



ALTEX Proceedings

3D Models & multi-organ-chips (MOC), human-organ-chips (HOC)

3R Centers in Europe & international – national and local centers

3Rs in education and academia

Advanced safety testing of cosmetics & consumer products and alternatives to animal testing in food safety, nutrition and efficacy

An integrated interdisciplinary approach to animal-free nano-material and chemical safety assessment: Results of the in3 project

Biological barriers

Disease models using human cells, tissues and organs

Ecotoxicology

Efficacy and safety testing of drugs, medical devices & biopharmaceutics



EUSAAT

*European Society for
Alternatives to Animal Testing*

The European 3Rs Society



LINZ 2019

22nd European Congress
on Alternatives to Animal Testing

EUSAAT 2019

19th Annual Congress of EUSAAT

www.eusaat-congress.eu

Ethical & legal issues

Free communications

**Implementing
EU Dir 63/2010 – update**

***In silico* models**

**Initiative for
implementing serum
free culture media**

***In vitro* techniques for
CNS toxicity and disease
studies**

Reduction & refinement

**Replacement – advanced
technologies**

**Specific endpoints of
toxicity**

**Stem cell models
and technology
(hIPS, ES, mES, mIPS...)**

**How to account for
uncertainties of reference
methods & data?**

**Animal experimentation:
Working towards
a paradigm change**

'Young Scientists' session





The world leader in innovative 3D reconstructed human tissue models ISO 9001 CERTIFIED

KEY FEATURES OF OUR PRODUCTS

Metabolically active, human cell-derived, 3D reconstructed tissue models
Objective, quantifiable endpoints
Excellent *in vitro* / *in vivo* correlation
Guaranteed long-term reproducibility
Availability of partial and full thickness tissue models
Availability of different tissue formats including high throughput screening plate
Price convenient testing kits as well as single tissues

EXCELLENT CUSTOMER SERVICE AND PROFESSIONAL SCIENTIFIC SUPPORT

Prompt reply to customer's requests and needs
Free scientific and technical consulting before purchasing of product
Monitoring of every single shipment
Dedicated trainings sessions in our facilities or on-site
International support provided by EU, US, Turkey and Japan representatives
More than 20 years of tissue quality control data summarized in open databases -
the most data of any tissue engineering company !
Since 2016 ISO 9001:2008 certified

INTERNATIONAL VALIDATIONS AND PROJECTS

EpiDerm™

ECVAM Skin Corrosion, Validated Assay - OECD TG 431
ECVAM Skin Irritation, Validated Assay - OECD TG 439
ECVAM Pre-Validated and ICH Accepted Phototoxicity Assay
Cosmetics Europe Validation Project on Genotoxicity Assays
German Skin Penetration Validation Study for Surfactants and Formulations
Irritation Potency of Extracts from Medical Devices Study (ISO 10993-10)

EpiOcular™

ECVAM/Cosmetics Europe Eye Irritation, Validated Assay - OECD TG 492
US EPA Accepted for Antimicrobial Products with Cleaning Claims (AMCPs)
COLGATE/IIVS Eye Irritation Validation Study
Con4Eye Project on Eye Irritation Testing Strategies

EpiVaginal™

NIH Funded HIV Research
CONRAD Microbicides Study

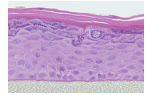
AFFILIATIONS AND MEMBERSHIP IN PROFESSIONAL OR- GANISATIONS AND CONSORTIA IN THE EU



TISSUE MODELS AVAILABLE FROM SLOVAKIA AND USA

EpiDerm™

Skin Corrosion, Skin Irritation, Phototoxicity, Genotoxicity
Micronucleus and Comet assay, Medical devices, Skin
Inflammation, Skin metabolism, Radiation Damage,
Percutaneous Absorption ...



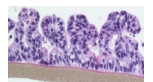
EpiOcular™

Ocular Irritation, "Sub-Draize" Ocular Irritation Testing (Mild,
Milder, Mildest), Specific Ocular Irritation of Surfactants,
Cosmetics and Consumer Products ...



EpiIntestinal™

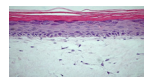
Intestinal Toxicity, Drug Delivery, Inflammation, Fibrosis, Infection,
Epithelial Restitution ...



TISSUE MODELS AVAILABLE FROM USA

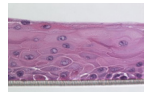
EpiDermFT™

Anti-Aging, Skin Longevity, Skin Hydration, UV Protection,
Percutaneous Absorption ...



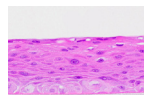
EpiCorneal™

Drug Delivery, Infection, Inflammation, Ophthalmic Product
Testing ...



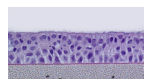
EpiOral™ and EpiGingival™

Mucosal and Oral Irritation, Transmucosal and Buccal Drug
Delivery, Gum Disease, Oral Cancer, Smokeless Tobacco
Effects, Oral Epithelial Proliferation, Antimicrobial Barrier
Function ...



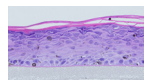
EpiAirway™

Drug Delivery, Respiratory Infection and Toxicology, Tobacco
Smoke Toxicology, Nano-particle Toxicology, Gene Expression
Analysis, RNAi/siRNA Therapeutic Drug ...



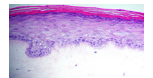
MelanoDerm™

Skin Lightening-Darkening, Skin Pigmentation Modulation,
Keratinocyte-Melanocyte Interactions ...



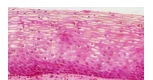
Psoriasis™

Anti-Psoriatic Drug Screening, Basic Psoriasis Research ...



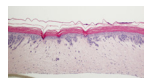
EpiVaginal™

Feminine Product Irritation, Microbicide Testing, Immuno-
competent, HIV-1 Infection Sexually Transmitted Infection,
Inflammation, Vaginal Drug Delivery ...



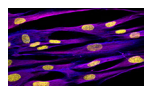
Melanoma™

Tumor Invasion, Anti-Melanoma Drug Screening ...



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A reconstructed human skin model containing macrophages to set up a delayed wound healing model of cutaneous leishmaniasis

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Cutaneous leishmaniasis (CL) is a vector-borne neglected disease caused by protozoan parasites of the genus *Leishmania*. Disfiguring and socially stigmatizing skin lesions develop at the bite site of the parasite-infected female sand fly [1]. Tissue damage and disease in CL are primarily caused by an excessive host immune response against the intracellular infection of dermal macrophages [2]. The dermal lesions persist for months or even years, but eventually heal on their own [3]. Treatment of CL is problematic, as long series of painful injections with the toxic pentavalent antimonials remain the standard therapy [1] and lesions are left alone to self-cure with the risk of secondary bacterial or fungal infection. New therapies for CL and CL lesions are urgently needed. Therefore, realistic CL lesion models are essential as a predictive experimental platform to identify more effective topical strategies.

To that aim we integrated for the first time *in vitro*-generated M1 polarized macrophages differentiated from the human monocytic THP-1 cell line into reconstructed human skin (RHS).

THP-1 derived macrophages were localized in the RHS dermal compartment and distributed homogeneously in accordance with native human skin. Standardized circular wounds were made with a 18 gauge blunt tip needle or by punch biopsy. In order to impair wound healing, wounded RHS was stimulated with intradermal application (for needles) or drops (for punch wounds) of IFN- γ in combination with LPS and/or hydrocortisone.

Wound healing was monitored on days 1, 3 and 7 after wounding by histological examination of RHS. Immunohistochemical (Ki67, K14, tenascin-C, laminin 5, α -SMA) and pro-inflamma-

tory cytokine analyses were performed pre- and post-skin wound and stimulation, to increase the characterization of the model and to assess the effects of IFN- γ , LPS and hydrocortisone in wound healing RHS models.

Early in healing, IFN- γ -LPS-hydrocortisone wounds displayed reduced proliferation and re-epithelialisation and heightened inflammatory response compared with control wounds. H&E-stained sections showed increased epidermal thickness and a lack of dermal epidermal junction in the wound zone.

In summary, we integrated functional THP-1 derived macrophages into RHS and induced a delayed wound healing to provide a unique experimental test platform to evaluate the effects of new topical treatments.

References

- [1] Murray, H. W., Berman, J. D., Davies, C. R. et al. (2005). *Lancet* 366, 1561-1577. doi:10.1016/S0140-6736(05)67629-5
- [2] Wijnant, G. J., Van Bocxlaer, K., Fortes Francisco, A. et al. (2018). *Antimicrob Agents Chemother* 62, e00631-18. doi:10.1128/AAC.00631-18
- [3] WHO (2010). Control of Leishmaniasis. *WHO Technical Report Series* 949, 1-187.

Submission declaration:

Conflicts of interest: The corresponding author declares that there is no conflict of interest with the authors.

Statement on ethics vote: No ethics vote is required.