



TITLE:

A Plasmacytoid Dendritic Cell-Based Assay to Predict Allergenicity Potential of Transdermal Drug Formulations

AUTHORS:

Seyoum Ayeahunie, Maureen Snell, Mitchell Klausner, and John Sheasgreen.
MatTek Corporation

ABSTRACT:

Purpose: All topically applied transdermal drug formulations must be screened for allergenicity. The goal of the present study is to develop a cost-effective in vitro assay system that utilizes human plasmacytoid dendritic cells (pDC) to predict the allergenicity potential of topically materials.

Methods: Human DC were generated from CD34+ progenitor cells and the pDC fraction (CD123+/CD11c-) was harvested using FACS sorting. The isolated pDC were further cultured for 10 days in pDC specific medium to expand the cell number. The generated pDC were then exposed for 18 hours to allergens (n=13) or irritants (n=13) using non-cytotoxic doses, as determined using propidium iodide (PI) staining. Un-stimulated cells were used as negative controls. FACS analysis was used to monitor CD86 expression and a stimulation index (SI) was calculated from the ratio of CD86 expression for pDC exposed to test formulations versus CD86 expression in unexposed pDC.

Results: All test material exposures resulted in <40% cytotoxicity, as determined by PI staining of the pDC. 13 allergens and 13 irritants/non-irritants were tested in pDC isolated from 2-5 donors. 12 of 13 allergens induced an SI >1.5 from at least 50% of the donors; 12 of 13 non-allergens resulted in SI < 1.5. Based on these results, a preliminary prediction model was developed to identify allergens. This prediction model has a sensitivity = 92.3% and a specificity = 92.3%.

Conclusion: CD86 expression in pDC appears to be a sensitive and specific predictor of allergenicity. The pDC assay is advantageous because high throughput screening of chemicals is possible, donor-to-donor variation can be monitored, the cells are of human origin, and the assay is cost effective. The pDC-based assay method will likely have broad utility to monitor drug and other formulations for contact sensitization.

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