

Dermal sensitizers - identification and potency ranking using IVSA and epiCS[®]

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Human 3D reconstructed skin epidermal equivalents have been shown to release IL-18 in response to a wide range of dermal sensitizing chemicals. The concentration of these chemicals that produce greater than a threshold positive response (Stimulation Index, $SI \geq 2.0$) is correlated to their potency or strength in an *In Vitro* Sensitization Assay (IVSA). In our experiments, 4-Nitrobenzyl bromide (NBB) and 2,4-Dinitrochlorobenzene (DNCB) were strong inducers of IL-18 secretion into the culture medium (SI-2 = 0.02% and 0.03%, respectively). The strong sensitizer p-Phenylenediamine (PPD) had an SI-2 of 0.13%. Cinnamaldehyde (CA) (SI-2 = 0.33%) and Isoeugenol (IE) (SI-2 = 0.56%) were moderate sensitizers, while Eugenol (EU) (SI-2 = 0.75), Resorcinol (RES) (SI-2 = 2.9%) and Hexylcinnamaldehyde (HCA) (SI-2 = 8.08%) were weak sensitizers. Sensitizer potency ranked using an SI-2 as follows: NBB > DNCB > PPD > CA > IE > EU > RES > HCA, with NBB, DNCB and PPD classified as strong, CA, IE and EU as moderate, and RES and HCA classified as weak sensitizers. Of the total of 18 chemicals tested, seven were irritants and two were non-sensitizers (Glycerol and Isopropanol); of these, only Chlorobenzene (50%) was incorrectly predicted as a sensitizer. epiCS[®] gave an Accuracy of 89% and Sensitivity of 89%, and all other Cooper Statistics (Specificity, Negative and Positive Predictivity) values were 89%. In summary, measuring IL-18 release from 3D tissues allows for highly accurate and sensitive identification of dermal sensitizers. Also, the ability to rank-order potency of these chemicals based on SI-2.0 values of IL-18 secretion is a powerful tool for further classification into potency categories.