MILLI-FLUIDIC BIOMIMETIC BIOREACTOR FOR DYNAMIC AIR–LIQUID INTERFACE CULTURE FOR SKIN TISSUE ENGINEERING INVESTIGATIONS

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Introduction

Epithelial tissues are naturally **exposed** to the **external environment**[1], a condition replicated in vitro using **the air–liquid interface (ALI)** approach[2]. Conventional ALI systems rely on **transwell inserts** to separate air and liquid compartments[3]; however, their **static nature fails to reproduce the dynamic exchange** of nutrients and gases occurring in vivo, often leading to uneven tissue development.

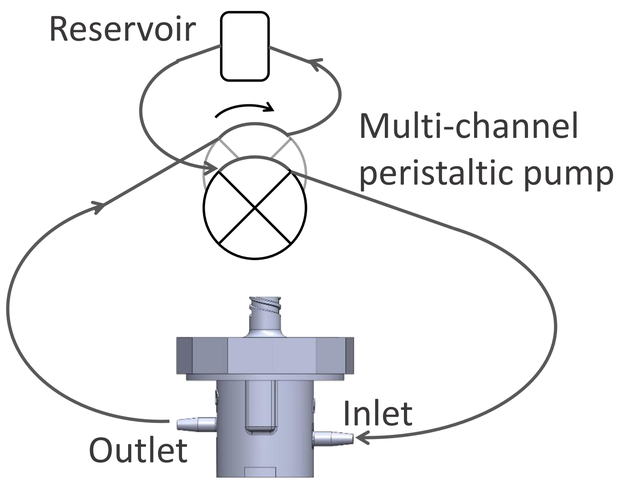
AIM: develop a biomimetic bioreactor, designed to support ALI culture with continuous medium recirculation to enhance physiological relevance for skin tissue engineering.

Design and manufacturing

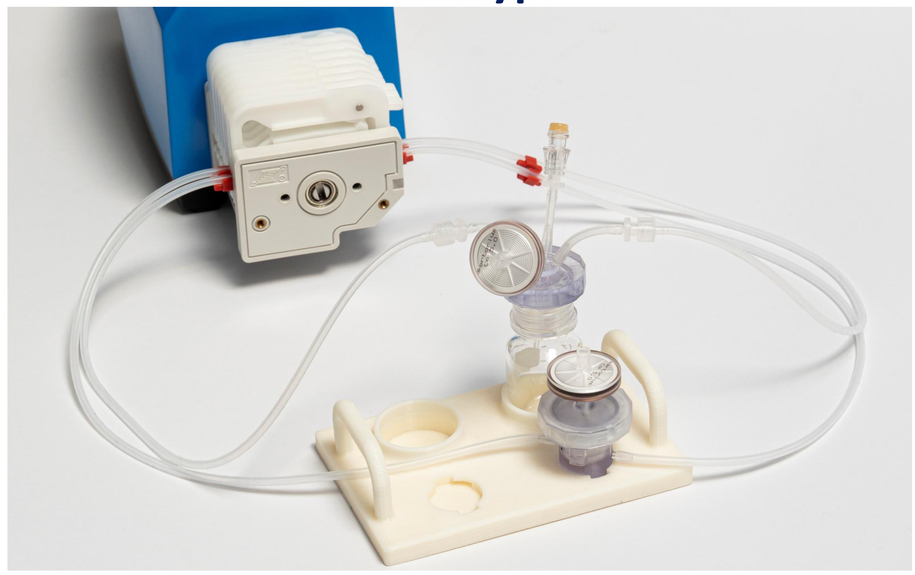
Culture chamber



Hydraulic circuit



Prototype

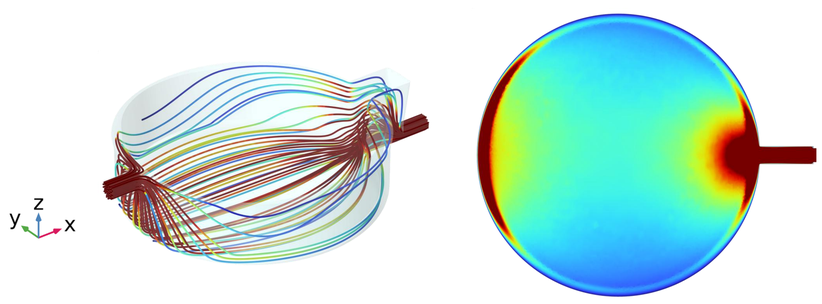


Computational fluid dynamic (CFD) simulations

3D stationary CFD simulations

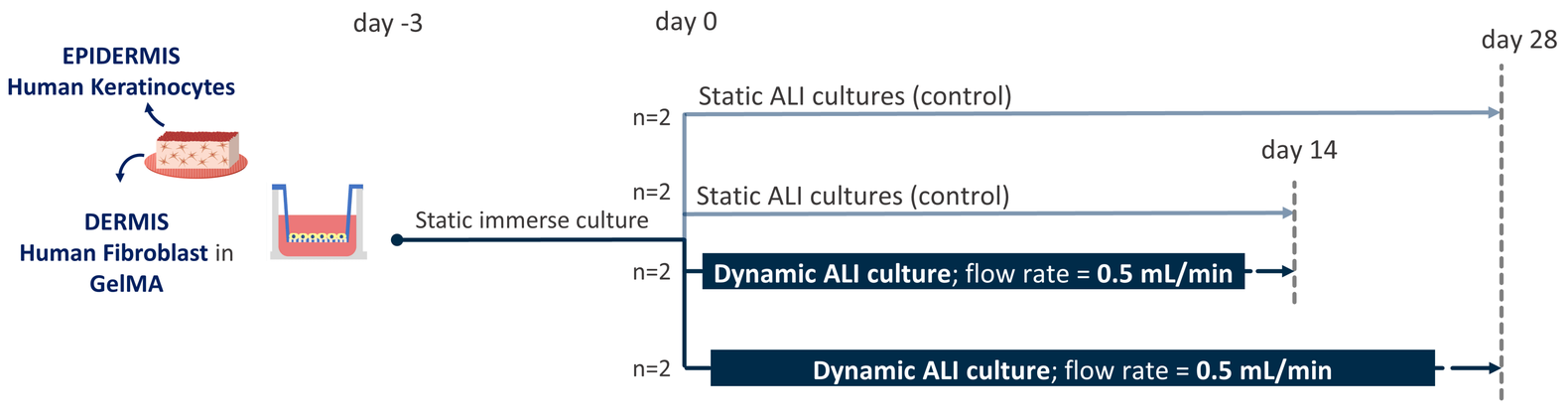
- Culture medium modelled as **incompressible Newtonian fluid at 37°C** (ρ = 9.943*10^2 kg/m^3, μ = 6.890*10^{-4} Pa*s)
- Imposed flow rates = **0.5 mL/min**

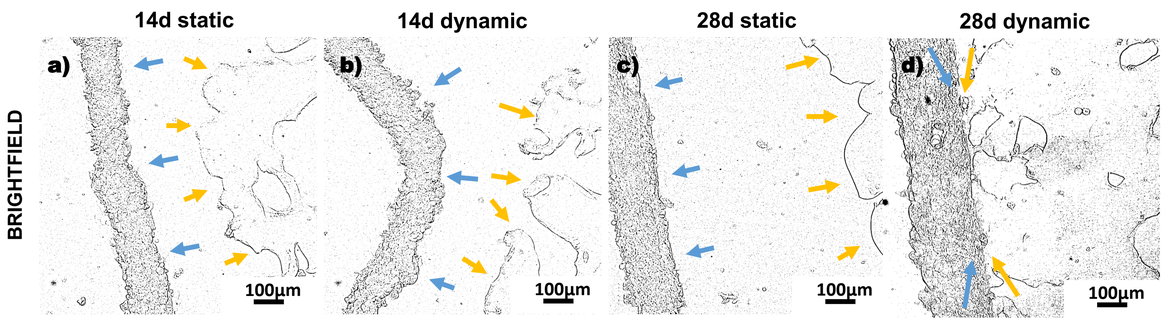
Velocity field (mm/s)



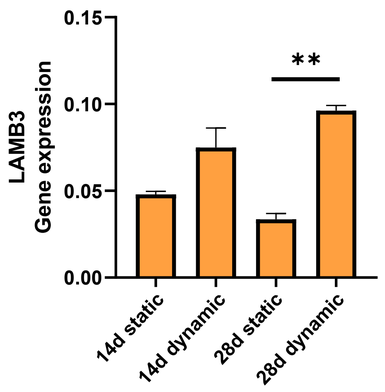
- ✓ **Absence of stagnation points** and recirculating zones
- ✓ **Average velocity v** in the range of **capillary blood velocity** (0.35 < v < 0.95 mm/s [2])

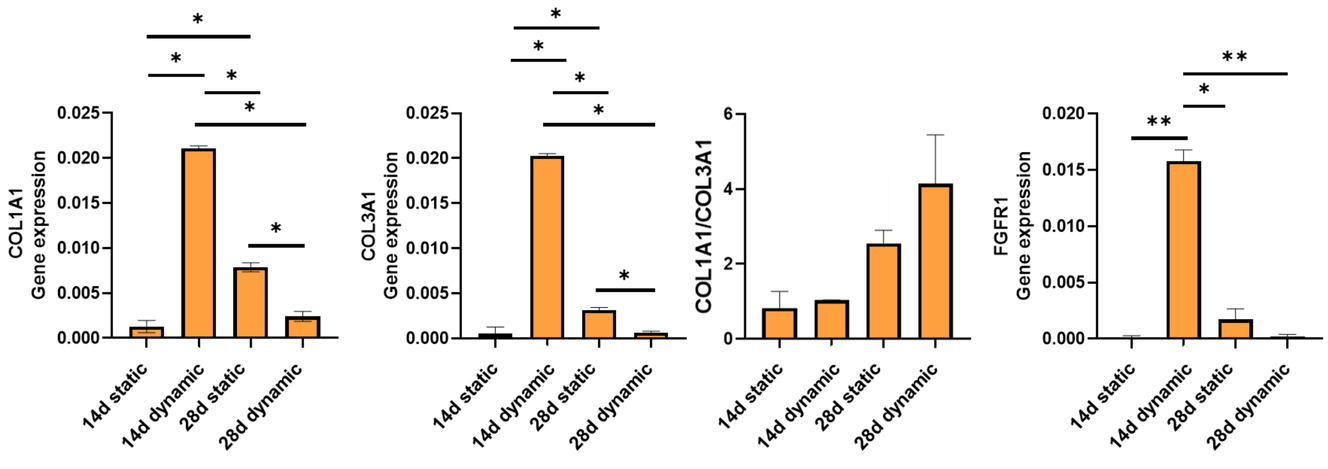
Biological experiments





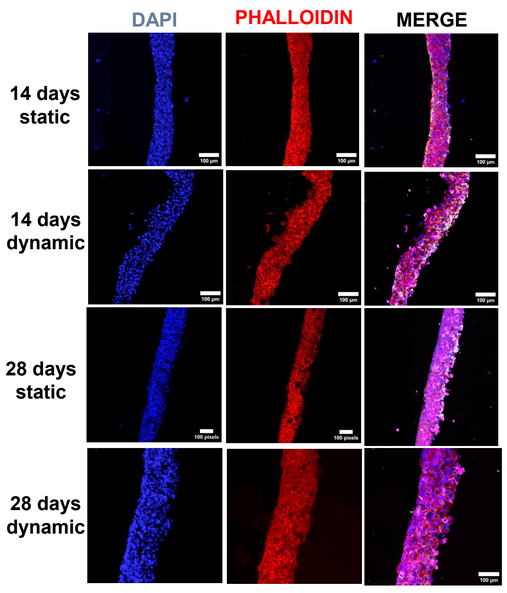
→ Epidermal compartment → Dermal compartment

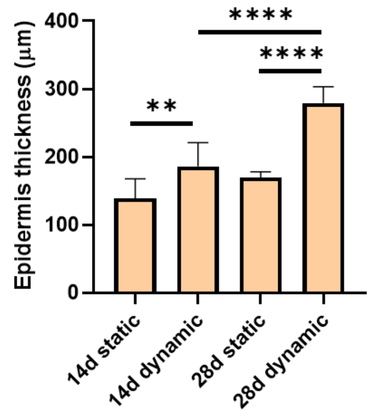




- ✓ Highly **active fibroblasts**
- ✓ High extracellular **matrix turnover**
- ✓ **Developing tissue**

Epidermis Thickness



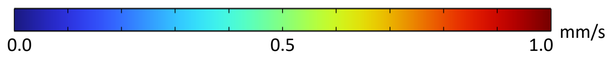


- ✓ **Dynamic culture significantly increased the epidermis thickness**
- ✓ 28 days of **dynamic culture increased** the **mechanical cohesion** and **structural integrity** at the **dermal–epidermal interface**

- ✓ **Versatile and powerful tool to investigate epidermal–dermal interactions**
- ✓ **High potential for advanced in vitro skin modeling applications**

References

1.Rimal, et al, Appl.Mater.Today, 2021.
2.Chen, et al, Reprod.Domest.Anim, 2019.
3.Bluhmki, et al, Sci.Rep, 2020.


0.0
0.5
1.0
mm/s