

“ CTIBiotech develops predictive Human skin models for dermatocosmetics, biomedical and pharmaceutical research and development.

World-class experts at CTIBiotech produce innovative solutions for efficacy and safety testing of active ingredients, formulated products, dermatocosmetics & medical devices.

CTIBiotech also designs custom-made 3D Bioprinted skin models for safety and efficacy testing.



## We provide

### Ex vivo biopsy models

Including skin, scalp, hair and on demand tissues.  
We work with a network of 200 healthcare professionals worldwide to procure healthy and diseased skin biopsies with ethical consent of donors.

### In vitro models

Different Human cell types from skin pre-clinical grade production by biomedical scientists with over 30 years experience. Human primary cells are isolated from tissues collected with ethical consent and regulatory authorisations.

### 3D Bioprinted full skin models

A flexible bioprinting platform to produce as many as 50 to 100 artificial skin models (dermis & epidermis) from one donor skin cells.  
5 years of extensive R&D nurtured this powerful technology to screen ingredients, finished products or for pre-clinical medium to high throughput evaluation.

## World first innovations for skincare R&D

Advanced **human cells and tissue models** including human **sebocytes** and **ex-vivo 3D sebaceous glands** for oily or dry skin, inflammation or acne R&D, **3D hair & scalp ex-vivo models**.

A unique **BabySkin model** world's first pediatric skin model adapted with OECD guidelines to mimic physiology & the reactivity of newborn baby skin to **evaluate products** for babies and children.



**Professor Colin McGuckin**  
**President & CSO of CTIBIOTECH**

“ CTIBIOTECH helps the world's leading cosmetics skincare companies develop their innovation and prove efficacy.

## Technical and analytical platforms

Including:

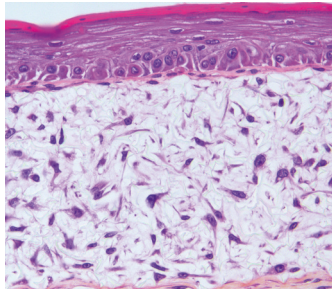
- 1200m2 laboratories
- Accredited human tissue and cell biobank
- Flow cytometric analysis
- Protein analysis
- 2D & 3D bioimaging
- Spectrophotometry, UV rays simulator, bioimpedance, bioreactors...

## Our offer

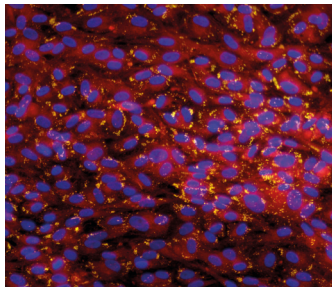
Biosourcing

Open Laboratory & Open Innovation for human tissue model development

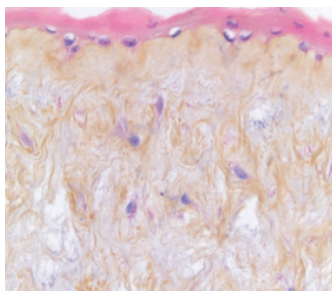
Contract testing



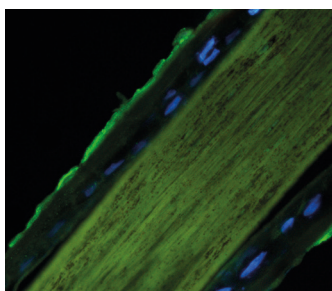
HES staining of a skin biopsy



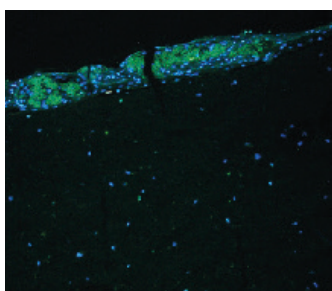
Nile red analysis of primary sebocytes showing lipid production



HES staining of full baby skin model (dermis and epidermis)



Immuno fluorescence staining of hair



Inflammatory response in 3D Immunised Skin model

## Ex-vivo biopsies

*3D skin models to test the efficacy and the safety of cosmetics ingredients & products and medical.*

Biopsies and cells are available with a diversity of phototypes, pathologies, body localisation, age. We only work with the highest ethics and therefore only use up-cycled tissues from living human donors.

## Sebaceous glands and primary sebocytes

Presented at  
IFSCC  
2017

*2D and 3D models developed to increase the significance of testing on acne, seborrhoeic and dry skin.*

These innovative models can be used to advance your research and development and develop efficient cosmetics, aimed at increasing or decreasing sebum production.

## Baby Skin Model

Presented at  
IFSCC  
2019

*Advanced testing of skincare efficacy, irritation and safety for dermocosmetics products.*

Developed as an alternative to animal testing, BabySkin is a highly sensitive model to test ingredients and cosmetics irritation potential. More and more, concerned parents want the safety of the products they use on infants and children to be thoroughly tested. Tested with reference to OECD guidelines.

## Hair and Ex-vivo Scalp model

*Designing bioassays for haircare products.*

In vitro hair and ex vivo scalp models to test hair-care products for efficiency, itchiness, hair growth, colour, dandruff or ageing. The practical, realistic, model we developed allows the test of active ingredients and haircare products. It brings robust honest scientific data to demanding customers.

## 3D Bioprinted Skin Models

Presented at  
IFSCC  
2020

*New technologies developed by us enable our researchers to reproducibly produce predictive human tissue models in large quantities.*

Bespoke 3D skin models to demonstrate the efficacy of ingredients, formulated products, drug candidates or medical devices. Our models include keratinocytes, fibroblasts and other cell types such as immune cells or sebocytes. This powerful and flexible platform opens new horizons for cosmetic solutions for dry, atopic, oily skin...

# Baby Skin Model

## Advanced testing of irritation and safety for cosmetics



The Baby Skin model is a new advanced procedure, taking tissue from newborn babies, that is normally thrown away. It is a highly sensitive model appropriate for testing of everything coming into contact with baby skin: creams, cleansers, wipes, food, clothes

Developed as an alternative to animal testing, Baby Skin is a highly sensitive model designed by CTIBiotech's expert team of bioengineers to test ingredients and cosmetics irritation potential.

The skin of the baby is highly sensitive to irritation compared to adult skin. More and more, concerned parents want the safety of the products they use on infants and children to be thoroughly tested.

HES staining photographs of fixed CTIBiotech's BabySkin models fixed. The model shows normal skin morphology.



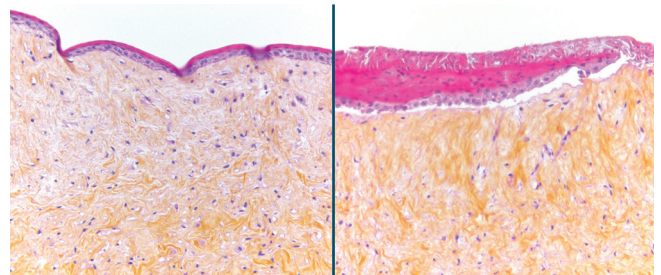
Since the sample is human and is not reconstructed, it provides an opportunity to understand penetration and effect of products applied on the skin and potentially to understand immune system complications which arise in children with sensitive skin.

Following CTIBiotech's strict ethical rules, Human samples are obtained from hospitals with appropriate legal approval and authorization as well as additional consent at the hospital.

All samples obtained are taken with ethical body approval and at no time is any Human harmed during the process.

Tested with reference to OECD guidelines, the Baby Skin model proved to be reproducible and sensitive. Both SDS and real ingredients were tested and the pertinence of the model demonstrated and compared to alternatives such as foreskin or reconstructed models.

Impact of irritant on Baby Skin, histology:



Impact of SDS irritant on the Baby Skin Model. On the left, untreated model, on the right 1 % SDS applied for 10 min. Histology using HES staining.

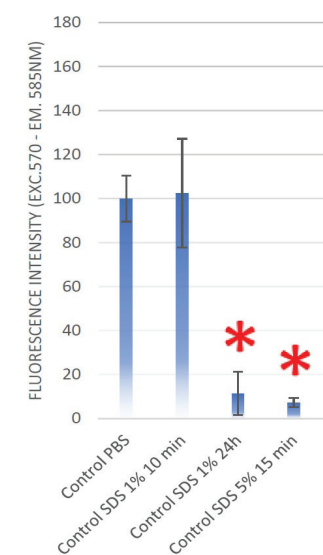
Following OECD guidelines, the Baby Skin model was tested with different concentrations of the irritant substance SDS. At 1% SDS a thicker epidermis formed. At 5% SDS this increased. As expected, a long 24 hours exposition of the skin to SDS was clearly unhealthy for the tissue.

**Baby Skin by CTIBiotech is the world's first ethical Human baby skin model.**



# Baby Skin Model

## Skin irritation evaluation on the model adapted from OECD guidelines

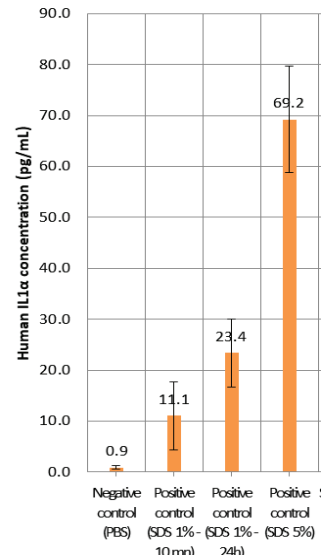


Mean of fluorescence intensity measured after Alamar Blue test realized 42h after sample application on BabySkin models.

### Impact of irritant on viability

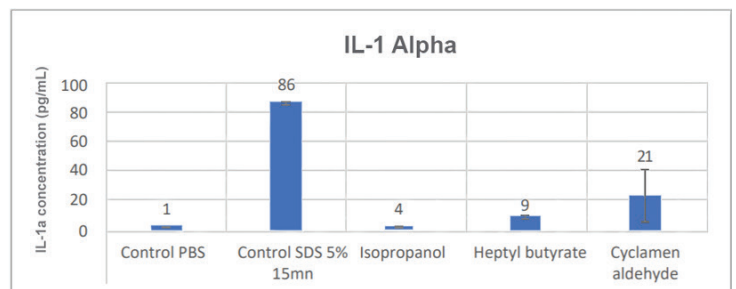
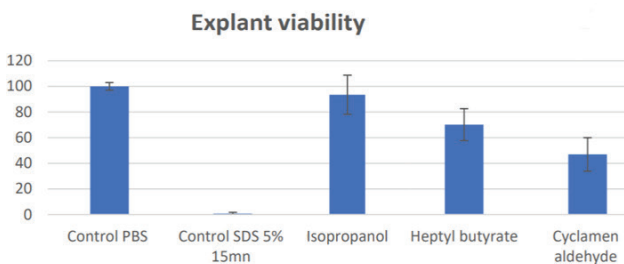
The viability of the skin is negatively impacted by irritants. Using Alamar Blue, a significant 10-fold decrease of viability between untreated negative control and positive controls was measured. This confirmed the high irritant effect of SDS applied in those conditions. No significant difference has been observed after SDS 1% application during 10 minutes.

Interleukin, a marker of sensitive skin 2h after treatment, 1% SDS application for 10 minutes increased slightly IL-1 alpha production. A significant increase was observed with SDS 1% applied during 24h or SDS 5% applied for 15 minutes: 25 and 75 fold increase respectively. The dose dependant effect shows the baby Skin Model sensitivity.



Mean of IL-1 alpha produced by CTIBiotech's Baby Skin models 42h after sample application

## Test of various molecules with known and different irritation potentials according to OECD guideline 437 :



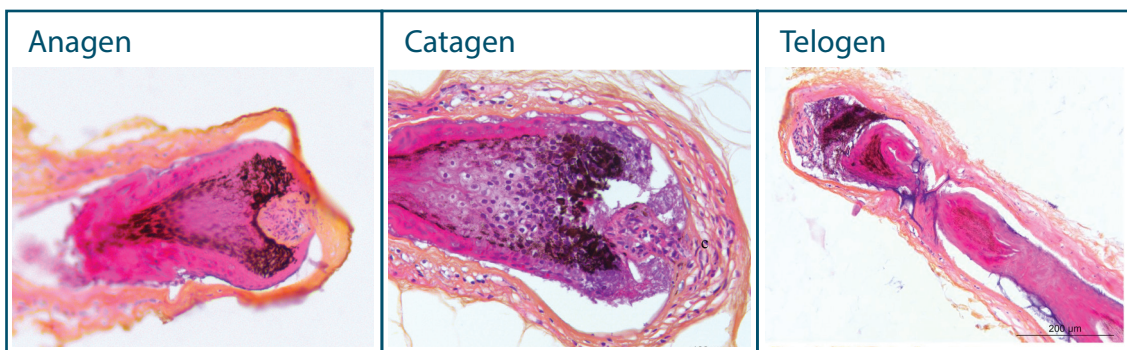
Chemical	In vivo score	UN GHS category	Test on BabySkin
Isopropanol	0,3	No Cat	No irritant
Heptyl Butyrate	1,7	No Cat (optionnal cat 3 = mild irritant)	mild irritant
Cyclamen aldehyde	2,3	Cat 2 (irritant)	Irritant

The Baby Skin model is a safe and ethical alternative to animal testing. The sensitivity of the model allows for thorough testing of ingredients and cosmetics for the specificities of the skin of infants. The dose dependant effect allows for optimal choice of target concentration.

# In vitro Hair Model

Test: itchiness, irritation, alopecia, hair growth and inhibition

Hair is an integral part of our personality and can be damaged by modern life, pollution, or rough treatments such as coloration and heat. The practical, realistic, model we developed allows the test of active ingredients and haircare products. It brings robust honest scientific data to demanding customers.

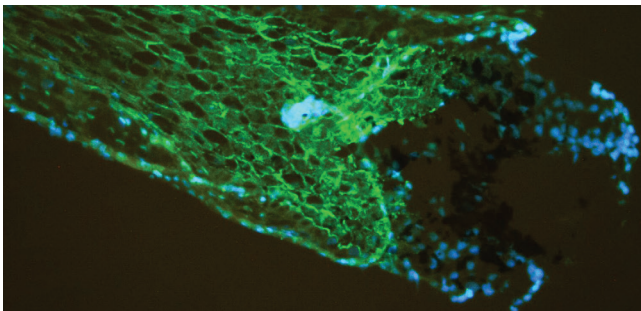


CTIBiotech's in vitro hair cycle through the 3 phases like in nature. HES staining.



## In vitro hair model

This innovative model was developed following clients demands and maintains hair natural cycle in culture. Analysis possibilities are manifold and can be carried out on each phase. Tests performed on this model validate the effectiveness of an active ingredient and add credibility to cosmetics. Tests can be performed by our team or by client's researchers in CTIBiotech's open laboratory.



## Applications

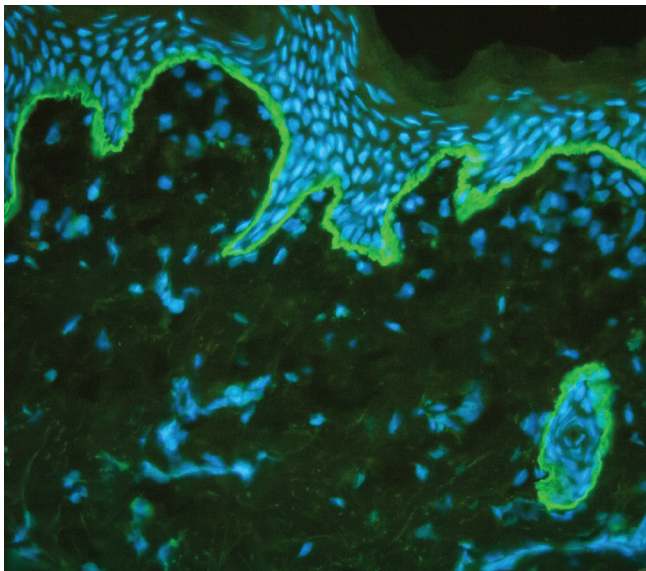
Itching: anti-itching components, test of irritation potential of a molecule  
Growth: hair loss, hair growth, alopecia  
Inflammation: folliculitis  
Treatment evolution: topical or systemic  
Pigmentation: hair colour, reaction to UV  
Research and development of new products, co-innovation

# Skin Biopsies

True to the skin of  
your target clients



With our wide network of health care partners we are able to propose a large range of human skin biopsies: by typology, skin colour, area of the body, age and gender. Our fresh samples, cultured up to 3 weeks in optimised medium, enable true cosmetics testing. We offer fresh, frozen or paraffin embedded samples of healthy skin and pathological samples.



Fluorescence microscopy of a skin biopsy highlighting dermal-epidermal junction integrity (Collagen 7 in green)

Easy testing on comprehensive system of  
biopsy model for realistic results  
Ingredient efficacy claims, attractive  
images and data for marketing, R&D

## Contract testing applications

- Topical treatment: cream or liquids are tested on the surface of the biopsy
- Actives systemic ingredients diluted in medium
- Irritation tests
- Cosmetics efficiency tests
- UV irradiation (solar lentigo)
- Skin ageing

## Tailored solutions for specific R&D targets

- Possibility to vary parameters on request
- R&D: understanding mechanism of action of your ingredients
- Open innovation: with our team of experts in modelisation and bioengineering, develop tomorrow's models

## Analysis

- Microscopy immuno-fluorescence
- Stratum corneum thickness
- Elastin
- Immunohistochemistry
- Histology
- Collagen analysis
- Determination of different cytokines by ELISA and/or CBA beads
- AFM to evaluate elasticity, tension, firmness, skin hydration
- 3D microscopic analyses of skin biopsies with advanced studies: of different components and the penetration of ingredients into the skin.



# Skin Biopsies

True to the skin of your target clients



## Pathologic skin

For specifics tests we provide pathological skin biopsies and cells:

- Atopic dermatitis
- Psoriasis
- Scar tissues
- Solar lentigo
- ... and other with our on-demand biosourcing



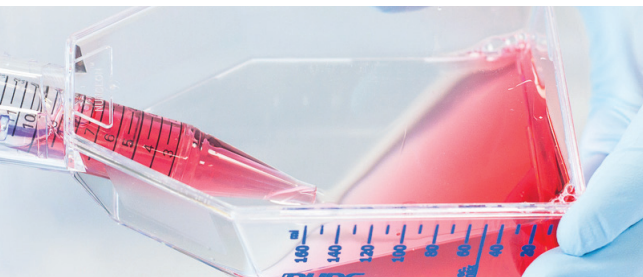
## UV irradiation

Sun radiation plays an important role in skin ageing. Using UV A or UV B irradiation, final product can be tested for UV protection or skin coloration. The influence of active ingredients on skin complexion can be measured at CTIBiotech. Several products from famous global or Asian brands are on the market using CTIBiotech's scientific data.



## Scalp models

Scalp and hair are a complex system. We use an ex vivo model to test active ingredients or products on the complete realistic hair environment for comprehensive results. We provide fresh, frozen and formalin fixed paraffin embedded scalp.



## Proprietary media

In order to complete our proposal we offer additional services :

- Special media for growth of specific cell types
- Formation and advice for tests
- OpenLab

# Ex vivo Scalp Model



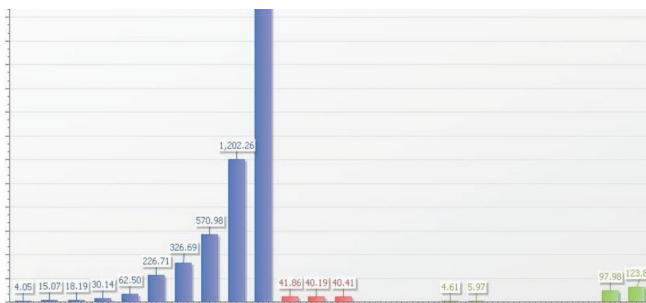
## Itchiness, irritation and dandruff tests on a comprehensive model

Scalp and hair form a complex system that must be carefully replicated when designing bioassays for haircare products. Our ex vivo scalp model delivers an efficient, realistic test for active ingredients for comprehensive scientific results. Your products can be tested in our laboratories, or the scalp model can be shipped to your facilities. We also offer open lab services for overseas customers, allowing them to perform their experiments in Lyon.



### Ex vivo Scalp model

Through the use of specific media developed at CTIBiotech and high working standards derived from clinical expertise, we are able to keep scalp biopsies in culture for 14 days. With our track record in innovation, we are able to help customers with protocols and project design through consulting and co-innovation services. We provide fresh, frozen and paraffined scalp.



TSLP dosage on ex vivo scalp model

### Analysis tools

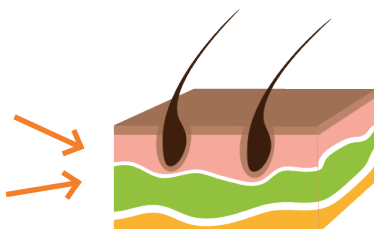
- Histology: Haematoxylin Eosin Safran (HES)
- Immuno-fluorescence: microscopy imagery for markers specific to customer needs.
- Cytokines: ELISA, cytometry (FACS), cytometric bead array.
- Thymic stromal lymphopoietin (TSLP)
- Hair growth measurement

### Applications

- Test of active ingredients
- Hair environment evolution
- Active ingredients' mechanism of action
- Hair psoriasis
- Irritation
- Dandruff
- Hair colour, pigmentation
- UV irradiation

Topical treatment

Dissolved actives



Scientific data  
Illustrations

Ingredient efficacy claims  
Images for marketing  
R&D



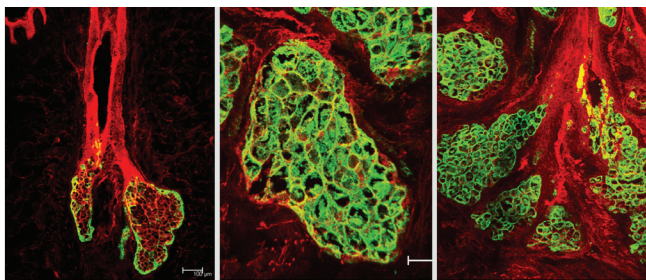
# Sebocytes & Sebaceous Glands



## Bioassays for drugs and cosmetics in acne, seborrhea, oily and dry skin

### Sebaceous gland: 3D ex vivo model

Sebaceous glands are essential in producing sebum and forming the lipid layer that protects our skin from harsh environmental conditions and pollution. Since existing models of sebaceous glands were lacking, CTIBiotech developed the world's first fully characterised 3D ex vivo human sebaceous gland model. We created proprietary media and culture conditions body adapted to sebaceous gland to insure an increased qualitative production of lipids similar to the human body. The model can produce specific sebaceous lipids, squalenes and wax esters.



Immunofluorescence, Muc-1 antibody (green)

©CTIBiotech, BASF

### Applications

These innovative models can be used to advance your research and development and develop efficient cosmetics, aimed at increasing or decreasing sebum production. As customers and regulators are increasingly demanding, the robust scientific data resulting from this model can be used for ingredient efficacy claims. The in-depth analysis of lipids quality can be of special interest for acne, pollution protection, seborrhoea, oily and dry skin or hair loss.

### Publications

de Bengy AF et al, 2018, Development of new 3D human ex vivo models to study sebaceous gland lipid metabolism and modulations, Cell Proliferation.

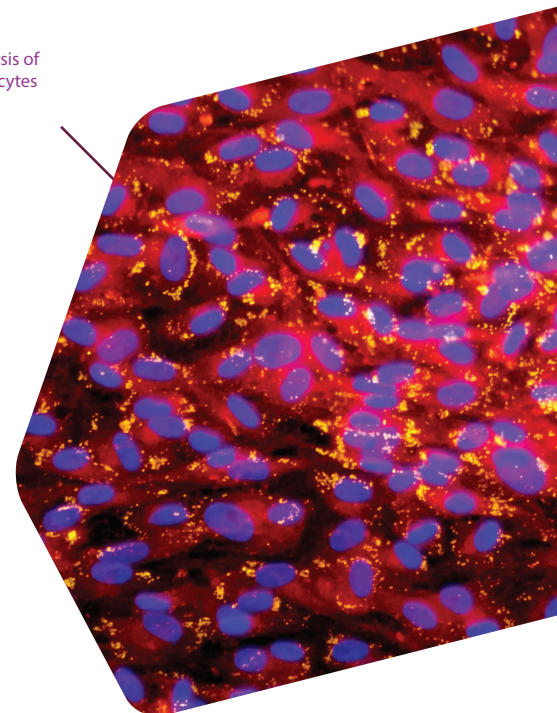
Pain S et al, 2017, Novel 3D human ex vivo sebaceous gland models to study skin lipid metabolism and modulation, IFSCC.

Pain S et al, 2018, Highly efficient plant extract against oily skin determined by 2D and 3D sebaceous models, IFSCC.

### Primary Sebocytes: in vitro testing

CTIBiotech also provide primary sebocytes that grow efficiently and produce natural skin lipids. They are suitable to test final products and cosmetics ingredients either at CTIBiotech or in your laboratory. We provide training on sebocytes growth, handling and staining and a range of sebocyte-specific culture plates and proprietary media to ensure customer satisfaction. Donors can be selected by gender, age, photo-type and body area. We can do 2D and 3D bio-imagery, histology, confocal microscopy and lipid quantification by fluorometry or flow cytometry and penetration scanning.

Nile red analysis of primary sebocytes showing lipid production

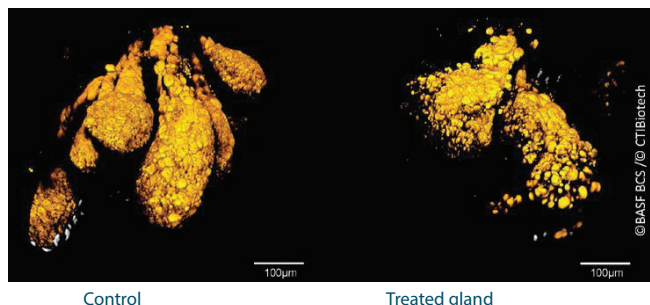


Test your cosmetics on advanced realistic models and add credibility to claim substantiation  
Donors can be selected with gender, age, phototype; body area can also be chosen

# Sebocytes & Sebaceous Glands

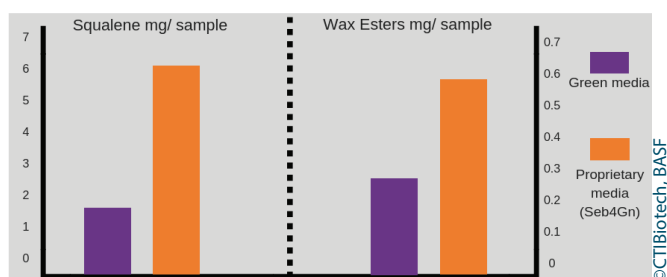


Bioassays for drugs and cosmetics in  
acne, seborrhea, oily and dry skin



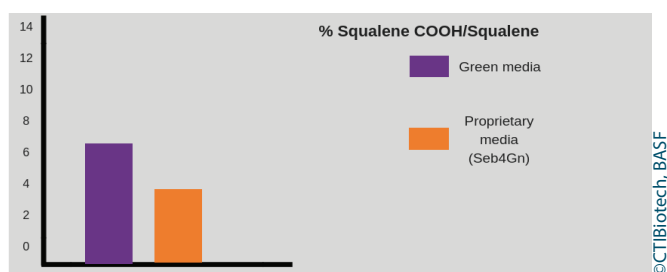
## Our 3D ex vivo sebaceous gland model

Confocal microscopy images show the model used to demonstrate the effects of an active ingredient (lipids in yellow). 3D models are more realistic; it allows the testing of drugs in a complete organotypic system. Actions on the gland and at cellular levels are taken into account. Results are therefore predictive of clinical studies on patients.



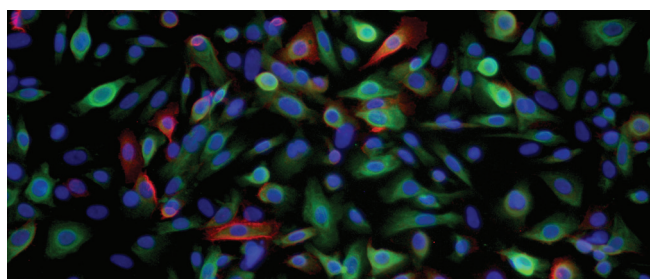
## True natural lipid production

Our proprietary media, simulates in vivo environment, in particular the production of specific sebaceous lipids, squalenes and wax esters. The figure shows the impact of the CTIBiotech proprietary media and culture conditions versus standard media on squalenes and lipid production.



## Quality of squalene

Our proprietary media allows good quality sebum production by decreasing peroxydized squalene level versus non peroxydized squalenes.



Primary sebocytes stained with cytokeratin 7 in green and Muc-1 in red

## Analysis

We can provide bio-imagery, histology, confocal microscopy, qualitative and quantitative lipid analysis by fluorometry or flow cytometry and by penetration scanning.