In vitro human SCAR Models

Human Skin Models

Human skin and scar models are cultured human skin cells, which serve as an alternative for animal testing and mimic the human reaction in vitro as closely as possible. VU medical center, department of Dermatology offers a broad range of state-of-the-art human skin models (for investigating how compounds can interfere with normal skin homeostasis and disease) and skin tissue engineering expertise. The skin models are an alternative for animal testing, can be used for screening of therapeutics and can be adjusted to your specific research needs.

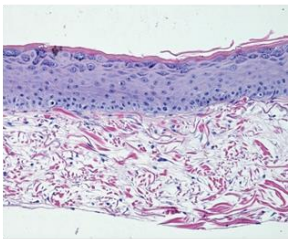
Human Scar, Hypertrophic Scar & Keloid Model

We are able to culture three different types of human scar models: e.g. normal scar, hypertrophic scar and keloid scar. Our human full-thickness scar models consist of keratinocytes and melanocytes on a fibroblast-populated dermal matrix resembling the human scars. The scar models can be constructed from adipose-derived mesenchymal cells. On demand we can culture different cell types/constructs (e.g. only epidermal or dermal layer). The culture process will take 4–5 weeks including an air-exposed culture period. The models are a robust, safe and animal free solution to screen a product or compound for positive effects on e.g. scar quality and healing (by using quantifiable scar and wound-healing parameters and biomarkers).

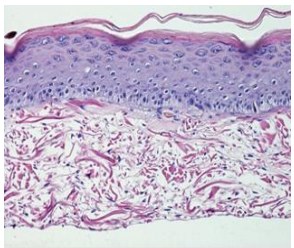
Read-out options for Scar Models are:

- Tissue histology (HE, IHC)
- Viability (MTT/Trypan blue)
- Proliferation, migration and contraction assays
- Apoptosis and Necrosis
- Dose finding/Dose Cytotoxicity
- Wound-healing factor secretion
- Effect of compounds on cytokine, chemokines & growth factor production
- Risk assessment of chemicals
- Screening of compounds and chemicals on positive effect on scar quality, reduction, refinement & prevention
- Effect of compound/chemical on thickness of dermis, contraction, Collagen 1 secretion, Epidermal cell layers.
- Outgrowth of epidermis, IL-6 & CXCL8 secretion.

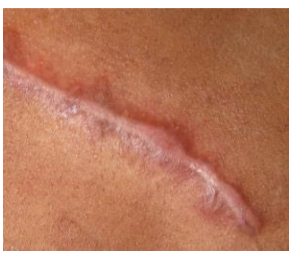
Hypertrophic scar model



Keloid scar model



Hypertrophic scar



Cultured Keloid scar

Assays and Techniques e.g:

- ELISA
- FACS
- Western Blotting
- qPCR
- Specific kits

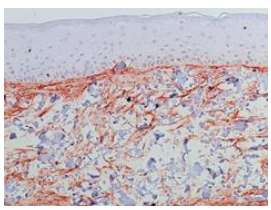
Application options compound:

- Topical
- Injection
- Systemic (in medium)

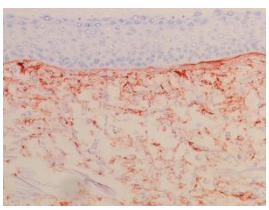
Time frame exposure e.g: 2, 4, 8, 24, 72 hrs.

Characterization and parameters scar models

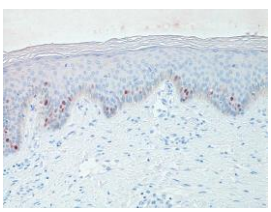
Collagen III



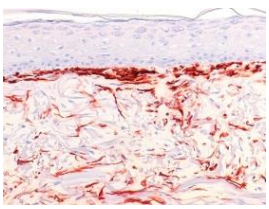
Collagen IV



Ki67



αSMA



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A-SKIN Contract Research Services

A-SKIN is a skin tissue engineering company culturing human skin, founded in 2006 as a spin-off company of the VU University Medical Center in Amsterdam. A-SKIN contract research services focuses on the development and usage of our broad range of in vitro human skin models. The skin models are an alternative for animal testing and can be used for screening of therapeutics and compounds, risk assessments, allergen prediction or sensitizing potential.

SKIN Tissue Engineering Research

The VU University Medical Centre (VUmc), established in 1964, is one of the leading academic centers in the Netherlands and focuses its core activities on healthcare, research and education. VUmc research is strongly translational: from bench to bedside to society. VUmc's studies focus on discovering, testing, implementing and disseminating new insights and on enhancing health care.

The Department of Dermatology is an internationally leading research group in the development of tissue engineered skin and other wound-healing management strategies for research purposes and clinical applications and works in close collaboration with A-SKIN. This special research uniit focuses on relevant clinical and pathophysiological aspects of chronic and acute wound-healing. Current research focuses on i) the clinical and pathological aspects of allergic and irritant contact dermatitis and ii) the development and application of tissue engineered skin substitutes for healing chronic wounds and burn wounds and iii)construction of human skin models such as a keloid, scar or immunological model for skin testing services.

Prof.dr. S. (Sue) Gibbs is Professor of Skin and Mucosa Regenerative Medicine, Head of the Dermatology Laboratory at VUmc, co-founder of A-SKIN. Sue Gibbs received her training in Biochemistry at the Sheffield University, UK, after which she obtained her PhD in 1991 at the Department of Molecular Genetics, Leiden University, NL. In her 25 year career, she has focused on research in the human skin and its cellular components. In 2005, she joined the Sixth Framework Programme “Sens-it-iv”, which focused on novel testing strategies for *in vitro* assessment of allergens. The resulting *in vitro* assays are currently being implemented in the cosmetics industry in order to reduce animal testing. With the publication of her work titled “Autologous full-thickness skin substitute for healing chronic wounds” in 2006, her career took a next step, opening the opportunity to expand the research on tissue engineered skin for *in vivo* wound healing and to develop skin models as animal alternative for testing and screening. Sue Gibbs is passionate about the reduction, refinement and replacement of animal testing by human *in vitro* skin models. In 2015 Sue Gibbs was awarded with the “Lef in het Lab” (“Courage in the Lab”) prize from the Dutch Society for the Protection of Animals for her commitment to the reduction of animal testing with her *skin-on-a-chip model* to study complex skin disease processes and to test new drugs without the use of animals.

Relevant publications

Quality of skin equivalents:

1. Reijnders C.M.A. et al. Development of a Full-Thickness Human Skin Equivalent In Vitro Model Derived from TERT-Immortalized Keratinocytes and Fibroblasts. Tissue Engineering Part A. September 2015, 21(17-18): 2448-2459
2. Kroeze KL et al. Autocrine regulation of re-epithelialization after wounding by chemokine receptors CCR1, CCR10, CXCR1, CXCR2, and CXCR3. J Invest Dermatol 2012;132(1):216-25.
3. Kroeze KL et al. Chemokine-mediated migration of skin-derived stem cells: predominant role for CCL5/RANTES. J Invest Dermatol 2009 June;129(6):1569-81.
4. Spiekstra SW et al. Wound-healing factors secreted by epidermal keratinocytes and dermal fibroblasts in skin substitutes. Wound Repair Regen 2007 September;15(5):708-17.

Drug and growth factor testing models:

1. van den Broek LJ, et al. Development, validation and testing of a human tissue engineered hypertrophic scar model. ALTEX 2012;29(4):389-402.
2. Kosten I.J. et al. MUTZ-3 derived Langerhans cells in human skin equivalents show differential migration and phenotypic plasticity after allergen or irritant exposure. Toxicology and Applied Pharmacology 05/2015; 85(1).
3. van den Broek LJ. et al. Suppressed inflammatory gene expression during human hypertrophic scar compared to normotrophic scar formation. Exp Dermatol. 2015 Aug;24(8):623-9.
4. Kerstin Reisinger et al. Systematic evaluation of non-animal test methods for skin sensitisation safety assessment. Toxicology in Vitro, Volume 29, Issue 1, February 2015, 259–270.

Inflammation, sensitization and irritation in vitro

1. Ouwehand K et al. Irritant-induced migration of Langerhans cells coincides with an IL-10-dependent switch to a macrophage-like phenotype. J Invest Dermatol 2011 February;131(2):418-25.
2. Ouwehand K et al. CXCL12 is essential for migration of activated Langerhans cells from epidermis to dermis. Eur J Immunol 2008 November;38(11):3050-9.
3. Kosten I.J. et al. Gingiva equivalents secrete negligible amounts of key chemokines involved in Langerhans Cell migration compared to skin equivalents. Journal of Immunology Research. In Press.

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