Advanced translational cosmetics: using the world's first non-invasive Bioimpedance 3D Bioprinted skin chips to link cosmetics lab testing to humans.

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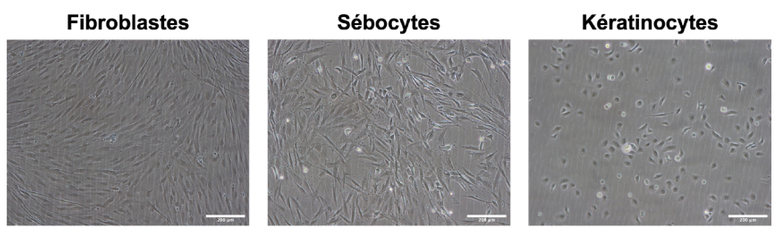
INTRODUCTION

In vivo cosmetics donor testing remains the most expensive stage to creating advanced safe cosmetics. Solutions to making safer cosmetics requires better testing which is why we have developed the world's first 3D Bioprinted oily skin model which can measure the same non-invasive electrical activity as on humans, while at the same time giving normal laboratory read-outs. Bioimpedance, which has long been used for general body composition testing can also be applied at the surface skin level, to evaluate changes in the local skin environment. Here we aimed to combine laboratory and in vivo parameters for better cosmetics testing.

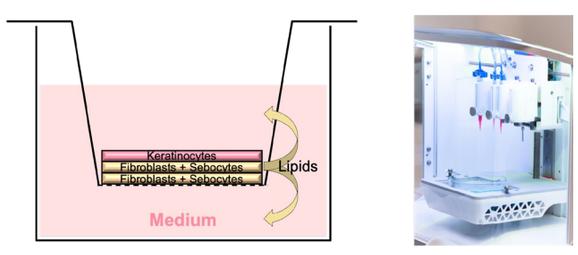
METHODS

EX VIVO MODEL



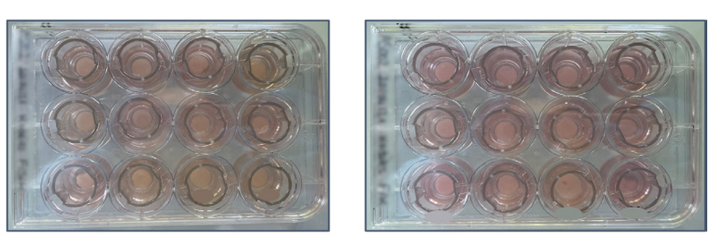
Fibroblasts, keratinocytes and sebocytes were isolated from human skin donors using enzymatic dissociation and grown in 6-well plates.

ACTIVE APPLICATION



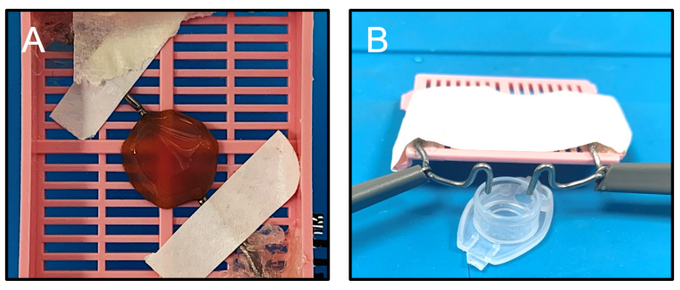
Cell were mixed with specific bioinks and transfered to a 3D Bioprinter (Bio X, Cellink). 3D models were produced layer after layer following selection of a Computer Aided Design (CAD).

METABOLIC ACTIVITY



In order to modulate lipid production, 3D models of sebaceous micro-glands were treated in triplicates for 5 days: Linoleic acid, and TOFA as controls and 3 test active ingredients A1, A2 and A3. Properties of the actives were not known at the time of the experiment and were blind tested.

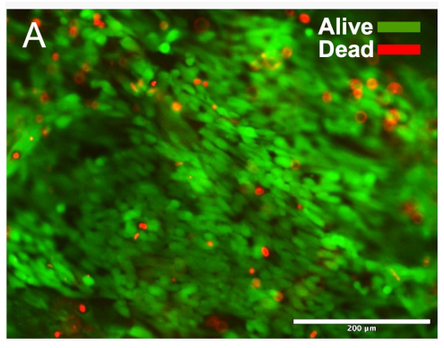
BIOLOGICAL IMAGING



To demonstrate the capability of bioimpedance to detect changes in lipid production, we collected supernatant at days 0, 1, 2 and 5 after treatment with lipid modulator, and performed bioimpedance readings using a Bioimpedance reader (East Tester®, China) calibrated in the 10 kHz range and connected to adapted biological probes (B). 3D models were also collected at the end of treatment to measure Bioimpedance in the bioink using specific probes (A)

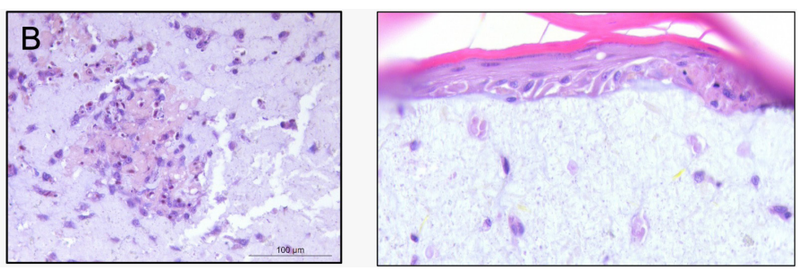
RESULTS

Live-Dead



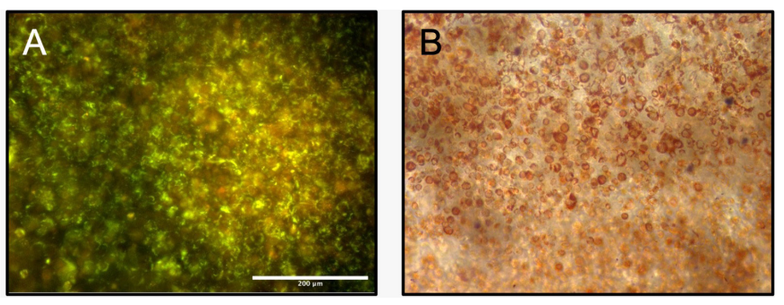
- Cell express a good viability and 3D structures similar to micro-sebaceous glands.

Hematoxylin, Eosin, Saffron staining



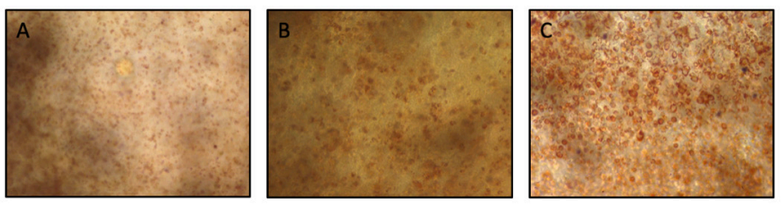
- HES coloration results showed multilayered, differentiated and cornified epidermis developed on the dermis.
- The dermal-epidermal junction (DEJ) was defined, separated, organised and differentiated.
- Significant reduction for TOFA, expressing a potential toxicity of TOFA under these conditions.

Nile Red staining

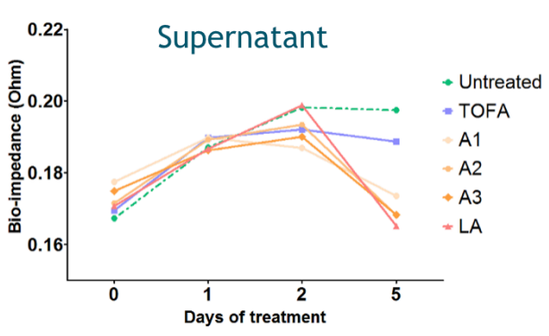


- Significant increase of lipid droplet after treatment with Linoleic acid (B), as expected, compared to the untreated condition (A). More lipid droplets as well as bigger lipid droplets inside the structures.

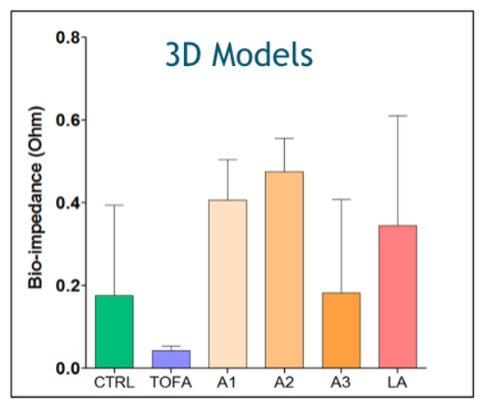
Oil Red O staining



- Lipid production of 3D models validated for the different conditions.
- Slight reduction was observed in TOFA condition (B) compared to the untreated control (A). On the opposite, a substantial increase was detected in Linoleic acid condition (C). Similarly to the Nile Red observations, Linoleic acid condition showed sebocytes rich in lipids.



- Due to lipids accumulation, bioimpedance levels increased over time from day 0 to day 2.
- At day 5, TOFA treatment, slightly reduced bioimpedance level, reflecting the inhibition of lipid accumulation.



- In contrast, significant decrease of the bioimpedance signal was observed for Linoleic Acid and actives conditions, probably expressing the release of lipids in the supernatant between day 2 and day 5.

CONCLUSION

- 3D bioprinted full skin model including microsebaceous galnds for lipids screening has been enhanced
- Validation of a rapid non-invasive technology, bioimpedance, for the detection of lipid secretion
- This model allow advanced translational lab-to-donor data to help bring sophisticated cosmetics ingredients to market faster, safely and more affordably.