
Poster: free communications

Gene expression analysis in chemical-treated dendritic cells: discriminating contact sensitisers and irritants employing the immune toxicity chip and a whole genome array

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The replacement of animal tests for the detection of the sensitising potential of chemicals is of great importance due to current legislation. In order to establish a test system for the identification of contact sensitisers, human immature dendritic cells (DCs) derived from peripheral blood monocytes were used as substitutes for Langerhans cells, the antigen presenting cells of the skin.

Concentration dependency of sensitiser-specific effects was determined employing flow cytometry by measuring dose-response curves for 7 contact sensitisers and 3 irritants. Gene expression in chemical-treated DCs was then compared to gene expression in solvent treated samples using a previously developed targeted microarray, the immune toxicity chip, and a commercially available whole genome microarray. Additionally, quantitative real-time PCR was performed in order to confirm treatment-related differences in gene expression detected on microarrays.

Statistical data analysis of the experiments performed with the immune toxicity chip revealed a panel of marker genes suitable for the discrimination of strong allergens and irritants. In addition, whole genome analysis identified genes not represented on the targeted array that were significantly differentially expressed after either allergen- or irritant treatment. Graphical visualization of the data by hierarchical cluster analysis showed 2 major groups for sensitisers and irritants and smaller subsets for the different chemicals. Furthermore, the predictive value of the detected genes for determining sensitising potential was assessed by leave-one-out-crossvalidation.

The results indicate that our test system based on the immune toxicity chip allows the identification of strong sensitisers and the differentiation of irritants. Furthermore, additional promising indicator genes for sensitisers and irritants were found with whole genome experiments. Including these genes in the chip design of the targeted array might also permit the identification of weak allergens.

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