

Lecture: free communications

Influence of “danger signals” on CD54 and CD86 marker expression in THP-1 cells – improvement by HaCaT-Coculture

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The prediction of the sensitizing character of substances is subject of intensive research work, as the 7th Amendment to the European Cosmetics Directive bans the use of animal testing for cosmetic purposes beginning 2013. As a result, test systems have to be established, doing both, reliably survey sensitizing properties of substances and provide information about the expected strength of the possible allergic reaction. To date, numerous test systems have been suggested, based on the culture of primary dendritic cells (DC) or related cell lines.

The *in vivo* situation in allergic response is mediated by a variety of different cell types. Nevertheless, the currently used *in vitro* systems concentrate on systems using only a single cell type. Although some effort has been made, the predictive capacity of these test systems is limited to the properties of the cellular system used.

One important aspect, missing in these prediction systems is described in the concept of “danger signals”. According to this, DCs get primed to differentiate on external stimuli; in addition, auxiliary signals are necessary from the surrounding tissue to finally establish the sensitization. Thus, not solely the DCs but also the environmental cells must react properly on external stimuli to establish an allergic reaction. Furthermore, xenobiotic metabolism of DCs is subject of discussion, with the majority of scientists believing in limited metabolic competence of dendritic cells. Keeping this in mind, the environment additionally supports the formation of allergic reaction by metabolizing the pro-haptens to active haptens.

Here we present data, stressing the necessity of supportive signals from skin cells in the prediction of sensitizing properties.

We show the influence of the well-known “danger signals” IL1alpha, IL1beta, IL6, IL8 and TNFalpha on the CD86 and CD54 marker expression of THP1-cells and present results about the influence of toxicity. We demonstrate, that THP1-cell mature in contact with cellular lysates. Interestingly, the expression of maturation markers is dependent on the cellular origin of the lysate. Additionally we show results on toxicity-related soluble factors (“danger-signals”) like ATP, Calcium or Prostaglandin E2. Finally, we give evidence in considerably improved secretion of the “danger signal” IL1beta, a well-known marker-protein in sensitization-prediction, by combining the THP1-cells with HaCaT-cells in a coculture system, thus stressing the need of auxiliary cell types for the prediction of sensitization.

Keywords: danger signals, toxic influence in sensitization, coculture, metabolic competence