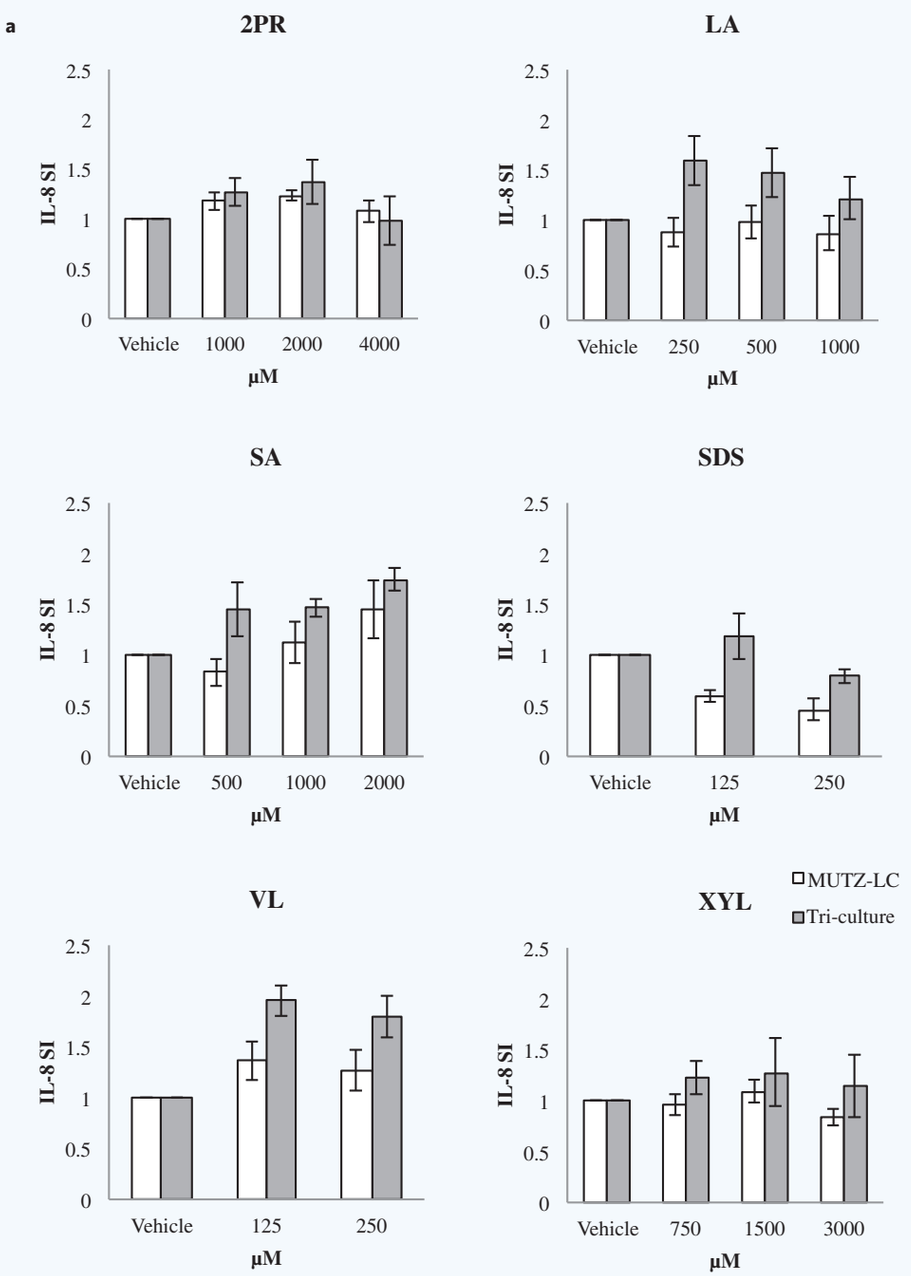
25. Ouwehand, K. *et al.* Comparison of a novel CXCL12/CCL5 dependent migration assay with CXCL8 secretion and CD86 expression for distinguishing sensitizers from non-sensitizers using MUTZ-3 Langerhans cells. *Toxicol. In Vitro* **24**(2), 578–585 (2010).
26. Nelissen, I. *et al.* MUTZ-3-derived dendritic cells as an *in vitro* alternative model to CD34+ progenitor-derived dendritic cells for testing of chemical sensitizers. *Toxicol. In Vitro* **23**(8), 1477–1481 (2009).
27. Kimura, Y. *et al.* Optimization of the IL-8 Luc assay as an *in vitro* test for skin sensitization. *Toxicol. In Vitro* **29**(7), 1816–1830 (2015).
28. Larsen, C.G. *et al.* Production of interleukin-8 by human dermal fibroblasts and keratinocytes in response to interleukin-1 or tumour necrosis factor. *Immunology* **68**(1), 31–36 (1989).
29. Taub, D.D. *et al.* T lymphocyte recruitment by interleukin-8 (IL-8). IL-8-induced degranulation of neutrophils releases potent chemoattractants for human T lymphocytes both *in vitro* and *in vivo*. *J. Clin. Invest.* **97**(8), 1931–1941 (1996).
30. Larsen, C.G. *et al.* The delayed-type hypersensitivity reaction is dependent on IL-8. Inhibition of a tuberculin skin reaction by an anti-IL-8 monoclonal antibody. *J. Immunol.* **155**(4), 2151–2157 (1995).
31. Takahashi, T. *et al.* An *in vitro* test to screen skin sensitizers using a stable THP-1-derived IL-8 reporter cell line, THP-G8. *Toxicol. Sci.* **124**(2), 359–369 (2011).
32. Toebak, M.J. *et al.* CXCL8 secretion by dendritic cells predicts contact allergens from irritants. *Toxicol. In Vitro* **20**(1), 117–124 (2006).
33. Bauch, C. *et al*. Putting the parts together: Combining *in vitro* methods to test for skin sensitizing potentials. *Regul. Toxicol. Pharmacol.* **63**(3), 489–504 (2012).
34. Almeida, A. *et al*. Insights on *in vitro* models for safety and toxicity assessment of cosmetic ingredients. *Int. J. Pharm.* **519**(1–2), 178–185 (2017).
35. Johansson, H. *et al.* A genomic biomarker signature can predict skin sensitizers using a cell-based *in vitro* alternative to animal tests. *BMC Genomics* **12**, 399 (2011).
36. Hirota, M. & Moro, O. MIP-1beta, a novel biomarker for *in vitro* sensitization test using human monocytic cell line. *Toxicol. In Vitro* **20**(5), 736–742 (2006).
37. Piroird, C. *et al.* The Myeloid U937 Skin Sensitization Test (U-SENS) addresses the activation of dendritic cell event in the adverse outcome pathway for skin sensitization. *Toxicol In Vitro* **29**(5), 901–916 (2015).
38. Saito, K. *et al.* Development of an *in vitro* skin sensitization test based on ROS production in THP-1 cells. *Toxicol. In Vitro* **27**(2), 857–863 (2013).
39. Takenouchi, O. *et al*. Test battery with the human cell line activation test, direct peptide reactivity assay and DEREK based on a 139 chemical data set for predicting skin sensitizing potential and potency of chemicals. *J. Appl. Toxicol.* **35**(11), 1318–1332 (2015).
40. Committee on the Design and Evaluation of Safer Chemical Substitutions: A Framework to Inform Government and Industry Decision; Board on Chemical Sciences and Technology; Board on Environmental Studies and Toxicology; Division on Earth and Life Studies; National Research Council. A Framework to Guide Selection of Chemical Alternatives. Washington (DC): National Academies Press (US); 2014 Oct 29. Appendix D, Overview of the GHS Classification Scheme in Hazard Classification. Available from: https://www.ncbi.nlm.nih.gov/books/NBK253967/
41. Basketter, D.A. & Kimber, I. Skin sensitization, false positives and false negatives: Experience with guinea pig assays. *J. Appl. Toxicol.* **30**(5), 381–386 (2010).

SUPPLEMENTARY INFORMATION

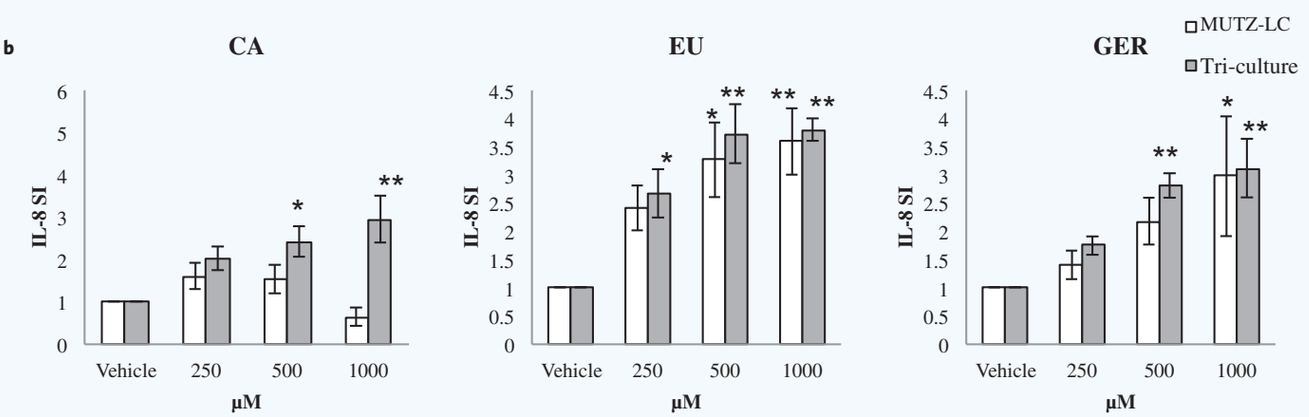
Supplementary Table 1 SVM prediction accuracy scores for MUTZ-LCs, tri-culture, and full-thickness skin model.

	Sensitivity	*Specificity*	*Accuracy*
MUTZ-LCs alone (top 2)	93.3%	79.6%	86.2%
Tri-culture (top 3)	92.7%	89.8%	91.1%
Full-thickness skin (top 4)[22]	92.0%	92.0%	92.0%

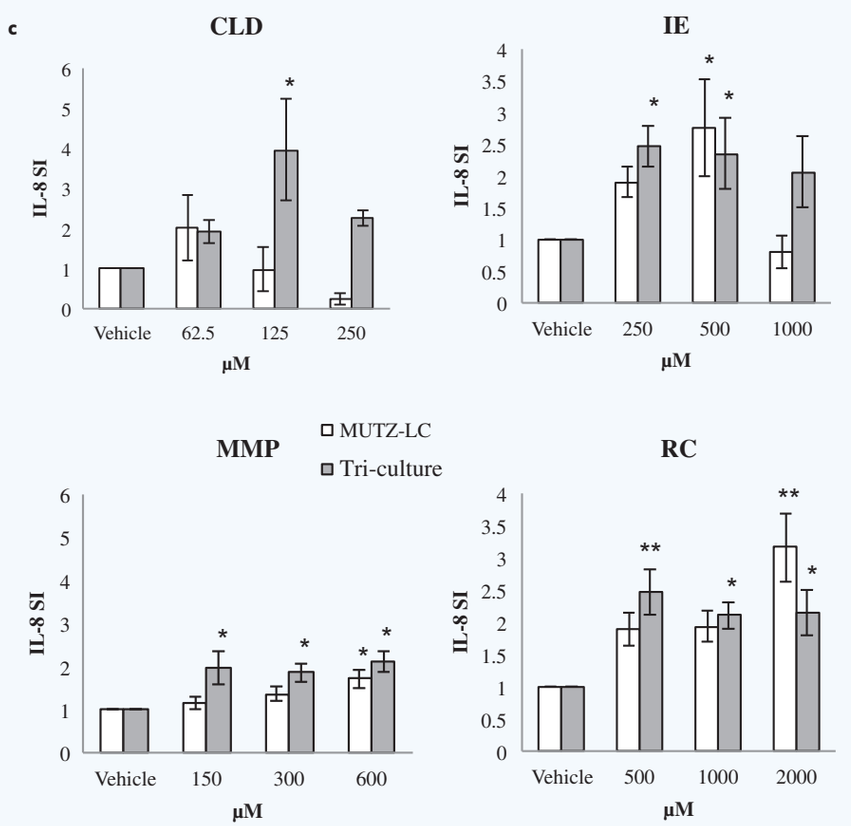
A comparison of SVM prediction accuracy, sensitivity, and specificity scores for the MUTZ-LCs alone, the tri-culture system, and the full-thickness skin model.



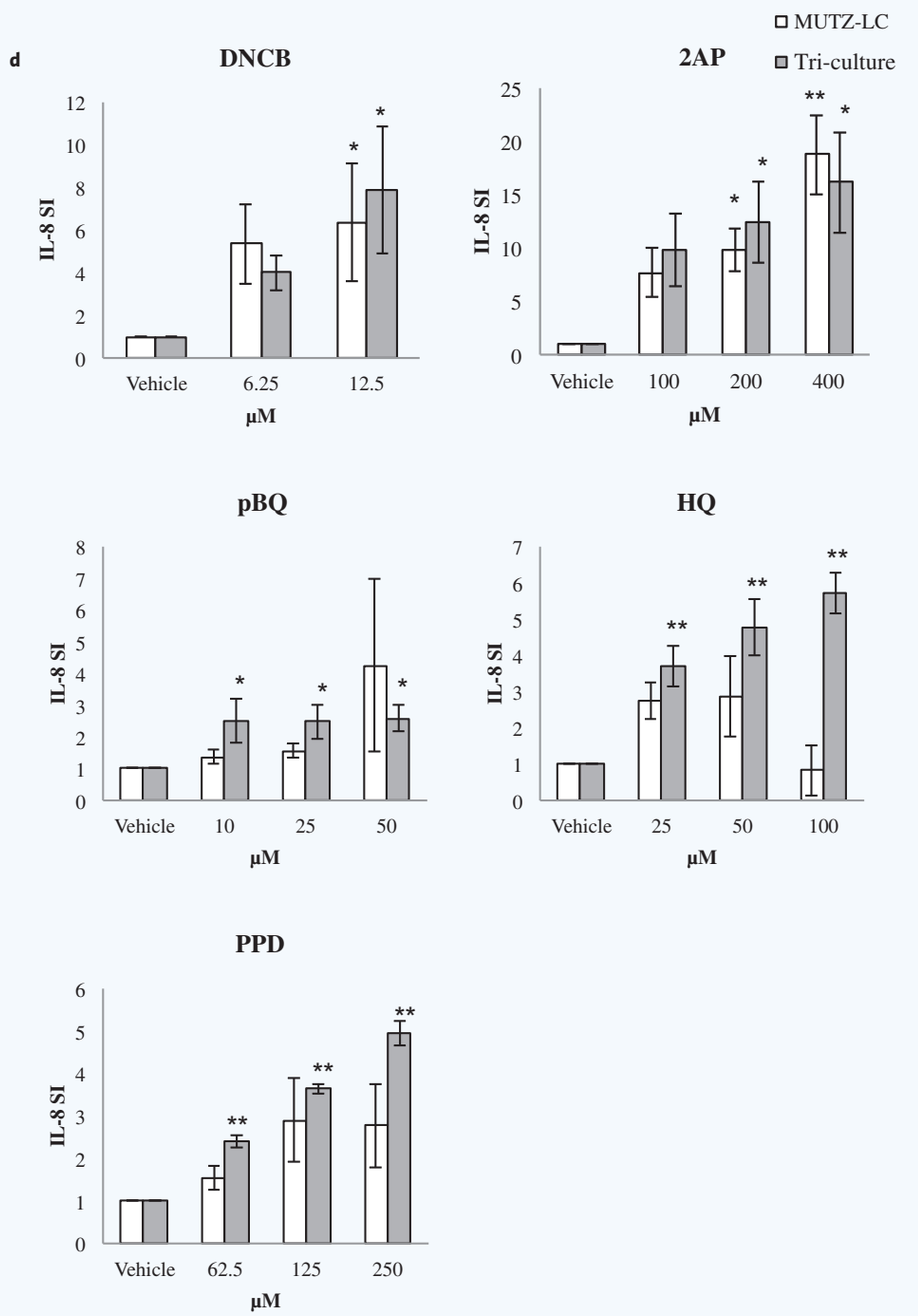
Supplementary Figure 1a ELISA analysis of IL-8 secretion by the tri-culture system and MUTZ-LCs alone in response to non-sensitizers isopropanol, lactic acid, salicylic acid, sodium dodecyl sulfate, vanillin, and xylene. No significant difference was found using Fisher's LSD post-hoc analysis for $n = 4$ independent replicates.



Supplementary Figure 1b ELISA analysis of IL-8 secretion by the tri-culture system and MUTZ-LCs alone in response to weak sensitizers cinnamic alcohol, eugenol, and geraniol. * indicates $p \leq 0.05$ and ** indicates $p \leq 0.005$ by ANOVA, Fisher's LSD post-hoc analysis for $n = 4$ independent replicates.



Supplementary Figure 1c ELISA analysis of IL-8 secretion by the tri-culture system and MUTZ-LCs alone in response to moderate sensitizers cinnamaldehyde, isoeugenol, 2-methoxy-4-methylphenol, and resorcinol. * indicates $p \leq 0.05$ and ** indicates $p \leq 0.005$ by ANOVA, Fisher's LSD post-hoc analysis for $n = 4$ independent replicates.



Supplementary Figure 1d ELISA analysis of IL-8 secretion by the tri-culture system and MUTZ-LCs alone in response to strong/extreme sensitizers dinitrochlorobenzene, 2-aminophenol, p-benzoquinone, hydroquinone, and p-phenylenediamine. * indicates $p \leq 0.05$ and ** indicates $p \leq 0.005$ by ANOVA, Fisher's LSD post-hoc analysis for $n = 4$ independent replicates.