

A cell-based in vitro alternative to identify skin sensitizers by gene expression

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ABSTRACT

The ethical and economic burden associated with animal testing for assessment of skin sensitization has triggered intensive research effort towards development and validation of alternative methods. In addition, new legislation on the registration and use of cosmetics and chemicals promote the use of suitable alternatives for hazard assessment. Our previous studies demonstrated that human CD34+ progenitor derived dendritic cells from cord blood express specific gene profiles upon exposure to low molecular weight sensitizing chemicals. This paper presents a classification model based on this cell type which is successful in discriminating sensitizing chemicals from non-sensitizing chemicals based on transcriptome analysis of 13 genes. Expression profiles of a set of 10 sensitizers and 11 non-sensitizers were analyzed by RT-PCR using 9 different exposure conditions and a total of 73 donor samples. Based on these data a predictive dichotomous classifier for skin sensitizers has been constructed, which is referred to as VITOSENS[®]. In a first step the dimensionality of the input data was reduced by selectively rejecting a number of exposure conditions and genes. Next, the generalization of a linear classifier was evaluated by a cross-validation which resulted in a prediction performance with a concordance of 89%, a specificity of 97% and a sensitivity of 82%. These results show that the present model may be a useful human in vitro alternative for further use in a test strategy towards the reduction of animal use for skin sensitization.

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