

Assessment of Chemical Skin-Sensitizing Potency by an In Vitro Assay Based on Human Dendritic Cells

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The skin-sensitizing potential of chemicals is an important concern for public health and thus a significant end point in the hazard identification process. To determine skin-sensitizing capacity, large research efforts focus on the development of assays, which do not require animals. As such, an in vitro test has previously been developed based on the differential expression of CREM and CCR2 transcripts in CD341 progenitor-derived dendritic cells (CD34-DC), which allows to classify chemicals as skin (non-)sensitizing. However, skin sensitization is not an all-or-none phenomenon, and up to now, the assessment of relative potency can only be derived using the in vivo local lymph node assay (LLNA). In our study, we analyzed the feasibility to predict the sensitizing potency, i.e., the LLNA EC3 values, of 15 skin sensitizers using in vitro data from the CD34-DC-based assay. Hereto, we extended the in vitro-generated gene expression data set by an additional source of information, the concentration of the compound that causes 20% cell damage (IC20) in CD34-DC. We statistically confirmed that this IC20 is linearly independent from the gene expression changes but that it does correlate with LLNA EC3 values. In a further analysis, we applied a robust linear regression with both IC20 and expression changes of CREM and CCR2 as explanatory variables. For 13 out of 15 compounds, a high linear correlation was established between the in vitro model and the LLNA EC3 values over a range of four orders of magnitude, i.e., from weak to extreme sensitizers.

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