Skimune®>3D

Adverse Immune Reaction Model



Skimune® 3D, developed by Alcyomics[®] in collaboration with REPROCELL, is the only commercially available autologous human skin model for testing adverse immune reactions.

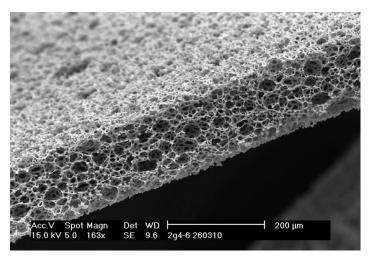




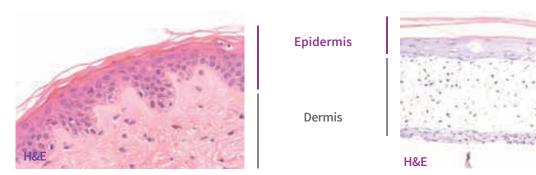
Understand Cell Function and Behaviour with Skimune[®] 3D

Skimune® 3D is made using **Alvetex™**, a polystyrene scaffold designed with three-dimensional (3D) cell culture in mind. Primary human skin cells and autologous immune cells are cultured together in **Skimune® 3D**, to create a co-culture system that is ideal for testing immunological reactions in human skin.

The **Alvetex™** scaffold allows cells to maintain their normal 3D shape and structure, and creates surroundings that maintain optimal growth, differentiation and function. In this 3D system cells form complex interactions with minimal exogenous interference, enabling a culture environment that is more physiologically relevant.



Skimune[®] 3D Under the Microscope



Skimune[®]3D Full-thickness 3D autologous human skin equivalent model



Skimune[®] 3D Combines Skin Tissue and Immune Cells from the same Donor

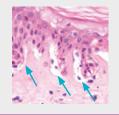
Skimune® 3D uses non-artificial human skin and blood samples from the same donor to accurately measure the efficacy and potential immunogenicity of large and small molecule therapeutics, cosmeceuticals and chemical products.



PBMCs +/- biopharmaceutical



Primary peripheral blood mononuclear cells (PBMC) +/– Mab of interest are co-cultured with Skimmune[®] 3D skin equivalent



- Immunohistopathology
- Laser scanning confocal microscopy
- mRNA expression analysis
- Cytokine analysis

In situ histopathological is evaluated for the severity of skin tissue damage.

Histological Analysis of Skimune® 3D in Action

In the following case study, Skimune[®] 3D was screened using known positive Mab (OKT3) and negative Mab (Tysabri[®]) controls and assessed for skin damage. Positive staining for heat shock protein 70 (HSP70), a marker of cell apoptosis, in the epidermis was indicative of damage in the skin model.

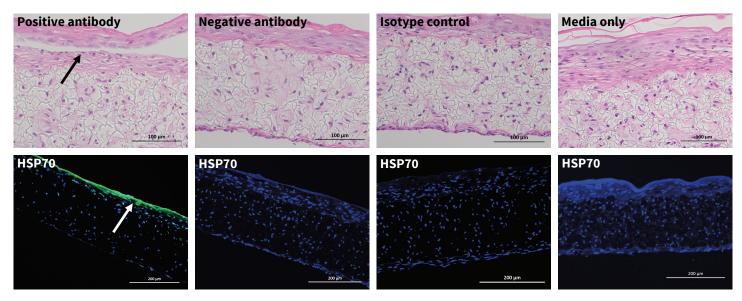


Figure 2: Screening of known biologics in Skimune[®]3D. Haematoxylin and eosin staining for positive antibody OKT3 (top left image) suggested tissue damage when compared to the negative control (Tysabri[®]) which showed normal expected structure with no damage. Positive immunofluorescence staining for the apoptotic marker heat shock protein 70 (HSP70) was shown in the positive control skin section (bottom left), but not the negative controls.

Cytokine Analysis of Skimune® 3D in Action

Damage in the skin sections correlated with cytokine release, demonstrated below by increased release of IFN γ and TNF- α in the positive Mab (OKT3) when compared to the negative Mab (Tysabri[®]) and other controls.

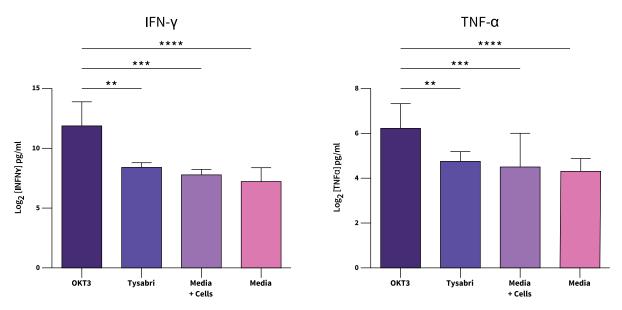


Figure 3: Skimune[®] 3D can be used to measure changes in cytokine release. Cytokine concentration is presented as Log2 [cytokine] pg/ml. * = $p \le 0.05$, ** = $p \le 0.01$, *** $p \le 0.001$.

Skimune[®] 3D advantages

- Cuts drug development costs
- ✓ Increases product safety profile
- ✓ Reduces the use of animal testing
- ✓ Accelerates hazard identification
- ✓ Solves the problem of the ban on animal testing for cosmeceuticals

Skimune[®] 3D applications

- Risk assess chemicals, compounds, novel drugs and biologics
- Assess potency of lead compounds and distinguish
 between sensitizers and non-sensitizers
- Analyse tissue histology via immunofluorescence
- Measure apoptosis in response to test compounds
- **Explore** test compound effects on chemokine, growth factors and cytokine levels

Skimune® 3D is a unique full-thickness human skin equivalent model providing an autologous in vitro system for safety testing of drugs, chemicals and cosmetics as an alternative to animal models.

- Dr Asif Tulah, BD Manager, Alcyomics®

REPROCELL Europe Ltd

Thomson Pavilion, Todd Campus West of Scotland Science Park Acre Road Glasgow, G20 0XA UK

T: +44 (0)141 465 3460 **E:** info-emea@reprocell.com



REPROCELL USA Inc

9000 Virginia Manor Road Suite 207 Beltsville, MD 20705 USA

T: +1 301 470 3362 **E:** info-us@reprocell.com

Alcyomics®

The Biosphere Draymands Way Newcastle Helix Newcastle upon Tyne, NE4 5BX UK

T: +44 (0)191 580 6158 **E**: info@alcyomics.com



www.reprocell.com