

High-Throughput In Vitro Models of Human Epidermis and Ocular Epithelium for Preclinical Safety and Efficacy Testing of Consumer Products and Pharmaceuticals

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Prior to introduction of new consumer products and cosmetics, or human testing of new therapeutics, animal experiments are traditionally utilized to screen for safety and efficacy. However, large numbers of lead candidates generated by modern high throughput technologies renders animal testing expensive and impractical. A growing need exists for high throughput in vitro models which can provide rapid, reliable safety and efficacy screening. The current poster describes development of in vitro models of human epidermal and ocular cultures in 96-well high-throughput screening (HTS) formats compatible with robotic manipulation. The HTS models are derived from normal human cells cultured at the air/liquid interface in 96-well microporous membrane plates to produce three-dimensional organotypic cultures. Culture histology of both models was evaluated by H&E staining of formalin fixed paraffin sections. The epidermal model displays a stratified and cornified differentiated structure, similar to native epidermis. The 96-well HTS ocular cultures are stratified squamous epithelium typical of in vivo ocular epithelium. Well to well (intraplate) and plate to plate (interlot) variability, as determined by the MTT viability assay, was generally found to be less than 10%. The HTS ocular model was also evaluated for compatibility with the EpiOcular Prediction Equation developed for predicting in vivo Draize ocular irritation scores with MatTek Corporation's standard EpiOcular product(OCL-200). When tested with various concentrations of chemicals including sodium dodecyl sulfate, Triton X-100, benzalkonium chloride, sodium hydroxide and others, the HTS ocular model gave predicted Draize scores that correlated well with standard EpiOcular predicted Draize scores and historical in vivo Draize scores. HTS epidermal and ocular models such as these may thus help to lessen bottlenecks currently encountered in safety and efficacy testing of consumer products and topical therapeutics. This work was supported by NIEHS grant 5R44 ES010237-03.

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