis

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Allergic contact dermatitis (ACD) induced by cosmetic ingredients varies among individuals, and human leukocyte antigen (HLA) polymorphisms have been implicated in this variability. In the pharmaceutical field, HLA polymorphisms are well known to influence drug hypersensitivity, with HLA-B57:01 playing a crucial role in abacavir-induced hypersensitivity reactions. Abacavir binds directly to the peptide-binding groove of HLA-B57:01, altering the peptide repertoire and triggering T-cell activation. Similarly, some cosmetic ingredients have been suggested to interact with HLA-B*57:01, but their ability to induce immune activation through the same mechanism remains unclear.

Our previous studies demonstrated that exposure to abacavir induces HLA-B*57:01-dependent endoplasmic reticulum (ER) stress responses in keratinocytes, suggesting that ER stress may contribute to skin rash development. To understand the mechanism of HLA-mediated drug-induced hypersensitivity, it is critical to identify the stress factors that trigger ER stress in response to abacavir exposure. Misfolded proteins and aggregates accumulate in the ER, leading to the dissociation of the molecular chaperone BiP from stress sensors such as IRE1 and ATF6, activating the unfolded protein response (UPR).

This study aims to analyze the intracellular localization of HLA-B57:01 in keratinocytes exposed to abacavir, its interaction with BiP, and the role of ER stress in immune activation. The findings could provide insights into HLA-associated immune activation and contribute to the development of novel risk assessment methods for ACD caused by cosmetic ingredients. By understanding how HLA-B57:01 interacts with specific compounds, this research may facilitate the establishment of personalized safety evaluation strategies, ultimately improving consumer protection against immune-mediated adverse reactions.