

**IN VITRO SCREEN FOR PHOTOTOXICITY OPTIMIZED DRUG DEVELOPMENT USES A HIGHLY DIFFERENTIATED SKIN MODEL.** Klausner, M., Neal, P., Kubilus, J. MatTek Corporation, Ashland, MA (USA).

**Poster Number:** W30302

**Date:** Wednesday, June 21, 2006

**Time:** 9 am - 4 pm (questions: 11:30 am – 12:30 pm)

**PURPOSE:** Both topically applied and systemically administered medications can induce photosensitivity. Photosensitivity includes both photo-allergic (immunologically mediated) reactions, and phototoxic effects, which occur following an initial exposure to a drug and sunlight. The majority of medications causing photosensitivity are systemic phototoxicants and phototoxicity is much more common than photo-allergy. In the development of new drugs, determining whether a new candidate is phototoxic is essential. Current in vitro methods result in a high percentage of false positives thereby eliminating good candidates from further development. In the current work, we investigated whether the 3-dimensional, highly differentiated EpiDerm skin model (EPI-200) could predict phototoxicity of systemically administered drugs.

**METHODS:** Fourteen known phototoxins, including fibrates, non-steroidal anti-inflammatory drugs (NSAIDs), tetracyclines, quinolones, psoralens, and histamine receptor antagonists, and 2 non-phototoxins were used in this study. EPI-200 tissues (n=2) were cultured for 3 hours in the presence of at least three concentrations of drug ranging from 0-200 mg%. The tissues were rinsed, placed in phosphate buffered saline, and exposed to a non-toxic dose of UVA (10 J/cm<sup>2</sup>) using a solar simulator. After irradiation, the tissues were again rinsed, cultured (37°C, 5% CO<sub>2</sub>) for an additional 18 hours in fresh medium, and evaluated for viability using the MTT assay. The viability of parallel non-irradiated, drug-exposed tissues (n=2) was also evaluated.

**RESULTS:** For tissues exposed to the phototoxic drugs, the viability of the irradiated tissues decreased by 33-75% more than the non-irradiated, drug exposed tissues, indicating phototoxicity. The assay was sensitive (14 of 14 phototoxins detected) and specific (2 of 2 negatives correctly identified).

**CONCLUSIONS:** The EpiDerm skin model will have utility in determining the phototoxicity of systemically administered drugs. Such an assay system will significantly improve the drug development process.