

In Vitro Evaluation of 3D Skin Models for congenital Ichthyosis

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For the testing of skin absorption, the OECD approved guideline 428 for in vitro testing legitimating the replacement of animal experiments by alternative tests. A German research consortium has previously validated an in vitro test protocol using reconstructed human epidermis to quantify skin absorption. In vitro models for skin diseases, however, are in their infancies only.

Thus, the aim of the present study was to appraise a recently established 3D model for congenital ichthyosis, a hereditary severe epidermal barrier function defect. Cultivating normal keratinocytes at the air-medium interface, control models and models mimicking congenital ichthyosis through RNAi-mediated gene knock down were generated. Moreover, keratinocytes from skin biopsies obtained from two ichthyosis patients were used to build up the disease models. The tissues were evaluated for permeation of OECD standard substances. Major and disease typical differences in permeability and barrier function were observed, as the permeability coefficients were markedly increased in patient and gene knock down models when compared to control samples. Moreover, the models were evaluated for the penetration enhancement by innovative nanocarrier systems, solid lipid nanoparticles and dendritic core-multishell nanotransporters. Loaded with Nile red as a model dye, both nanoparticles demonstrated strongly enhanced penetration into control models and healthy human skin compared to conventional cream. Penetration was even more pronounced in models created from patient samples thus once more reflecting the defective epidermal barrier. In conclusion, standardized procedures were successfully applied to characterize in vitro disease skin models rendering future investigations on potential new drug targets possible.