Wissenschaftliche Posterausstellung: Poster 21

Organotypic Models mimic Premature Ageing and Cutaneous Squamous Cell Carcinoma

*Christian Zoschke (a), Lilian Julia Löwenau (a), Suvara Wattanapitayakul (b), Hans-Friedrich Merk (c), Günther Weindl (a) and Monika Schäfer-Korting (a)**

a: Institute for Pharmacy, Freie Universität Berlin, Berlin, Germany
b: Department of Pharmacology, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand
c: Department of Dermatology and Allergology, University Hospital RWTH Aachen, Aachen, Germany

Corresponding Author:
Prof. Dr. Monika Schäfer-Korting
Freie Universität Berlin, Institute for Pharmacy (Pharmacology and Toxicology)
Königin-Luise-Str. 2+4, 14195 Berlin, Germany
Phone +49 30 838-53283
Fax +49 30 838-470871
E mail monika.schaefer-korting@fu-berlin.de

Abstract:
The failure of investigational new drugs in clinical trials (95% for all indications [1] emphasizes the need for relevant human-cell based approaches. This can be due to the low predictive value of animal-generated pharmacological data for humans [2]. Underestimation of age-related changes might be of relevance, too. Considering skin, ultraviolet (UV) irradiation causes the most prevalent skin disorders in later phases of the life span, skin aging and cutaneous squamous cell carcinoma [3]. However, current drug development relies on (animal-based) disease models using juvenile rodents. In this study, we aimed to transfer the effect of UV irradiation to the lab scale by introducing organotypic models of premature ageing and cutaneous squamous cell carcinoma.

To induce premature ageing [4], we reconstructed epidermis from irradiated juvenile normal human keratinocytes with UV-B light (9.6 to 30 mJ/cm^2; single-dose). UV irradiation causes elevated ß-galactosidase expression in keratinocytes. The model showed irregular structure of stratum corneum and stratum granulosum with altered expression of epidermal differentiation markers (keratin-10, -14, involucrin, and filaggrin) and elevated IL-8-expression. Normal reconstructed human epidermis was built from non-irradiated keratinocytes.

To induce premature ageing [4], we reconstructed epidermis from irradiated juvenile normal human keratinocytes with UV-B light (9.6 to 30 mJ/cm^2; single-dose). UV irradiation causes elevated ß-galactosidase expression in keratinocytes. The model showed irregular structure of

stratum corneum and stratum granulosum with altered expression of epidermal differentiation markers (keratin-10, -14, involucrin, and filaggrin) and elevated IL-8-expression. Normal reconstructed human epidermis was built from non-irradiated keratinocytes.

To mimic cutaneous squamous cell carcinoma we co-cultured human squamous cell carcinoma cells (SCC-12) with juvenile normal human keratinocytes on a dermal equivalent consisting of normal human dermal fibroblasts [5]. Normal reconstructed human skin was built without SCC-12 cells. Alteration of culture conditions allows controlling the tumor stage from carcinoma in situ to the invasive disease. Tumor nests show malignant histology and increased proliferation (Ki-67).

In conclusion, disease models on the cutting edge of tissue engineering offer test platforms for investigational new drugs. Further studies will focus on the absorption and metabolism profiles of our disease models.

References

[1] Hartung et al.: ALTEX. 2013. 30: 275-291.
[2] Tralau et al.: Environ Health Perspect. 2012; 120: 1489-1494.
[3] Stockfleth et al.: Eur J Dermatol. 2008,18: 651-659.
[4] Lewis et al.: Mol Biol Cell. 2008, 19: 1346-1353.
[5] Ali-von Laue et al.: Skin Pharmacol Physiol. 2014, 27: 173-180