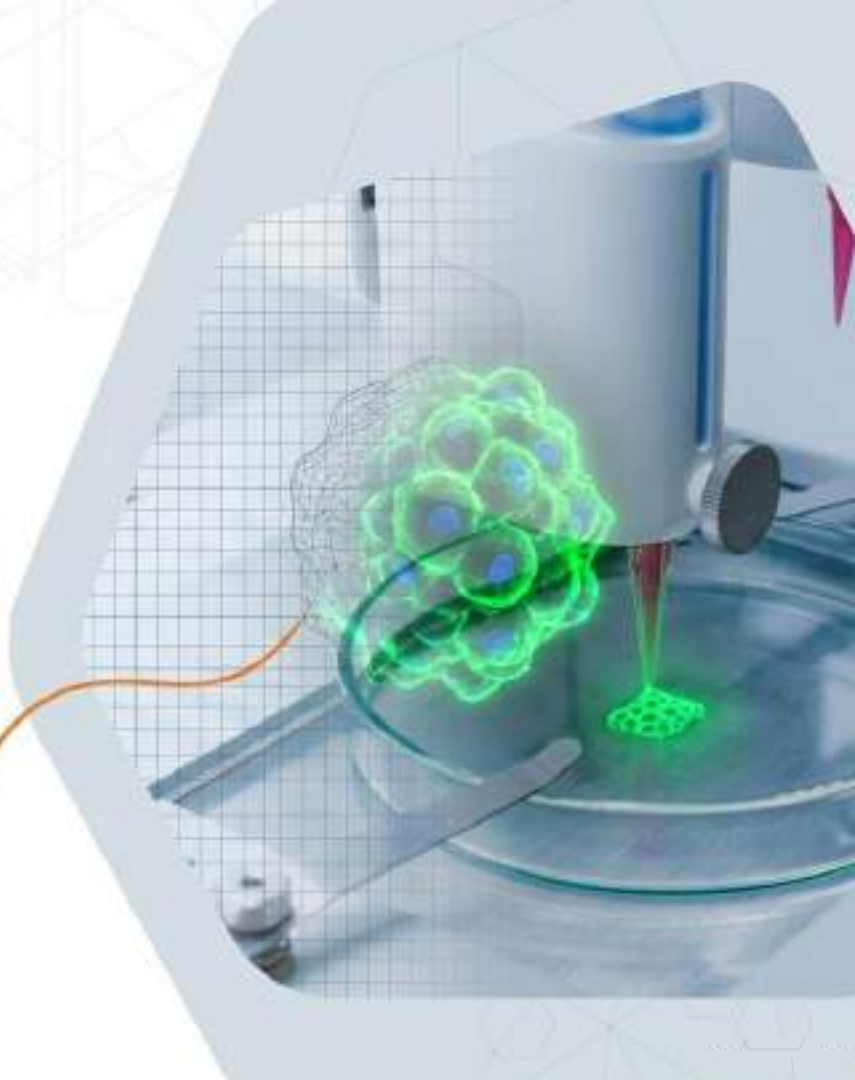
cti BIOTECH™
VISIONARY SCIENCE

3D Autologous Approaches in Immuno-Oncology

Bioprinting and Primary Spheroids for Long-Term Therapeutic Screening



Dr Nico Forraz – Chief Executive Officer

Nelly Dubrulle – Innovation Account Manager

Three Poles of Biological Excellence

cti BIOTECH™ VISIONARY SCIENCE

cti BIOSOURCING

Manufacturing of biological models, human tissues, and cells.

cti PHARMA

Development of bioassays to accelerate the development of drugs, medical devices, and cell therapies.

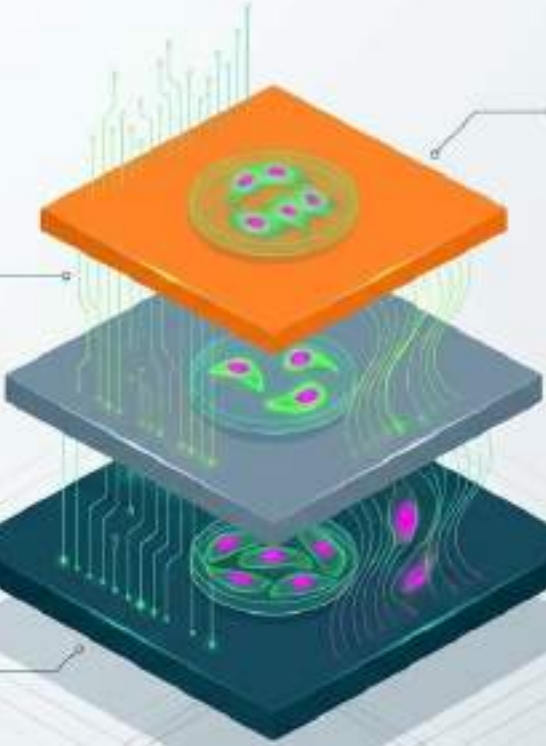
cti SKIN

Development of advanced human skin models to test new product ideas for dermatology and cosmetics.

3 Types of Models

- **Ex Vivo:** Skin biopsies, baby skin, sebaceous glands.
- **In Vitro:** Thousands of samples (Keratinocytes, Fibroblasts, Melanocytes, Cancer cells, CAFs, immune cells).
- **3D Bioprinted:** Full skin & microtumours derived from single human donors.

The Human Tissue Engineering Technology Stack



Pinnacle Layer (The Application)

3D Tissue Engineering & Bioprinting (Reconstructed tumors, proprietary bioinks, multi-layered models, mini-livers, artificial micro-organs).

Over 100 Publications

NASA Collaboration

Validation Layer (The Proof)

Analysis (Flow cytometry, immuno-fluorescence, ELISA, qPCR, tumor characterization).

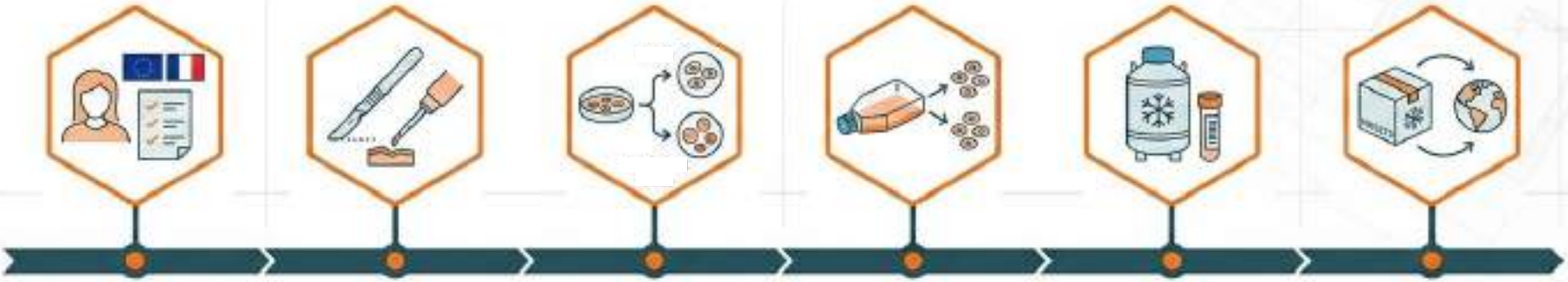
World's 1st mini-liver

950m² state-of-the-art laboratories

Foundation Layer (The Source)

Cell Culture (isolation, processing with enzymatic/mechanical dissociation), **Stem Cells** (cord blood, dental pulp MSCs, bone marrow), and **Biobanking** (clinical grade reagents, cell line production).

Biological supply chain:
From donor sample to ready-to-use model



Donor Management
Ethical Consent (EU/FR compliance)

Biopsy Collection
Clinical excision

Isolation & Differentiation
Isolation protocols for cancer, immune and NAT cells

Cell Amplification
Cell expansion with proprietary media

Cryopreservation
Cryopreservation to ensure high thawing yield

Worldwide Shipping
Dry ice / Dryshipper to UN3373 standard

Accredited by France Ministry of Research & national IRB

Capacity for **50,000** samples

Network of over **200** healthcare professionals

A Comprehensive Atlas of Human Tissues and Cells

Pathological Models

- Breast cancer
- Ovary cancer
- Pancreas cancer
- Lung cancer
- Liver cancer
- Prostate cancer
- Lymphoma
- Atopic dermatitis
- Solar lentigo
- Cancer associated

Healthy Baselines

- Skin (full thickness, cells)
- Dermal papilla
- Subcutaneous adipose tissues
- Neonatal tissues
- Peripheral blood (and cells)
- Bone marrow (and cells)
- Cornea

cti BIOTECH™
VISIONARY SCIENCE

Visionary Science for Healthcare Innovation

Why Choose Us ?

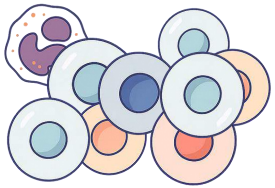
Published Research

40 years experience in medical research & cosmetic research

ISO certified

A commitment to ethics and traceability

Wide choice of cells & donors



Donor consent form

Reproducibility and reliability

Contact us for any questions

cti BIOSOURCING™ by cti BIOTECH VISIONARY SCIENCE

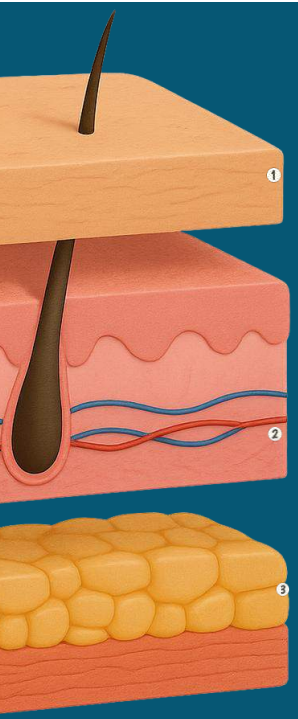
Manufacturing of biological models, human tissues and cells

- Accredited by France Ministry of Research and national IRB.
- Capacity for 50,000 samples.
- CTIBIOTECH™ has a network of 200 healthcare professionals
- Healthy and Diseased donors
- Extensive know-how in human tissue cryopreservation for pre-clinical and regenerative medicine

Samples for research use only

Understanding Human Skin A Complex and Vital Organ

The skin is the largest organ of the human body and serves as a protective barrier against the external environment. It plays crucial roles in immunity, thermoregulation, sensation, hydration, and synthesis of vitamin D.



A Layered Structure

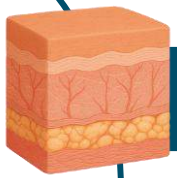
1. **Epidermis** : The outermost layer, mainly composed of keratinocytes. It acts as a waterproof shield and contains melanocytes, responsible for skin pigmentation.
2. **Dermis** : The middle layer, rich in collagen and elastin fibers mainly composed of fibroblasts. It supports the skin's strength and elasticity and contains blood vessels, nerve endings, sebaceous glands (sebocytes), and hair follicles.
3. **Hypodermis** (Subcutaneous tissue) : The deepest layer, composed primarily of adipocytes. It provides insulation and energy storage

Key Cellular Players

- **Keratinocytes** : Form the bulk of the epidermis and ensure its protective function.
- **Fibroblasts** : Produce and maintain the extracellular matrix and collagen, essential for skin strength, elasticity, and wound healing.
- **Melanocytes** : Produce melanin, the pigment that gives skin its color and protects against UV damage.
- **Sebocytes** : Produce sebum, an oily substance that lubricates and waterproofs the skin.
- **Adipocytes** : Store energy in the form of fat and provide insulation and cushioning for the skin and underlying tissues.

Human Skin Tissues for Research

- Adult human Skin, Full Thickness and defatted
- Aged human Skin, Full Thickness
- Juvenile human Skin, Full Thickness
- Dermatomed Skin



Adult & Aged :
- Skin Disc 2mm to 40 mm
- Skin square 1cm² / 200cm²

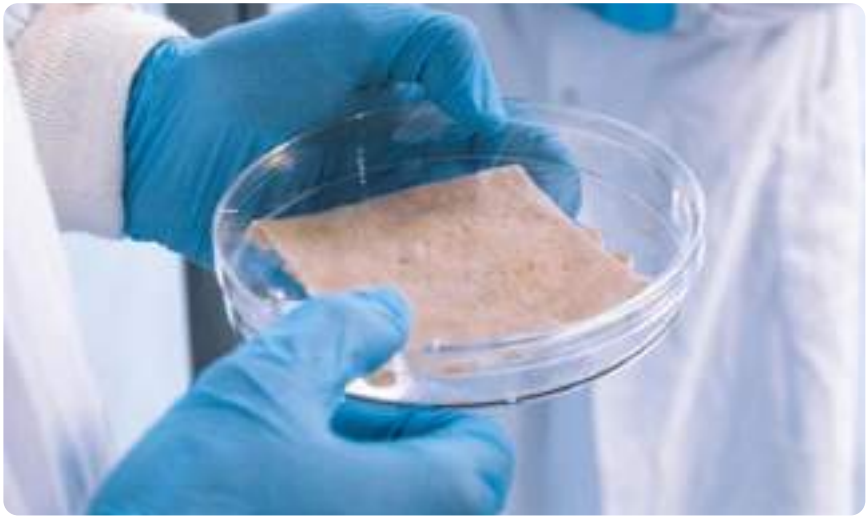
Juvenile :
- Skin Disc 2mm to 8mm
- Whole foreskin

Fresh or Flash frozen

FFPE & OCT

Access a complete range of skin phototypes from the lightest to the darkest

- Human skin samples from male ♂ and female ♀ donors
- Body zones : abdominal, arms, thighs, face, eyelids, adipose tissues



CTIBIOTECH™ provides human tissues for research, in full compliance with EU and French regulations.

We ensure fresh skin supply from various body areas, with carefully selected male and female donors.

Worldwide delivery available to support global research needs.

Skin Cells

Biosourcing

independentbiobank.com

Primary Human Skin Cells

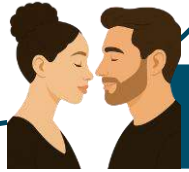
- Adult human Skin
- Aged human Skin
- Juvenile human Skin

Adult , Aged & Juvenile

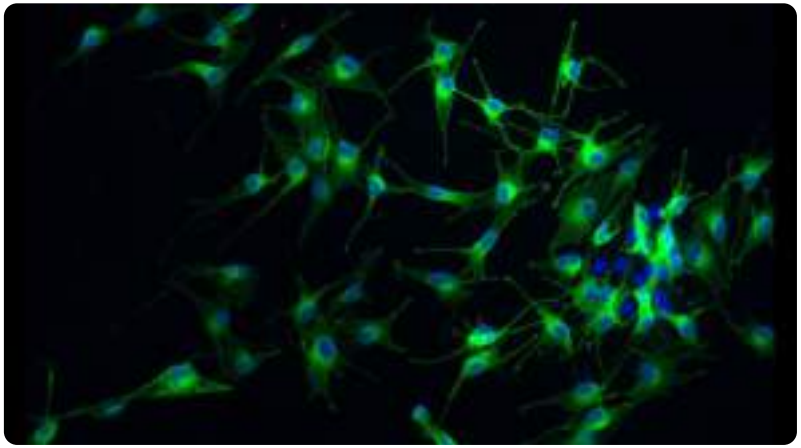
- 1.106 cells
- Fibroblasts, Keratinocytes, Melanocytes, Sebocytes, Adipocytes

Cryopreserved

Access a complete range of skin phototypes from the lightest to the darkest



Human skin samples from male ♂ and female ♀ donors



CTIBIOTECH™ Skin Cells are ethically sourced and prepared in our labs to offer a reliable, high-performance material.

They support the development of treatments, skincare, and in vitro studies, helping to understand skin mechanisms and test active ingredients.

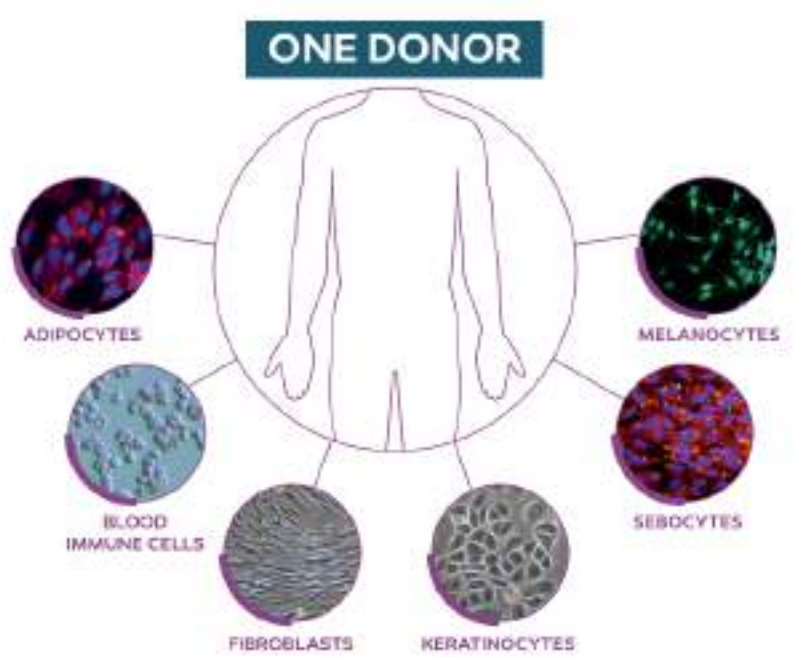
Available with expert support, they are a key tool for innovation in health and dermo-cosmetics.

Single Donor Kit

Biosourcing

independentbiobank.com

CTISkin® Single Donor Kit provides you with up to 6 different primary cell types from one single donor to reduce biological variations in your in vitro / tissue engineering assays. All kits are provided with defined cell culture media suitable for each specific cell type and recommended protocol as a turnkey solution for your safety or efficacy tests.



Single Donor Kit options:

Ex vivo

Biosourcing

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The Ex vivo kit from CTISkin® is a standardised and ready to use solution for your efficacy and safety tests. Collected just after the surgical intervention, we provide you with the freshest possible skin biopsies. According to the declaration of Helsinki, all skin samples are collected with donors informed consent and tested for HIV, HCV and HBC to ensure a negative serotyping. Provided with adapted culture medium, those biopsies can be used up to 11 days after the surgical resection. We can provide you regulary with fresh Ex Vivo skin.

Time to use

Babyskin

Biosourcing

independentbiobank.com

The product CTIBABYSKIN Kit ® from CTIBIOTECH™ contains an advanced solution to allow you to carry out your tests on fresh ex vivo Human biopsies. 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. Supplied fresh with culture media created by CTIBIOTECH™ , this product allows you to have access to a study model as close as possible to in vivo conditions. The original tissues have been obtained after informed consent of patients under the provisions required by French Law

Turnkey Solution For Preclinical Testing

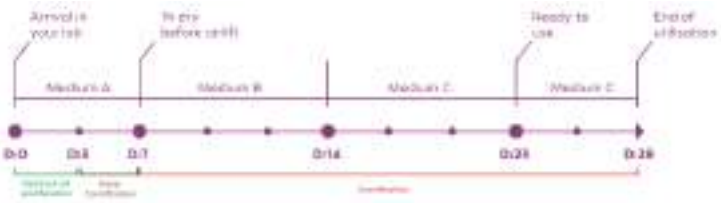
Including

Gel for transport

CTIBABYSKIN Reagent

250ml of Medium A
125 of Medium B
250 of Medium C

Time to use



Hair

Biosourcing

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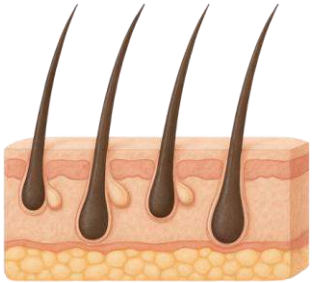
Human hair, for your in vitro tests

CTIBIOTECH™ offers human scalp models incorporating hair follicles, isolated sebaceous glands, and individual hairs, developed in our laboratories from bio-sourced human tissue.
These models are designed to meet the needs of the dermocosmetic, pharmaceutical, and academic sectors.
Our models offer a relevant alternative to traditional tests, with better biological representativeness and high adaptability to your research or development projects.

Human scalp with hairs follicles



Fresh or Flash frozen

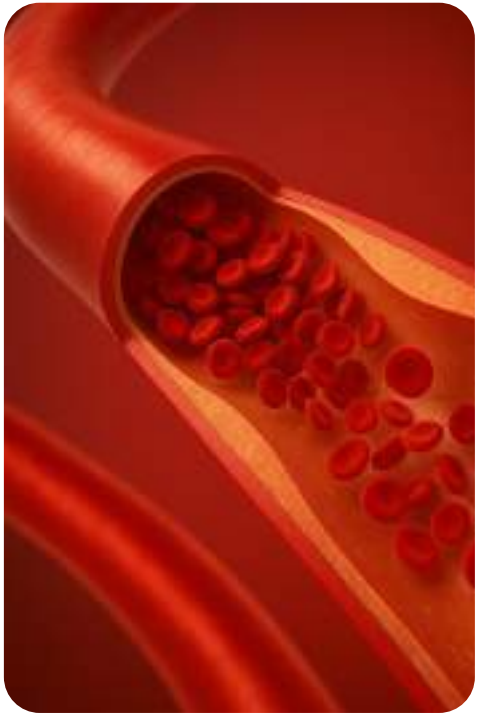
Human hair follicles (1 hair follicle)

Fresh or Flash frozen

Human Sebaceous gland

Fresh or Flash frozen

Human Blood: A Vital Resource for Innovative Research



Peripheral Blood

Origin: voluntary adult donors, in partnership with certified centers.

- **HIV, HCV, HBV testing**

Anticoagulant

- CPD
- K2EDTA
- K3EDTA
- ACD
- CITRATE
- NaHep

Blood derivatives

- Leuko-Platelets bag
- Whole peripheral blood Collect/Ship same day
- Peripheral blood serum / Pooled donors
- Peripheral blood plasma / Pooled donors
- Peripheral blood Buffy coat
- Peripheral blood Buffy coat on CPD

Cord Blood

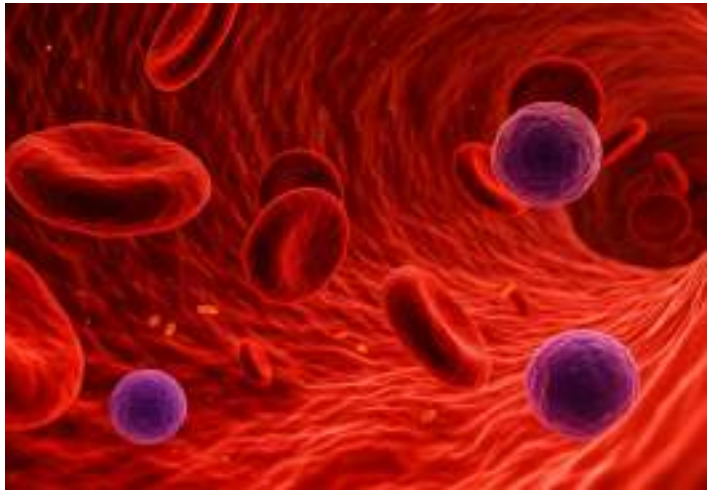
Origin: collected at birth (umbilical cord).

- **HIV, HCV, HBV testing**

- Whole cord blood on K2EDTA fresh or frozen : tube
- Whole cord blood Collect/Ship same day
- Cord blood serum / Pooled donors
- Cord blood serum plasma / Pooled donors

High-quality Immune Cells for your research

Thanks to our expertise, we provide high-quality cells to study immune responses in near-physiological conditions.
They offer reliable data to evaluate the immunological effects of your products.
CTIBIOTECH™ is a trusted partner for your scientific projects.



Our Immune cells

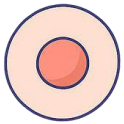
We offer fresh and cryopreserved immune cells from adult peripheral and cord blood, tailored to your preclinical research needs.
Each batch is quality-controlled to ensure high viability and functionality.

PBMC

T-Helper Cells
(CD4+)

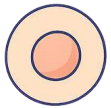
T-Killer Cells
(CD8+)

T-Regulatory Cells
(CD25+)



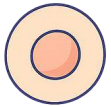
Monocytes
(CD14+)

NK Cells
(CD56+)



T-Cells
(CD3+)

B-Cells
(CD19+)



Hematopoietic stem cell
(CD34+)

Tumor cells

CTIBIOTECH™ provides cryopreserved human tumor cells for research, fully compliant with French and EU regulations.
We offer a wide diversity of tumor types (lung, ovary, pancreas, liver, prostate, lymphoma, etc.), stages, and grades from both male and female donors.
Available formats include primary tumors, dissociated tumor cells (DTCs), and PDX cells in defined quantities (0.5 or 1 million cells).
By covering detailed donor criteria, CTIBIOTECH™ enables personalized approaches in oncology research.

Available Conditions

By offering extensive donor criteria, including sex and medical history, CTIBIOTECH™ supports advanced, personalized approaches to oncology research. PDX cell lines are also available to help replicate the complexity of real tumors and provide more predictive preclinical models.

1. Cells type:

-Primary Tumor Ex-Vivo,
-Primary Dissociated Tumor Cells (DTCS),
-Primary Dissociated PDX Cells
-Cell models from PDX
-Cancer Associated Fibroblasts

2. Cancer Type (lung, ovary, pancreas, liver, prostate, lymphoma and more)

- **Sexe/Age/Medical history**

cti BIOSOURCING by cti BIOTECH

Microtumors
Biosourcing
independentbiobank.com

Replicating Microtumor Reality to Better Predict Tomorrow

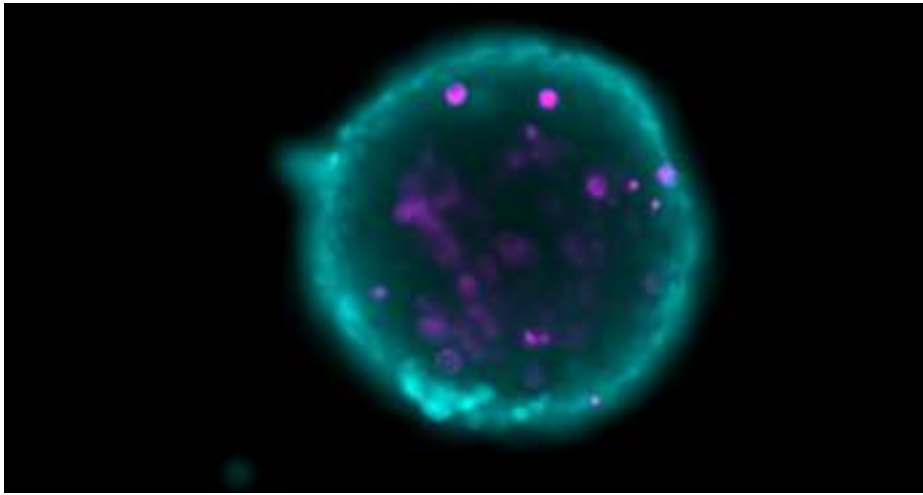
At CTIBIOTECH™ , we provide high-quality biosourcing solutions to support your preclinical testing with precision and relevance.
Our advanced 3D microtumor models, deliverable directly to your lab, replicate tumors in their natural environment.
These models improve the prediction of product responses, making CTIBIOTECH™ a reliable partner for your research projects.

Available Conditions

Our microtumors are selected based on specific criteria to best match your preclinical research needs:

- Cancer Type

- Sex
- Age
- Medical history



High-quality Stem Cells for your research

At CTIBIOTECH™, we focus on the powerful capabilities of human stem cells to design and produce complex, functional in vitro models that push the boundaries of biomedical research.

Whether pluripotent, mesenchymal, or adult stem cells, these unique biological sources provide unmatched versatility for recreating key human tissue functionalities under physiological and pathological conditions.

Our stem cells are carefully expanded under controlled conditions and cryopreserved at defined passages to ensure optimal viability, phenotypic stability, and batch-to-batch consistency.

Once thawed, they retain full capacity for proliferation and differentiation into relevant human cell types, including epithelial, hepatic, neural, or immune-related lineages.

Our Stem Cells

We source our adult stem cells from ethically obtained human tissues such as bone marrow, dental pulp, and adipose tissue. These origins offer distinct differentiation potentials and immunological profiles, allowing the creation of tailored models for applications in oncology, immunology, regenerative medicine, and metabolic disease.

Through our expertise in stem cell biology, controlled differentiation protocols, and advanced 3D structuring, we deliver biologically meaningful models that closely mimic native tissue organization and function. These models serve as high-value platforms for drug screening, toxicology testing, and disease modelling with enhanced predictability and translational relevance.

Bone Marrow Adipose Tissue Wharton Jelly

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Medium
Biosourcing
independentbiobank.com

Optimized Medium for Tumor and Skin Models

At CTIBIOTECH™, we deliver high-quality biosourcing and formulation solutions to support your preclinical research with precision and scientific relevance.
Thanks to our expertise and advanced technologies, we develop and supply specialized culture media tailored to the needs of tumor models and skin-derived cells. These optimized media enhance cell viability, functionality, and model accuracy by closely replicating physiological conditions. With a strong focus on innovation and reliability, CTIBIOTECH™ stands as a trusted partner in advancing your scientific projects.

Our Media*

*After opening, the culture media is usable for a period of two months

Our culture media are specifically developed to recreate a highly realistic human environment, supporting optimal growth of cell models, organoids, and complex tissues.
The Lipid Droplet Stimulator can also be added to modulate lipid accumulation in relevant models.

Medium for Sebocyte Growth and Differentation (500ml)

Medium for Fibroblasts (500ml)

Medium for Keratinocytes (500ml)

Medium for Melanocytes (500ml)

Medium for Cancer Cell N°1-11 (500ml)

see the details of the cancers supported by the medium on the catalogue

Medium for Adipose Tissue Derived Cells (500ml)

Lipid Droplet Stimulator (LDS) (500 µL)

Custom requests

Biosourcing

independentbiobank.com

Your project, Our expertise

The process :

- Custom request
- Feasibility by our team
- Quotation

CTIBIOTECH™ offers a fully tailored service, through three key steps a custom request to define your specific needs a feasibility assessment conducted by our team to evaluate your project then a quotation provided based on your criteria, we supply healthy or pathological tissues with various preservation options available FFPE, OCT, DTC, FRESH or FLASH FROZEN.

All types of matrix

- Plasma
- Tissue
- Serum
- Cells
- Urines
- Saliva
- Swab
- Other..

Why Choose us :

- informed consent
- Validation by the French ethics committee (IRB approved)
- > 200 healthcare partners & Biobanks

Contact us

ctiSKIN™ by ctiBIOTECH™ VISIONARY SCIENCE

Development of advanced human skin models to test new product ideas for dermatology and cosmetics

- Ex Vivo: skin biopsy, scalp biopsy, "baby skin" model, sebaceous gland model, etc...
- In Vitro: several thousands of cell samples from donors of different ages, genders, phototypes, Keratinocytes, Fibroblasts, Sebocytes, Melanocytes, Dermopapilla cells.
- 3D Bioprinted models: Full skin models. These models are derived from single human donors and can be designed according to the desired efficacy claim.

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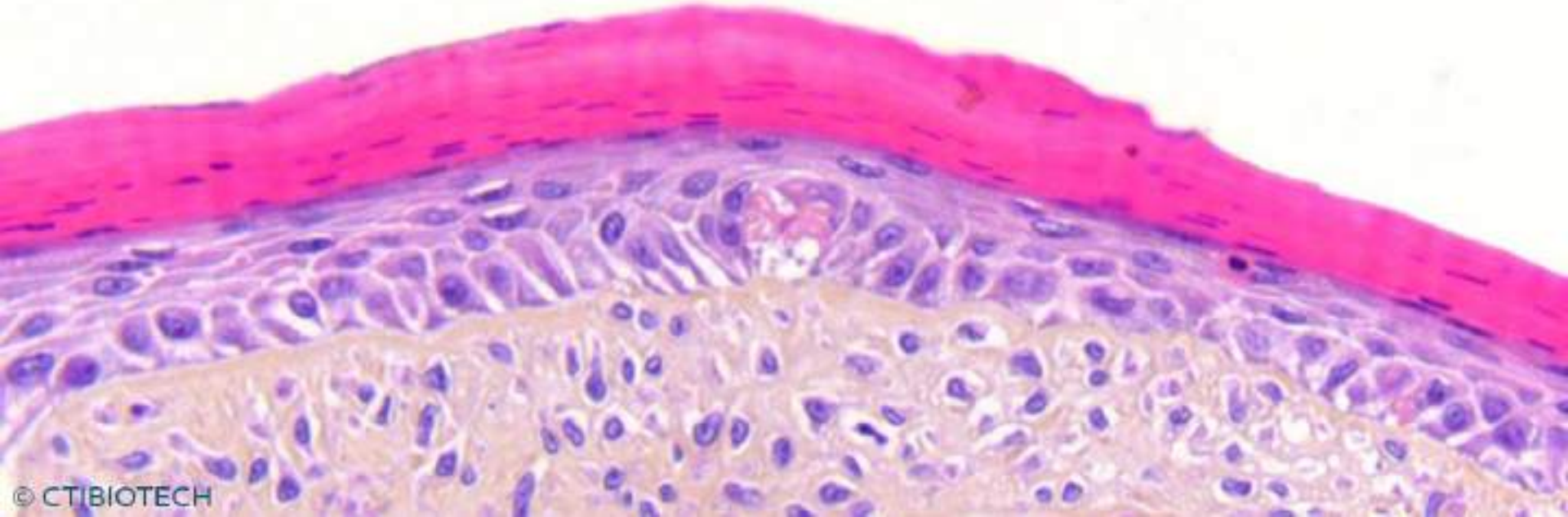
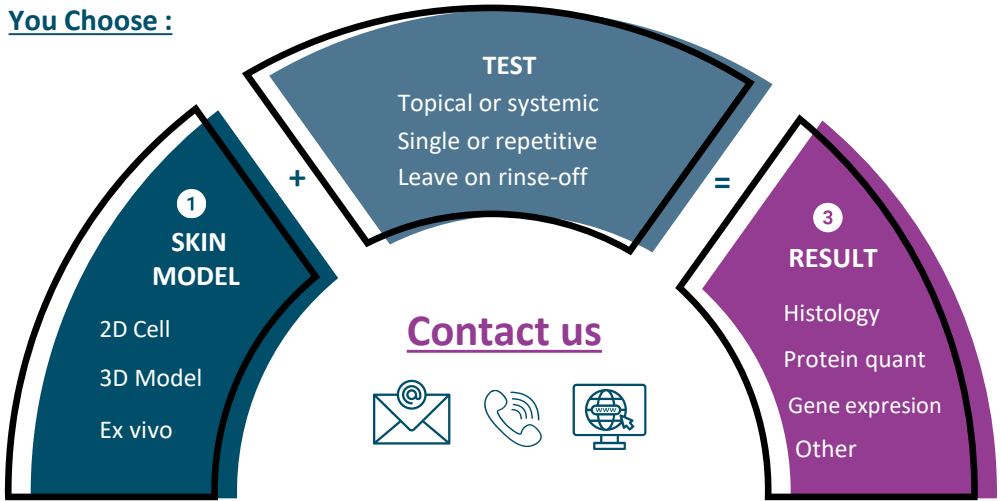


Your Project, Our Expertise

CTIBIOTECH™ supports you in the design and implementation of tailor-made projects, carried out directly in our laboratories.
Our team provides its scientific and technical expertise to develop innovative solutions adapted to your specific needs.
We also assist you in exploring approaches not yet defined by regulations, and in the formulation of your product claims based on solid scientific data.

You Choose :

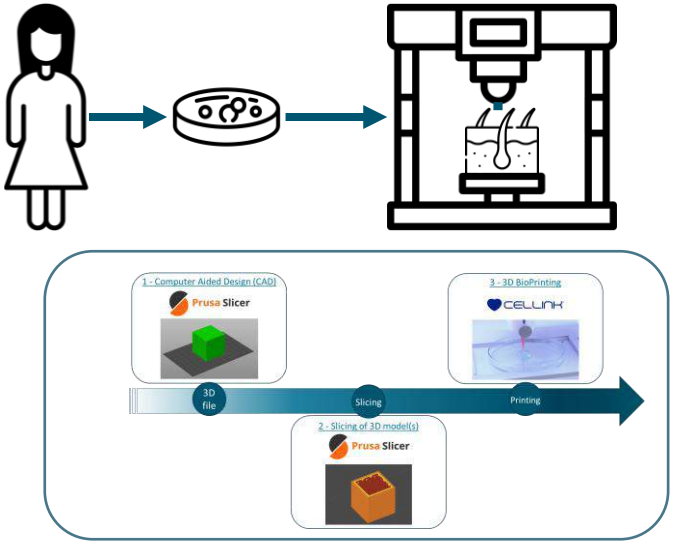


Why Choose us :

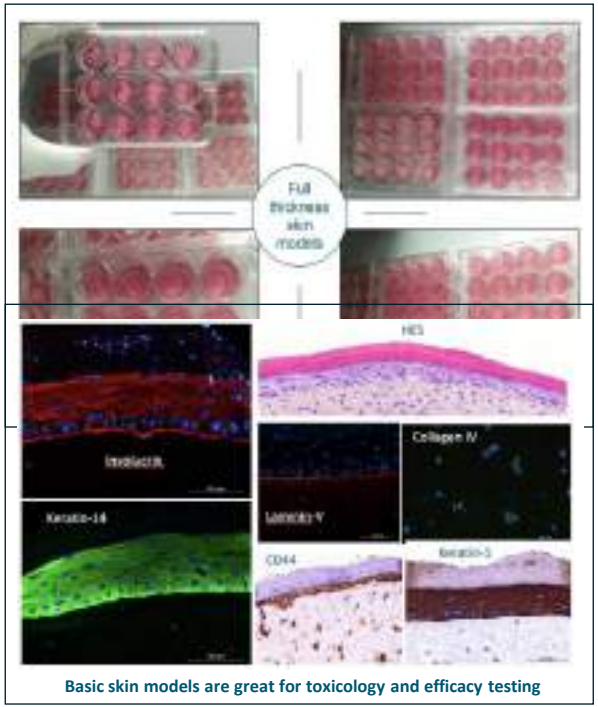

Recognized expertise

Innovative projects


A commitment to ethics and traceability

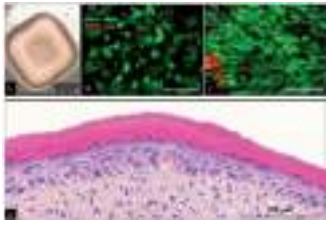


- Modularity: Customize the skin tissue to meet your specific needs
- Repeatability: Print the same model consistently
- Reliability: Ensure the accuracy of the printed model
- High-throughput: Efficiently produce hundreds of models in an hour.



Basic skin models are great for toxicology and efficacy testing

CTIMULTISKIN - **immune system induction and modulation of inflammation / irritation**



Structure and development of 3D bioprinted skin models

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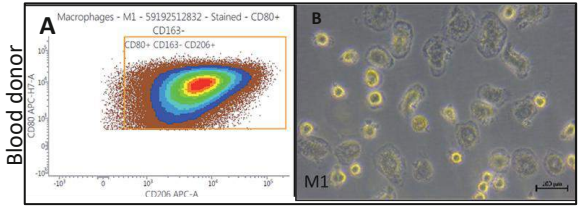
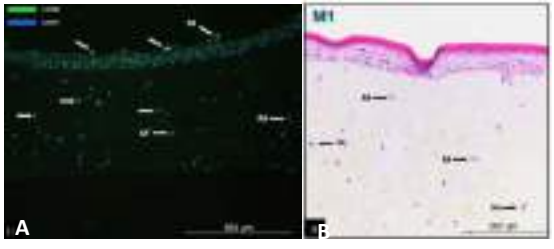
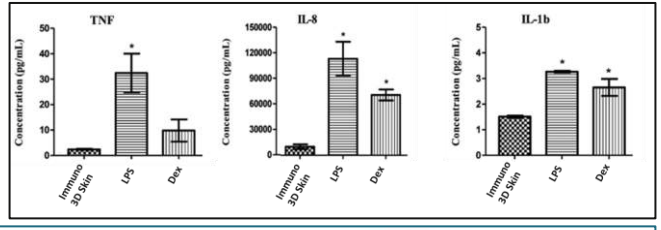


A) M1 FACS characterization; B) M1 2D culture



3D immunized skin models with M1 macrophages. A) Immunofluorescent staining (blue : dapi; green : CD68); B) HES staining (arrow : CD68)



The World's First 3D Bioprinted Immune Skin Model Suitable for Screening Drugs and Ingredients for Normal and Inflamed Skin

3D Immunised Skin models for clinical and medical device

Inserm

INSTITUT PASTEUR

Cold Plasma Medical Device

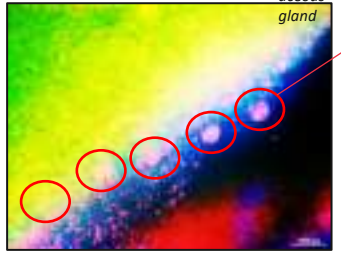
to support burn wound healing

CTIMULTISKIN - with Microsebaceous glands

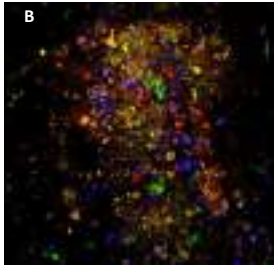
Beiersdorf

3D Bioprinted SeboSkin models

HES staining of 3D bioprinting skin including microsebaceous gland



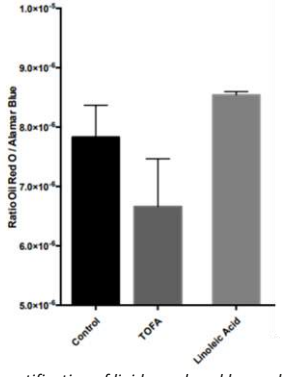
Nile Red staining of 3D skin modls with microsebaceous gland observed by confocal imaging (bleu : dapi, green : neutral lipid, red: total lipid, orange : both)



DAPI
NEUTRAL LIPID
TOTAL LIPID
BOTH

Nile Red staining observed by confocal imaging : A) Structure of 3D Bioprinted microsebaceous model; B) 3D Printed Oil Glands

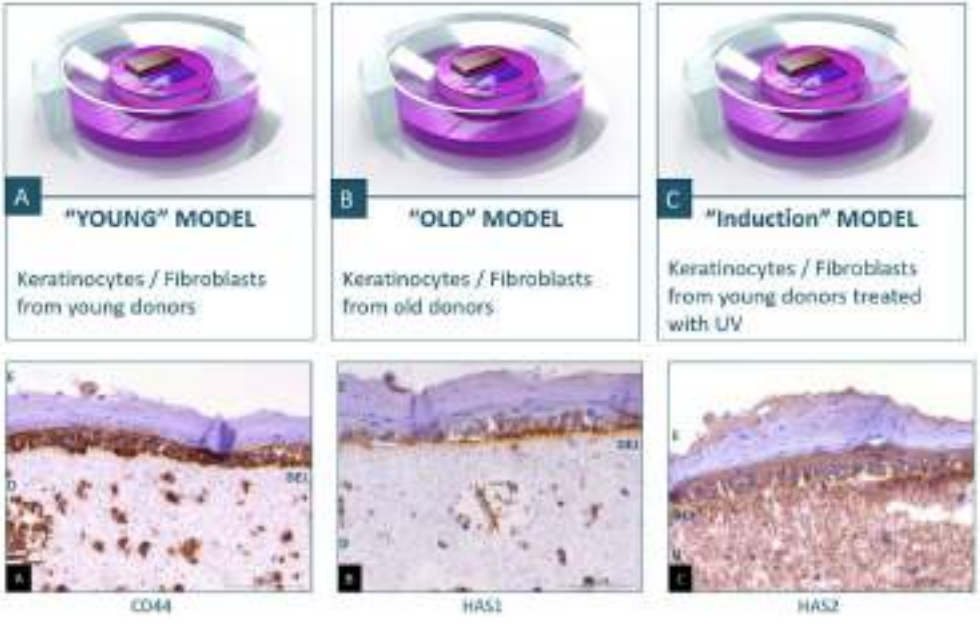
Dry and oily skin testing is now possible



Quantification of lipids produced by models in reponse to key molecules

→ model is functional and able to respond to the molecules tested by significantly modulating lipid production

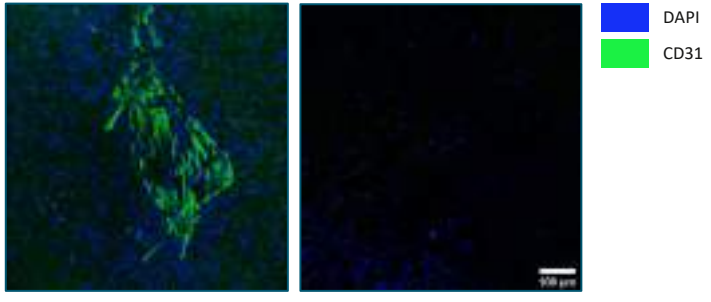
Cosmetics for everyone requires testing for all ages : creation of 3D Bioprinted old and young skin models for real efficacy testing



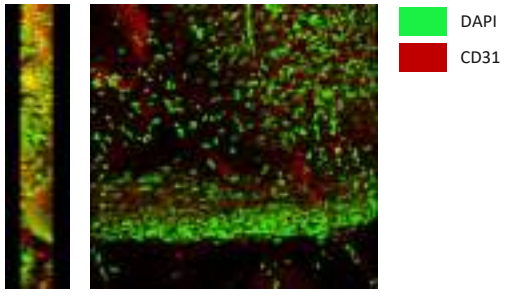
CTIMULTISKIN – **with Blood Vessels**

3D Bioprinted Vascularized skin models

3 cell types used : Keratinocytes / Fibroblasts / HDMECs



3D bio-printed vascularized dermis observed by confocal microscopy (blue : dapi; green CD31/HDMECs)

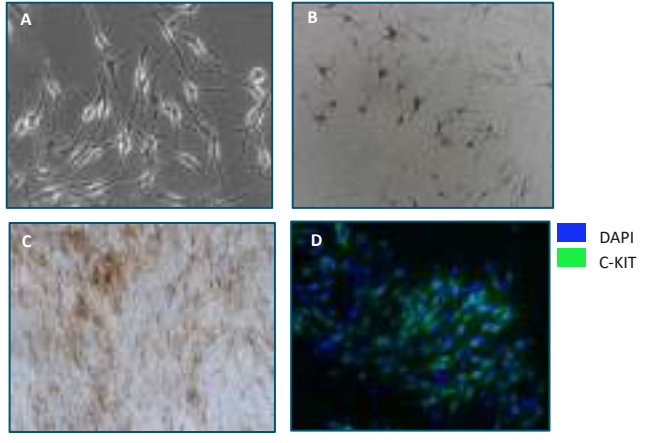


3D bio-printed vascularized dermis observed by confocal microscopy (green : dapi; red : CD31/HDMECs)

→ Vascular bed formation was seen upon stimulation with pro-angiogenic component (VEGF)

CTIMULTISKIN – **pigmented skin**

3D Bioprinted pigmented skin models



A) B) C) Pictures of functional 2D melanocytes culture; D) Immunofluorescent staining of functional melanocytes (blue : dapi, green : c-kit).

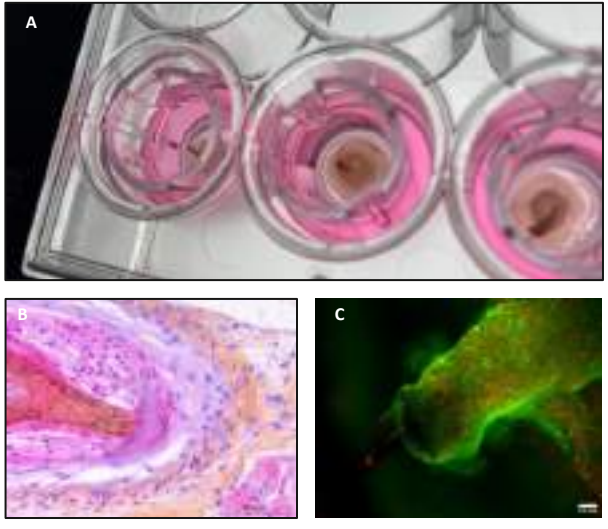
It's important to test EVERY color and type of skin

3D Bioprinted Pigmented skin models

→ Responses of pigmented 3D models to UV exposure

CTIMULTISKIN – **3D Bioprinted skin with growing hair**

CLARINS



A) 3D bioprinted skin models with Hair Follicle (HF). B) HES staining of the HF integrated in the model C) HF Live Dead staining (green : alive, red : dead).

→**Hair follicle integration in 3D skin model** significantly prolongs follicle viability.

→ The **3D microenvironment supports follicle function** through:

- **Cellular interactions** with surrounding skin cells.
- **Mechanical support**, mimicking physiological conditions.

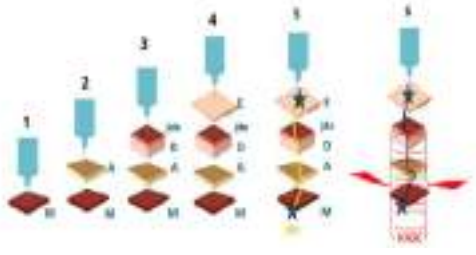
World's thickest 'close to real life' artificial human skin with muscle, hypodermis, dermis and epidermis for modelling of ageing skin, wrinkles and cosmetics development.

IFSCC2025-783

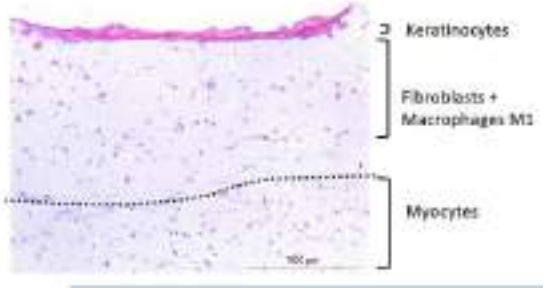
Clément Milet [1], Alizé Vialle [1], Anne-Laure Dearochies [1], Pauline Payen [1], Mathieu Laoroix [1], Tiffany Luangvanaasy [1], Niels Louiler [1], Nice Forraz [1], Colin McGuckin [1]*.

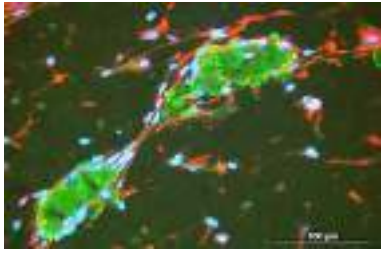
[1] CTISKIN, CTIBIOTECH, Mayalau, France; * Colin McGuckin, +33667107455, c.mcguckin@ctibiotech

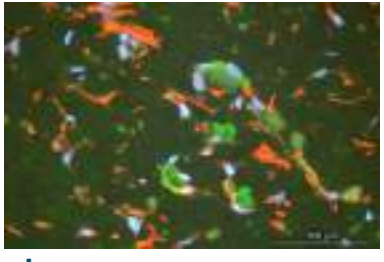
Making the world's most sophisticated lab-generated skin



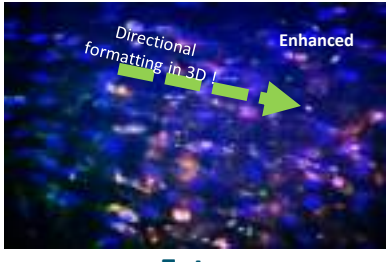
HES coloration







Muscle



Fat

IFSCC CONGRESS

THE FUTURE IS SCIENCE

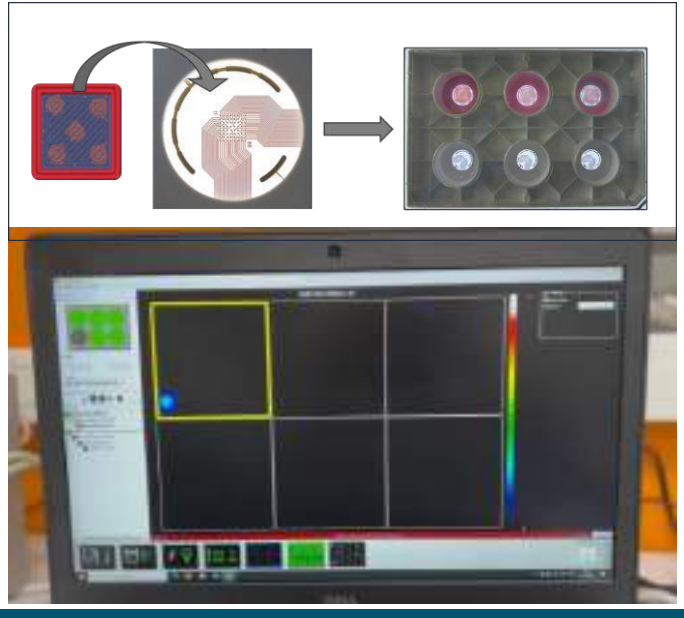
World's first computer-connected lab grown human bioprinted skin with a sensory nervous system for instantaneous cosmetics and fragrance testing.

Alizé Vialle [1], Anne-Laure Bearoches [1], Pauline Payen [1], Clément Milet [1], Stuart Prime [2], Nico Ferraz [1], Colin McGuckin [1].

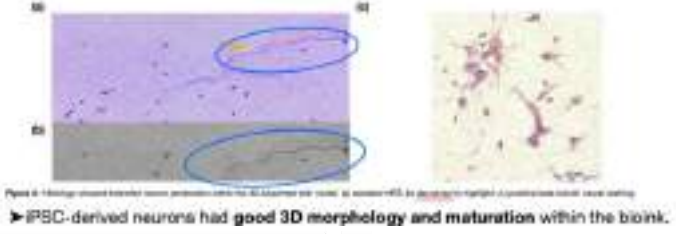
[1] CTISKIN, CTIBIOTECH, Meyzieu-LYON, France; [2] Axol Bioscience, Cambridge, United Kingdom

IFSSC 2025

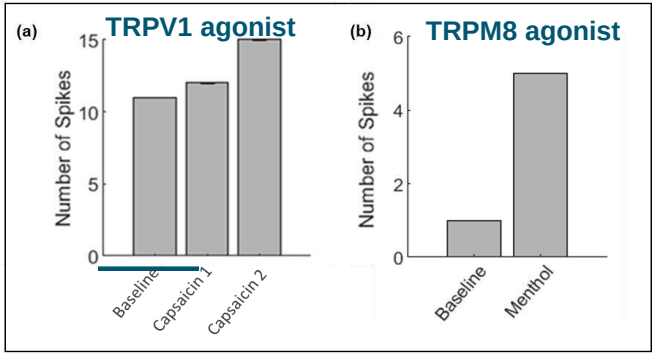
On-Chip Multi-Electrode Array (MEA) plate.



sensory neurons in the 3D skin model respond to thermosensory molecules



➤iPSC-derived neurons had **good 3D morphology and maturation** within the biolnk.



sanofi

iDEA-TECH Awards Europe

La Région Auvergne-Rhône-Alpes

FRANCE 2030

European Commission

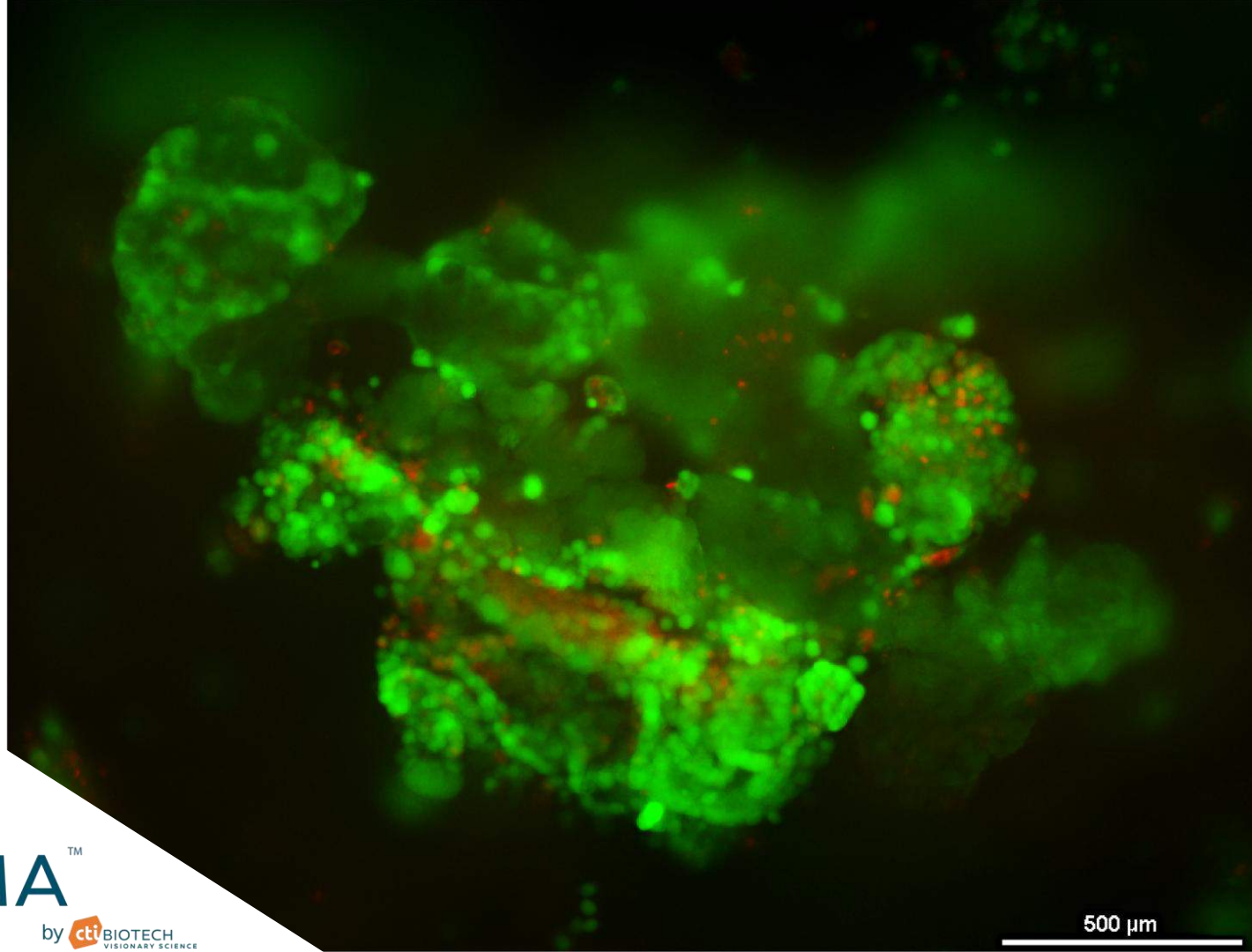
MÉTROPOLE GRAND LYON

ctiBIOTECH VISIONARY SCIENCE

- ***SAFESKIN3D: aims to make human skin injection sites with 3D bioprinting for better prediction of vaccine tolerance at early stages of development.***
- ***SAFESKIN3D: will make it possible to model injection sites to screen hundreds of vaccine formulations a day without animal testing.***

Development of bioassays to accelerate the development of drugs, medical devices and cell therapies

- Ex Vivo: tumor explant, organs biopsies
- In Vitro: Cancer cells, CAFs, immune cells, haematopoietic stem cells etc.
- 3D Bioprinted models: microtumour models. These models are derived from single human donors.



cti PHARMA™
by cti BIOTECH VISIONARY SCIENCE

3D Mictorumors

Pharma

ctipharma.fr

CTIMICROTUMORS for predictive and personalized medicine

By combining excellence in cancer research, tissue engineering and 3D bioprinting, CTIBIOTECH™ has developed the building blocks to produce large-scale, reliable, robust, reproducible, predictive, personalized 3D biological models of human tumors in sufficient quantity to accelerate the development of drug candidates for cancer chemotherapy and immunotherapy.

The Power of 3D to Drive Your Projects Forward

At CTIBIOTECH™, we offer a fully customized service: you choose the test you want to perform, and we carry it out in our own laboratories using our 3D models.
All the steps outlined above are handled by our expert team, according to your specific needs in oncology.
These innovative models, positioned between the limitations of 2D cell cultures and the ethical concerns of animal testing, provide a human-relevant, reliable, and predictive alternative for your R&D projects.

1. Model design

- Cancer type
- Cell types
- 3D design

2. Treatments

- Tumoral toxicity
- Tumor size reduction
- Comparison to known chemotherapy

3. Readouts

- Live dead
- Confocal imaging
- Caspase activity
- Other

CTIBIOTECH™ 3D MODELS

3D bioprinted

- Ethics ✓
- Close to human ✓
- Limited cost ✓
- Fast ✓
- Wide choice of pathological models ✓
- Reliable ✓

The Translational Gap in Pre-Clinical Oncology

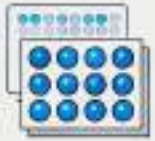
Patient-Derived 3D Systems

- Generating patient-specific models dramatically reduces reliance on animal-based preclinical testing.
- Evaluating ultra-low-attachment (ULA) culture and 3D bioprinting across primary ovarian, breast, and pancreatic cancers.

Next-Generation Oncology Platform: Complementary 3D Tumor Modeling

Platform utilizes patient-derived primary cells to create two complementary 3D systems—manual tumoroids and bioprinted microtumors—to provide more accurate, reproducible, and long-term drug response data for ovarian, breast, and pancreatic cancers.

MANUAL TUMOROID SPHEROIDS (ACUTE TESTING)



RAPID HIGH-THROUGHPUT SCREENING

Optimized cell seeding (2,000–15,000 cells/well) in ULA plates for fast drug-response profiling.

DOSE-DEPENDENT CYTOTOXICITY ANALYSIS

Reliable assessment of metabolic activity, apoptosis, and proliferation within 48 hours of treatment.

STRUCTURAL INTEGRITY

Models maintain cohesive 3D morphologies and hypoxic cores even under therapeutic stress.

ACUTE TESTING CAPABILITIES	
Typical Study Duration	48 – 72 Hours
Primary Focus	Acute Cytotoxicity
Cancer Types	BRE, PAN, OVA

3D BIOPRINTED MICROTUMORS (LONG-TERM MODELING)

EXTENDED CULTURE LONGEVITY

Maintains high cell viability for long-term studies, reaching up to 60 days post-print.

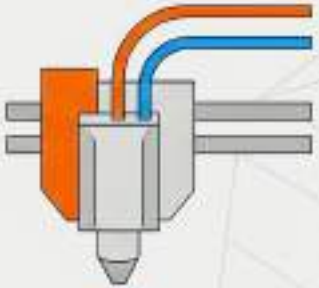
ADVANCED TISSUE RECAPITULATION

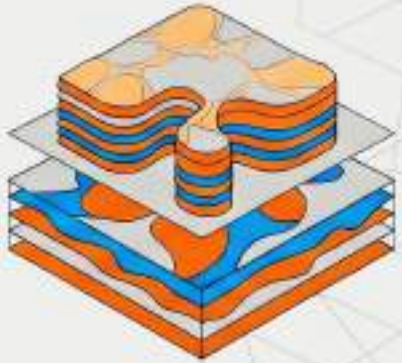
Enables the formation of differentiated mammary ductal carcinomas and pancreatic adenocarcinomas.

BIO-INK INTEGRATION

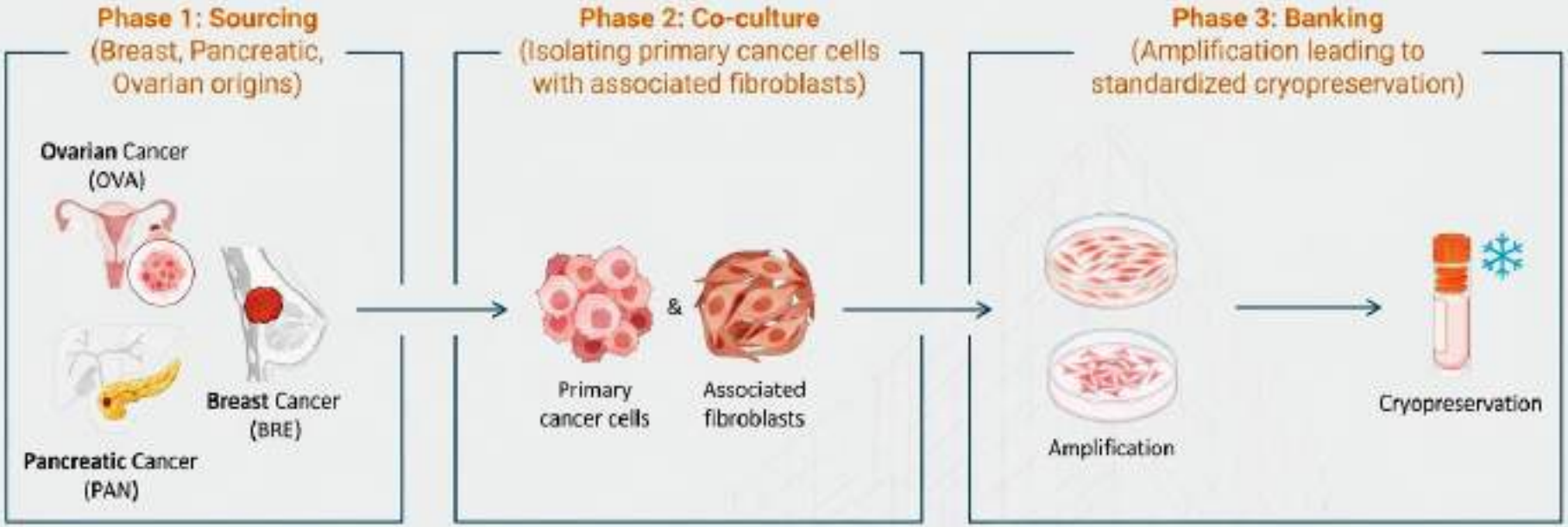
Combines patient-specific primary cells and associated fibroblasts with specialized bio-inks.

LONG-TERM MODELING CAPABILITIES	
Typical Study Duration	25 – 50+ Days
Primary Focus	Tissue Differentiation
Cancer Types	BRE, PAN



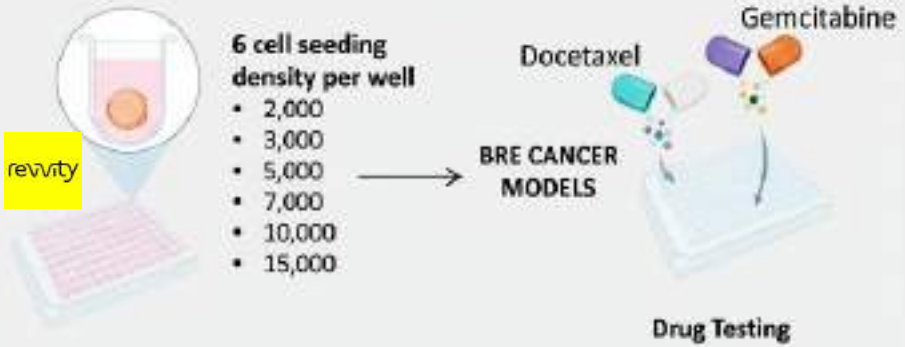


Standardizing Primary Cancer Cell Production



Two Advanced 3D Methods

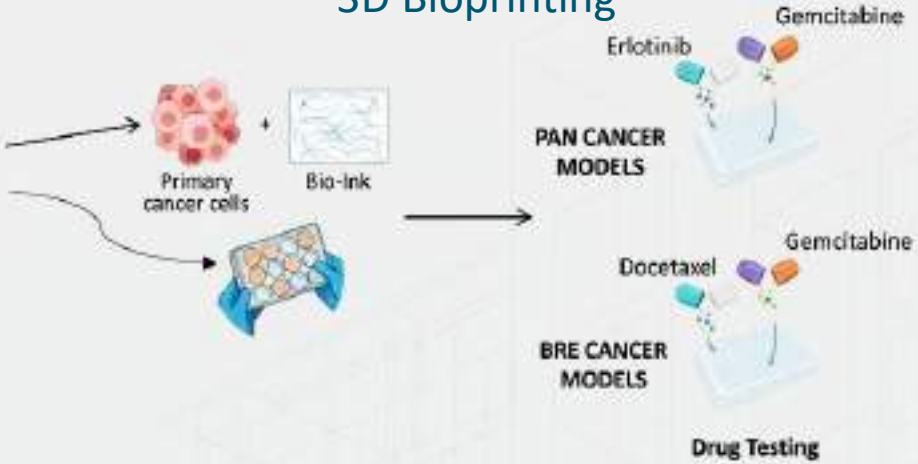
Manual spheroids



Key Parameters:

- **6 seeding densities** (2,000 to 15,000 cells/well)
- **Testing**: Breast cancer models treated with Docetaxel and Gemcitabine

3D Bioprinting



Key Parameters:

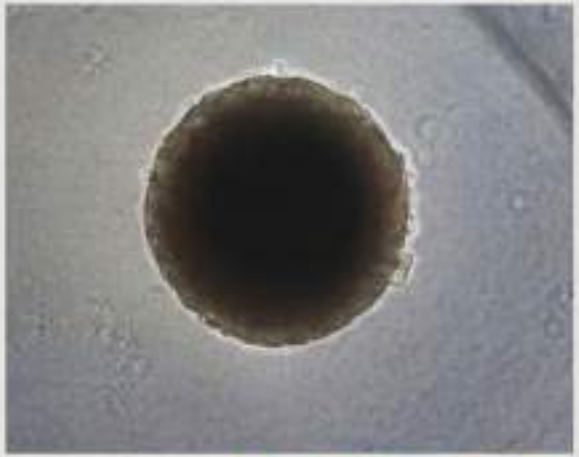
- **Primary cells** combined with specialized Bio-Ink
- **Testing**: Pancreatic models (Erlotinib/Gemcitabine) & Breast models (Docetaxel/Gemcitabine)

Shared Downstream Analytics:

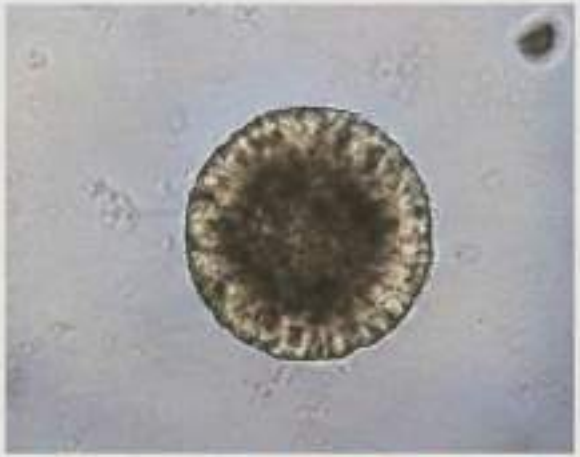
Metabolic Activity • Live/Dead Survival • Immunofluorescence (Proliferation, Apoptosis, Hypoxia)

Morphological Integrity Under Chemotherapy (48hrs)

Untreated Control



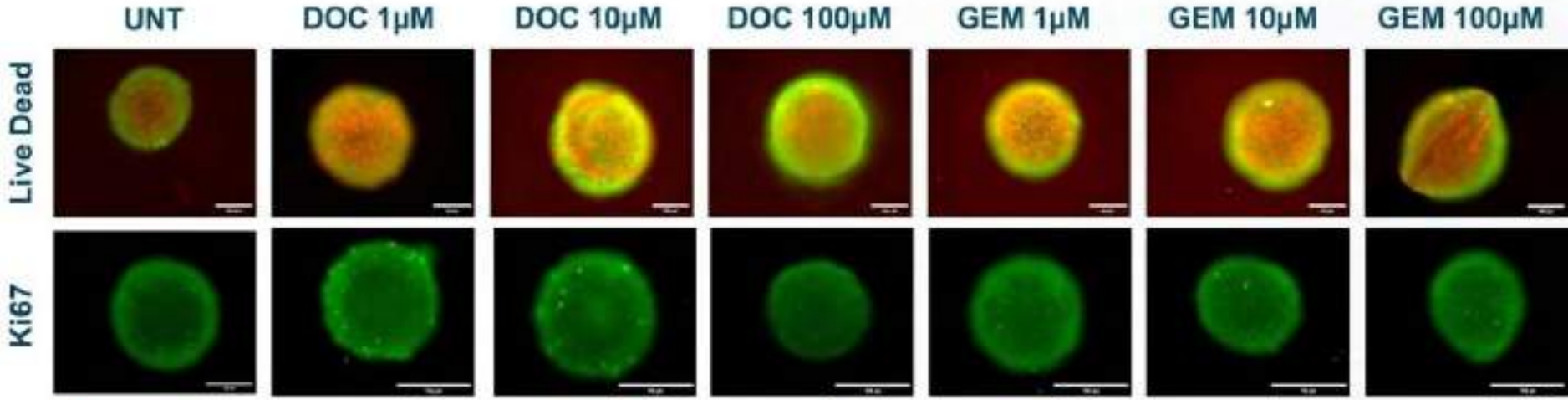
DOC 10µM **(Moderate Stress)**



DOC 100µM **(High Stress)**

- Breast cells form cohesive 3D organoids proportional to seeding density.
- After 48 hours of treatment, overall spheroid morphologies remain intact.
- High-dose Docetaxel visibly impacts internal structures while maintaining the outer boundary.

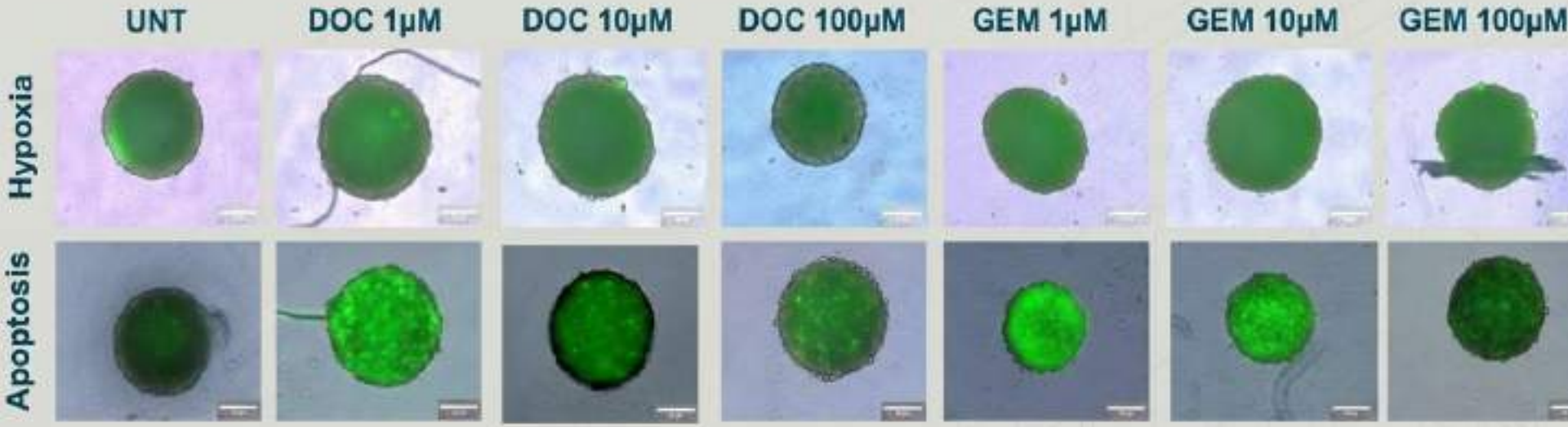
Cytotoxicity Profiling: Survival vs. Proliferation



Survival (Top Row): Concentration-dependent increase in cell death (Red) against viable cells (Green) under DOC and GEM exposure.

Proliferation (Bottom Row): Strong baseline proliferation shown by Ki67 (Green) in controls is progressively eradicated by treatment.

Cellular Stress: Hypoxic Cores and Apoptotic Spikes

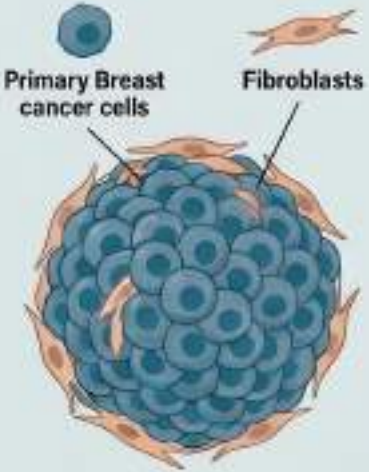


Baseline Feature: All models display a consistent hypoxic core (**Green**), comparable across all conditions. This establishes a normal 3D architectural baseline.

Drug-Driven Response: Caspase-3/7 staining reveals a massive concentration-dependent spike in apoptosis (**Green**) at 100μM for both DOC and GEM.

Manual Tumoroids: A Reliable First Approach for Immuno-Oncology Research

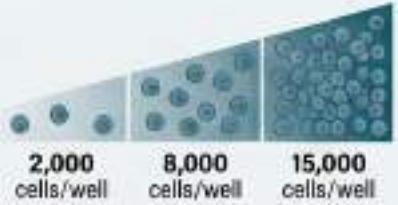
MODEL GENERATION & SETUP



Patient-Derived 3D Cohesion

Primary Breast (BRE) cancer cells and associated fibroblasts form cohesive 3D organoids.

Scalable Seeding Densities



Manual seeding remains reliable across densities ranging from 2,000 to 15,000 cells per well.

ULA Plate Methodology

Ultra-Low Attachment (ULA) Plate

ULA Plate Methodology

Utilizing Ultra-Low Attachment culture to ensure consistent, spherical 3D morphology for testing.

VALIDATION & THERAPEUTIC RESPONSE

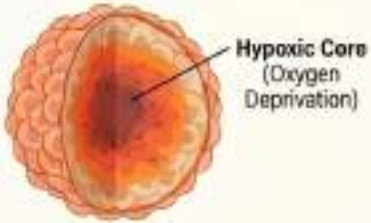
Dose-Dependent Cytotoxicity

Untreated (UNT)
Strong proliferation; mostly viable (green) cells.

1–10 µM (DOC/GEM)
Moderate but consistent decline in metabolic activity.

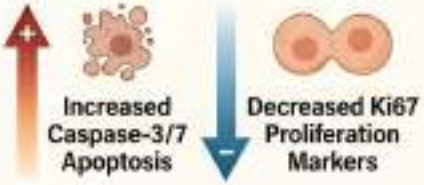
100 µM (DOC/GEM)
Strongest decrease in activity; high concentration of dead (red) cells.

Recapitulating Tumor Microenvironments



Models successfully displayed a hypoxic core, mimicking the internal conditions of solid tumors.

Proliferation & Apoptosis Tracking



Treatments showed a clear increase in Caspase-3/7 apoptosis while decreasing Ki67 proliferation markers.

Synthesis: Model Efficacy Matrix

Modality	Structural Integrity	Viability Window	Drug-Response Profiling
ULA Tumoroids	High (Cohesive 3D shapes, size proportional to seeding density)	Confirmed stable at 48hrs post-treatment	Excellent (Clear dose-dependency in Apoptosis, Ki67, and Metabolic activity)

➔ **3D Bioprinting: The next logical step beyond manual 3D culture limitations**

Synthesis: Model Efficacy Matrix

Modality	Structural Integrity	Viability Window	Drug-Response Profiling
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➔ **3D Bioprinting: The next logical step beyond manual 3D culture limitations**

Tissue Engineering using 3D Bioprinting technology

1. Computer Aided Design (CAD)

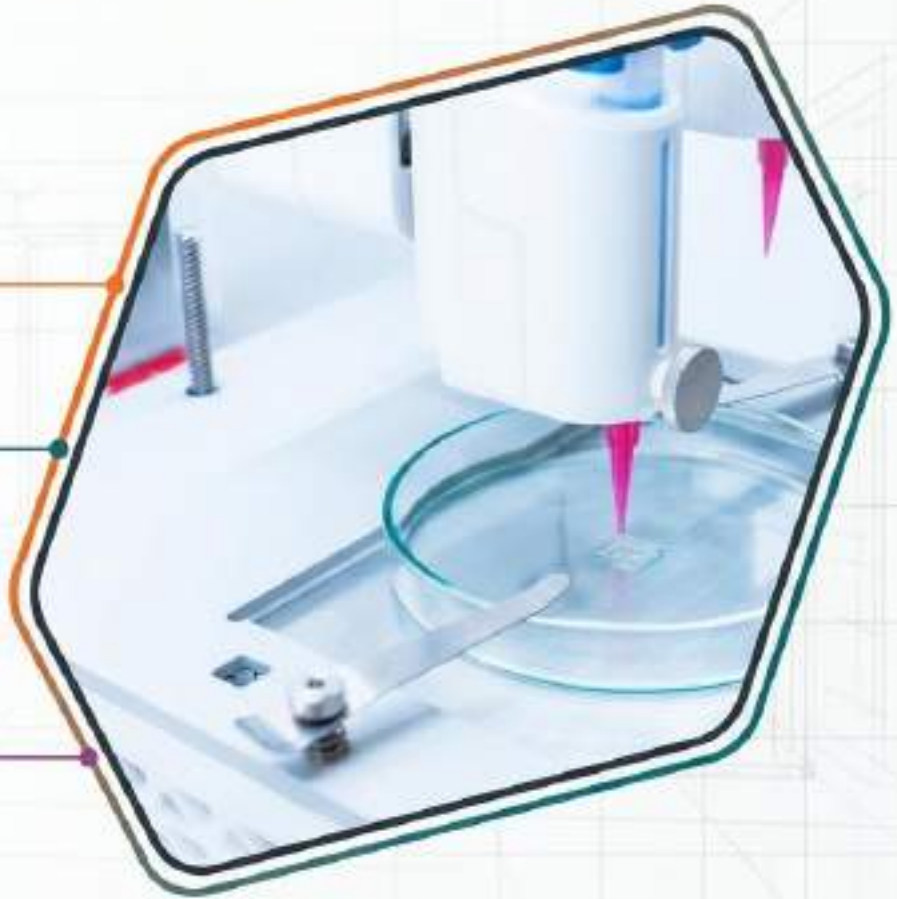
Generating the exact 3D file based on internal/external biopsy analysis.

2. Slicing

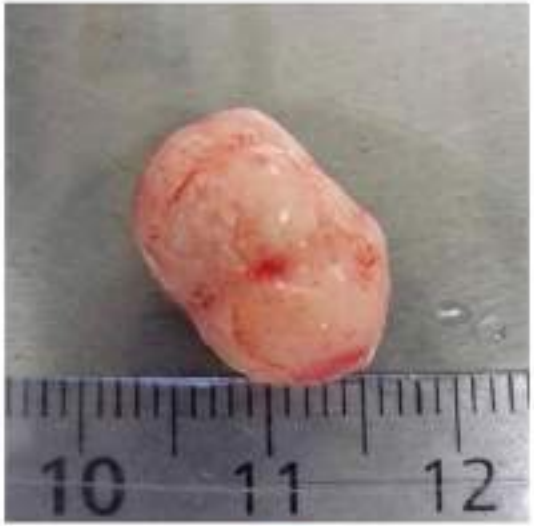
Converting the 3D computer model into highly precise printable biological layers.

3. 3D BioPrinting

The physical robotic reconstruction combining proprietary bioinks and isolated cells to form complex microtumours.

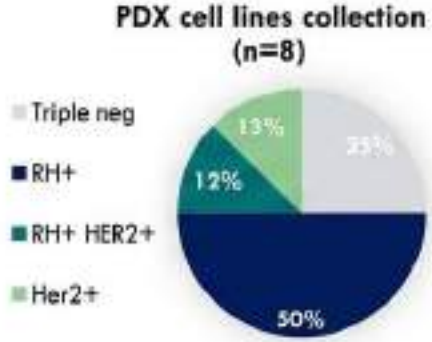


Clinical Foundation: Diverse, Patient-Derived Sourcing



IMODI

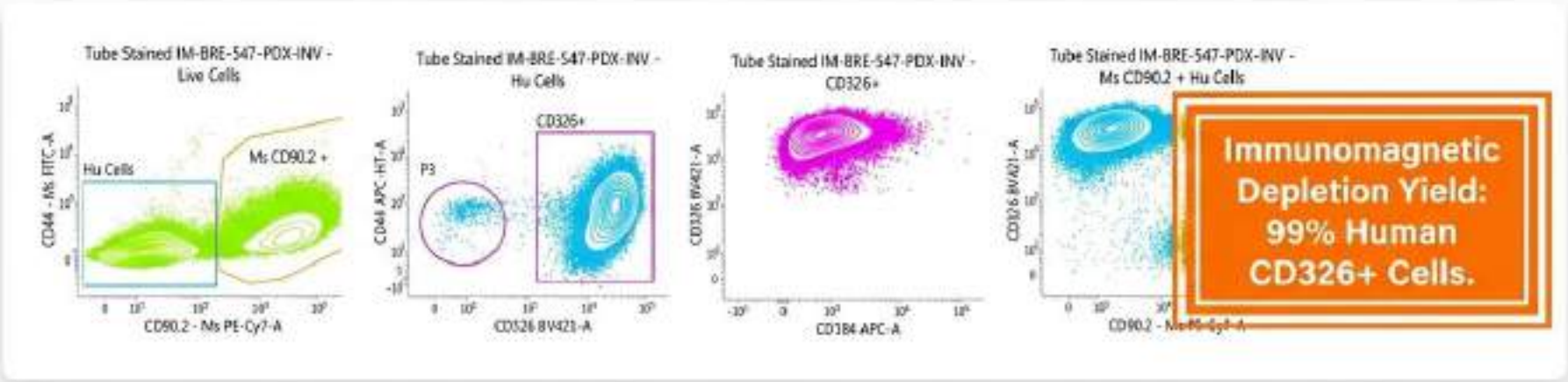
INNOVATIVE MODELS INITIATIVE AGAINST CANCER



Strategic collection across distinct breast cancer sub-types (Primary and PDX) ensures platform versatility and robist representation of complex microenvironments.

Precision Cellular Isolation & Depletion

Mechanical/Enzymatic Dissociation → Isolation → Expansion → Immunomagnetic Depletion → Banking



Complete removal of mouse fibroblasts ensures the isolated cells are Human, eliminating cross-species artifacts in pharmacological studies.

Standardizing the 3D Micro-Tumor Architecture

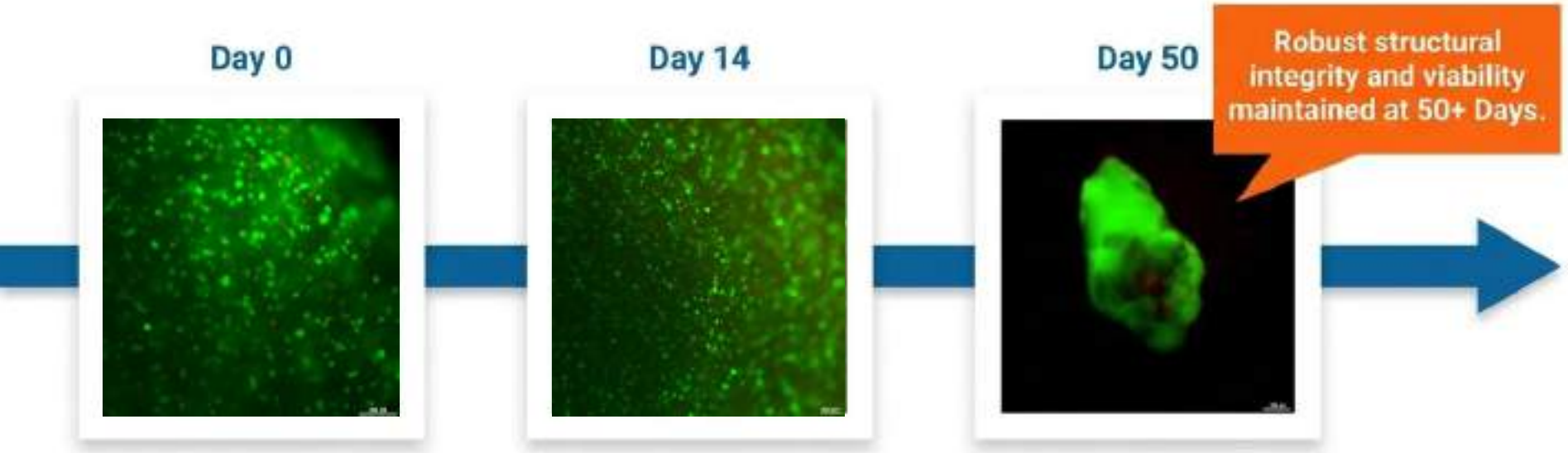
Blueprint

Cells

3D models

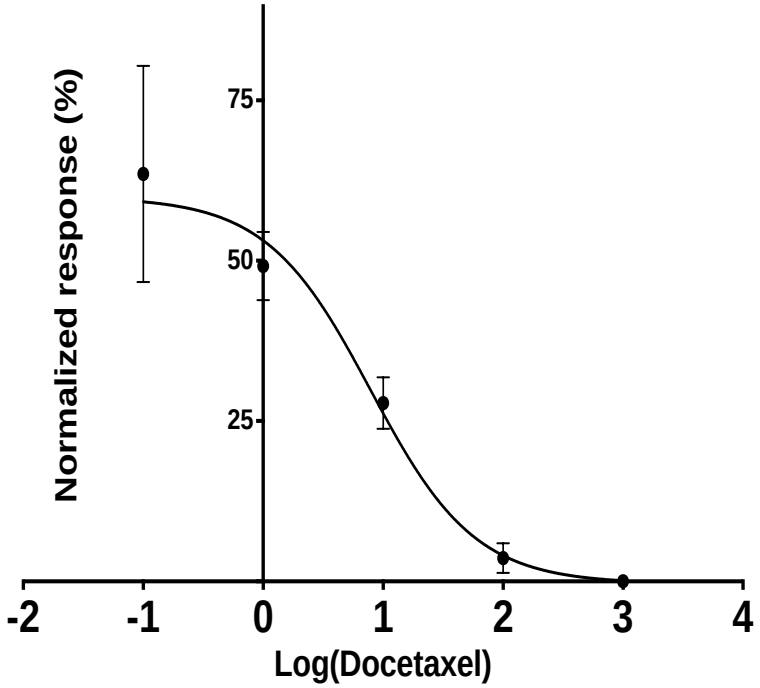
High-throughput 3D bioprinting translates cancer cells into standardized structures, enabling highly reproducible multri-well pharmacological screening.

Longitudinal Viability: Surpassing 2D Limitations



Unlike traditional 2D cultures, 3D MicroTumors sustain long-term cellular viability, uniquely enabling chronic and repeated-dose toxicity testing treatment.

Pharmacological Efficacy: Docetaxel Dose-Response



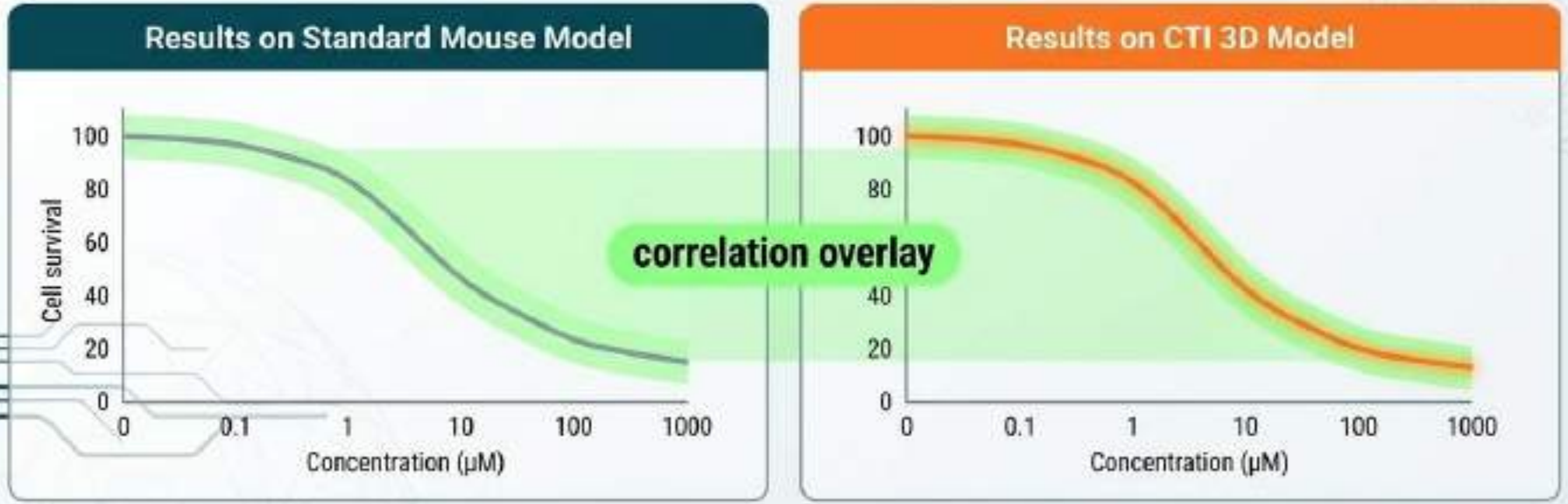
Calculated IC_{50} = 7.879 µM

R^2 = 0.9241

The BRE-547 3D model demonstrates a highly predictable, dose-dependent cytotoxic response to standard Docetaxel treatment, establishing a robust baseline for novel compound screening.

Clinical Correlation: Dose-Dependent Efficacy

Testing Agent: Docetaxel (Concentrations: 0, 0.1, 1, 10, 100, 1000 µM) applied to BRE-547 breast cancer models.



1. Clear **dose-dependent effect** observed in the autologous 3D model.
2. **High correlation** with the standard in vivo baseline, validating the 3D model's predictive accuracy without requiring animal subjects.

cti PHARMA

+

transgene

Strategic Application Case Study

Metastatic CRC (Colorectal Cancer) donor recruitment and model generation.

Utilizing the CTI BioTumor platform to engineer patient-specific advanced models, accelerating the validation of targeted therapies in highly complex, immune-competent microenvironments.

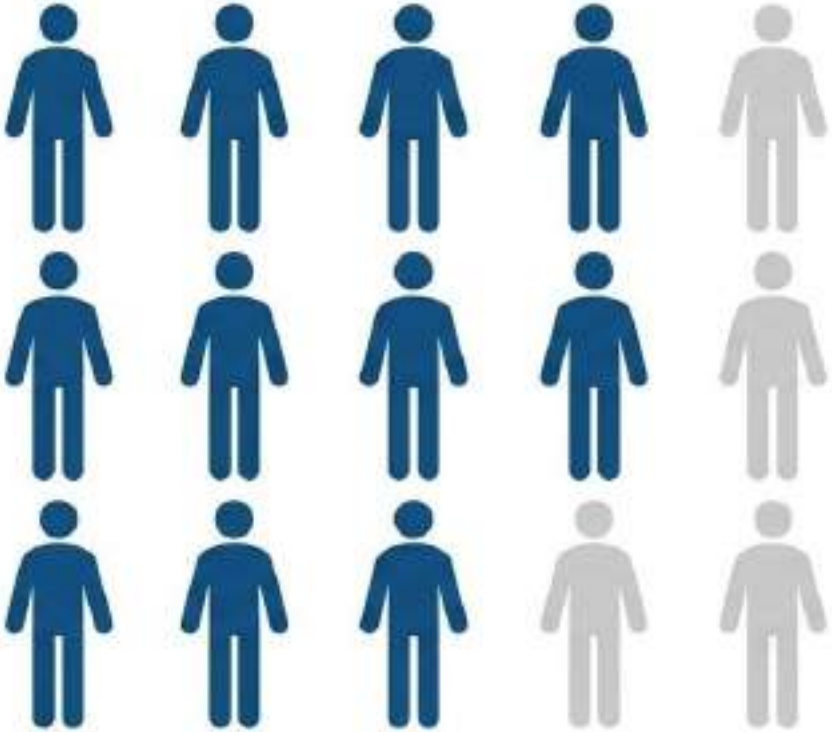
Materials & Methods: Patient Procurement & Bio-Processing

CLINICAL INPUT PROFILE
Patient Profile: 74-year-old Male
Diagnosis: Primary colorectal adenocarcinoma
Extent: Metastatic
Input Material: 3.66g tumor sample

Sample Receipt → **Mechanical Dissociation** → **Enzymatic Dissociation** (Collagen IV/Dispase) → **Automated Cell Counting**

➔ **Securing high yields through the power of standardized dissociation protocols**

Reliable Expansion of Patient-Derived Microtumors



75%

Success Rate
(9 of 12 patients)

Despite extreme variations in primary metastatic sample sizes (0.23g to 6.98g), 75% of patient samples successfully yielded stable, long-term 3D bioprinted organoids suitable for Oncolytic Virus (OV) screening.

Validates the bioprinting protocol as a highly repeatable preclinical tool for solid and metastatic cancer modeling.

Materials & Methods: High-Throughput Spatial Engineering

Bioink: RGD-bound alginate + nanofibrillar cellulose

Viscosity: 3–20,000 Pa/s

Cellular Density: 15 million cells/mL

Extrusion: 25-gauge nozzle (0.25 mm), 8–10 kPa pressure

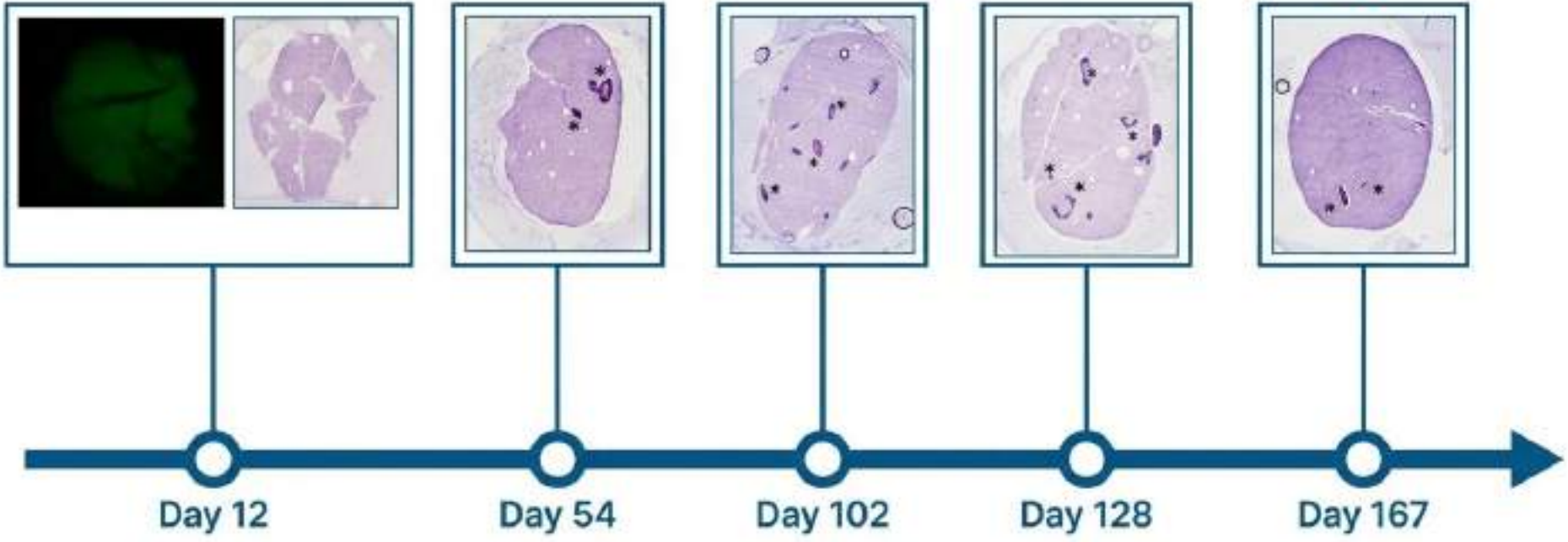
Crosslinking: CaCl2 for 1-5 minutes

Dimensions: 0.5 cm diameter, 0.05 cm thickness

Scalability: 173 identical models printed per hour from initial expansion.

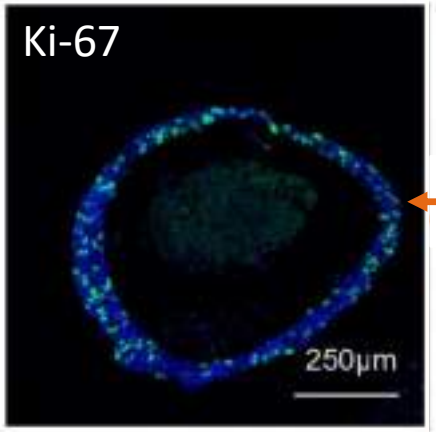
Results: Unprecedented Longitudinal Viability (>5 Months)

Stable microtumors maintained in vitro for nearly half a year, enabling genuine multidrug resistance and mutagenesis tracking

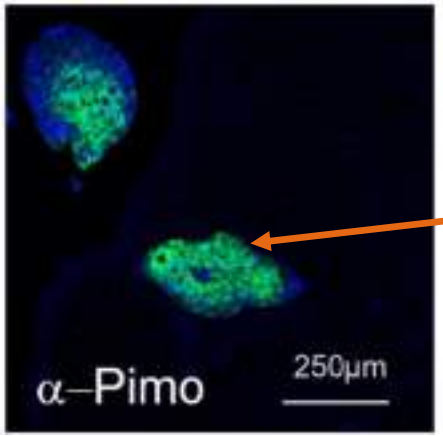


Results: Recapitulating In Vivo Tumor Heterogeneity

The 3D bioprinted model natively develops a necrotic center surrounded by highly proliferative cells. This complex micro-architecture perfectly mirrors *in vivo* human colorectal tumor dynamics, providing a physiologically relevant barrier for drug penetration screening.

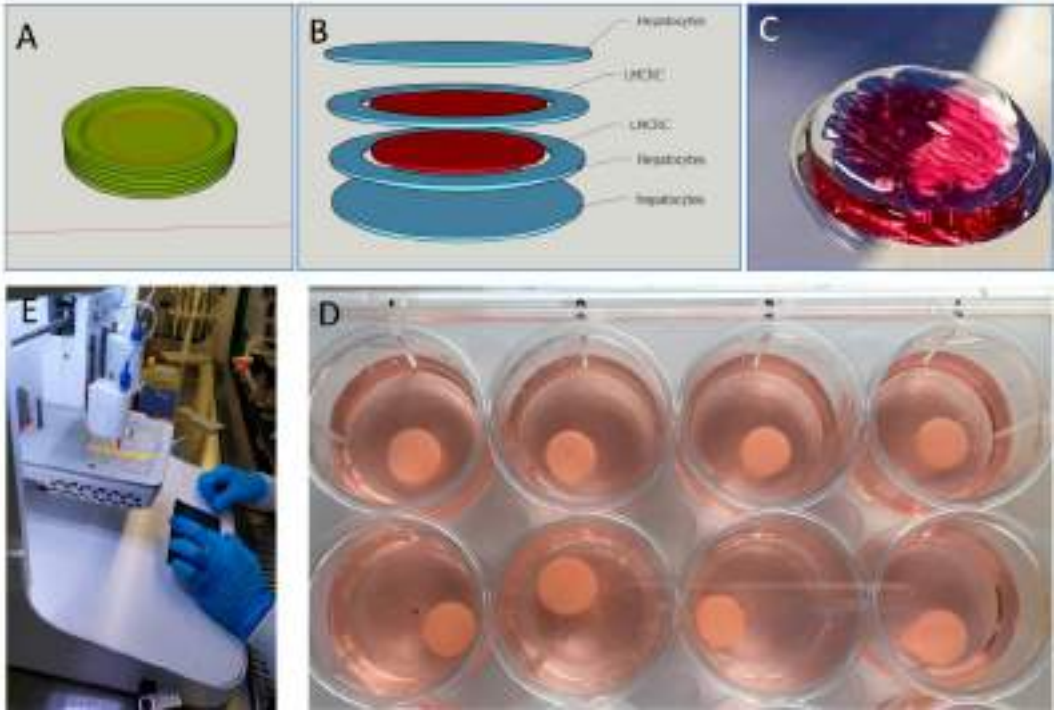


Active Proliferative Ring



Treatment-Resistant Hypoxic Core

Results: Advancing Toward Complex 3D Models

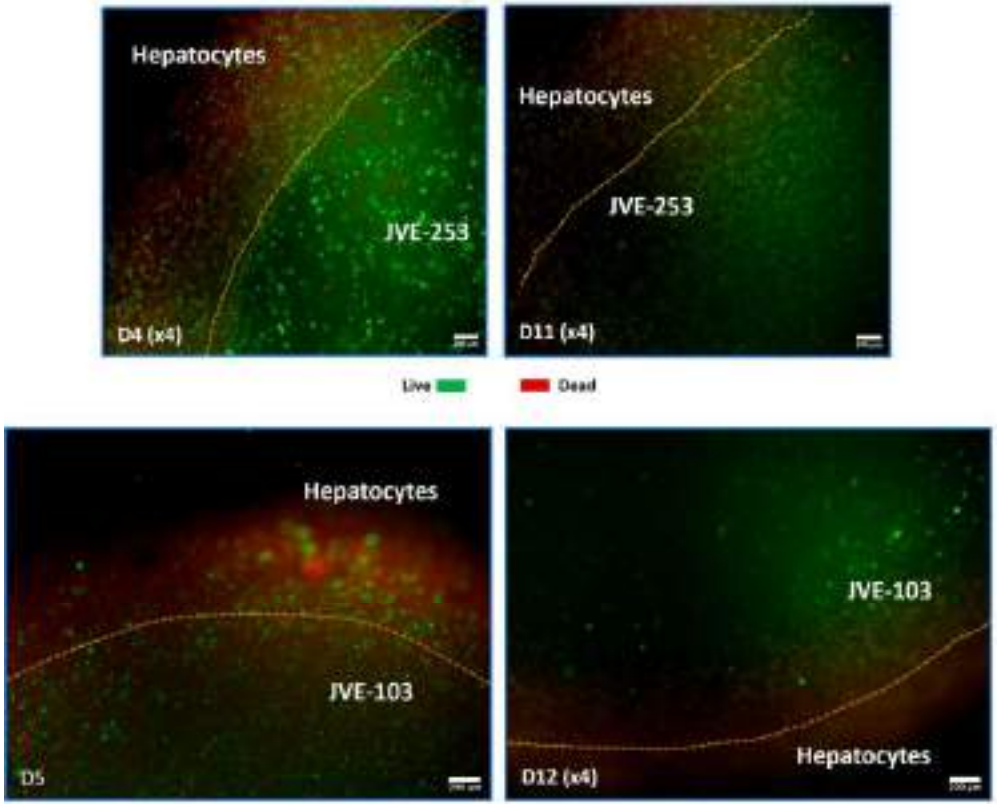


Streamlined Workflow: Simple software design and easy transfer to the CELLINK printer.

High Throughput: >60 highly reproducible prints per session (requires strict room temperature control).

Robust for Transport: Models survive off-site shipping with uncompromised cell viability, facilitating collaboration.

Results: Advancing Toward Complex 3D Models

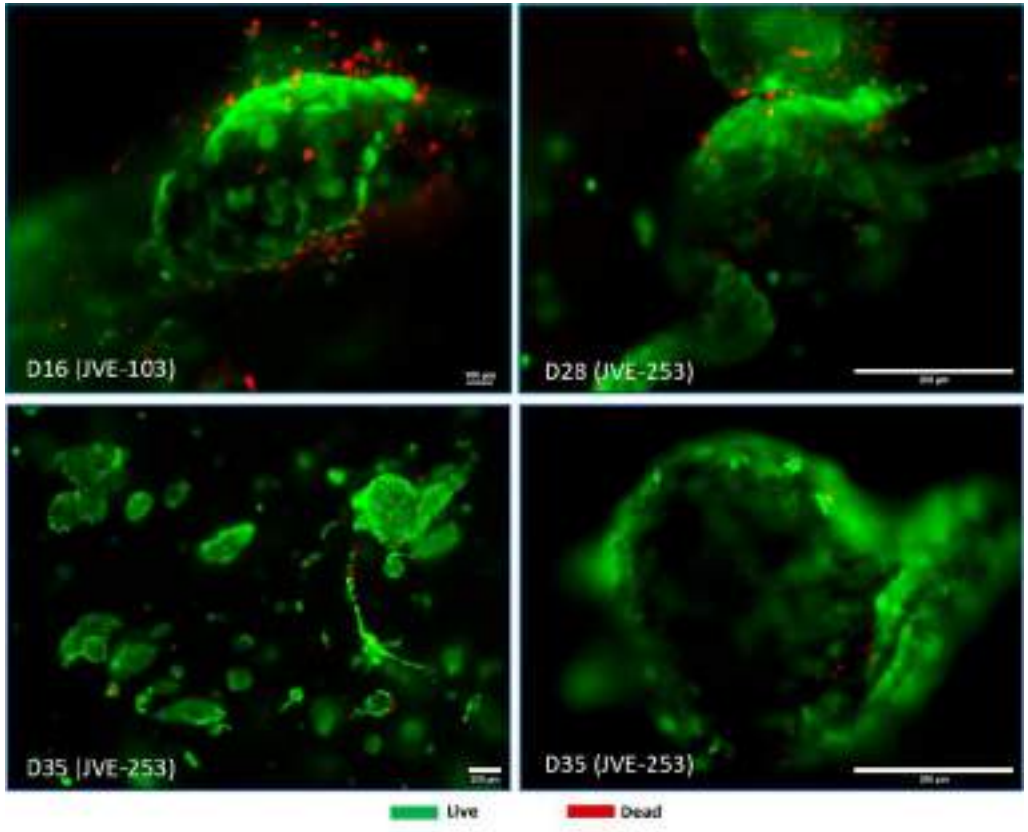


Advanced Co-culture: Successfully models metastasis by combining tumor cells and hepatocytes.

Strategic Research: Enables precise genetic analysis and drug migration studies.

3D Spatial Accuracy: Maintains clear, realistic organization between different cell types.

Results: Advancing Toward Complex 3D Models



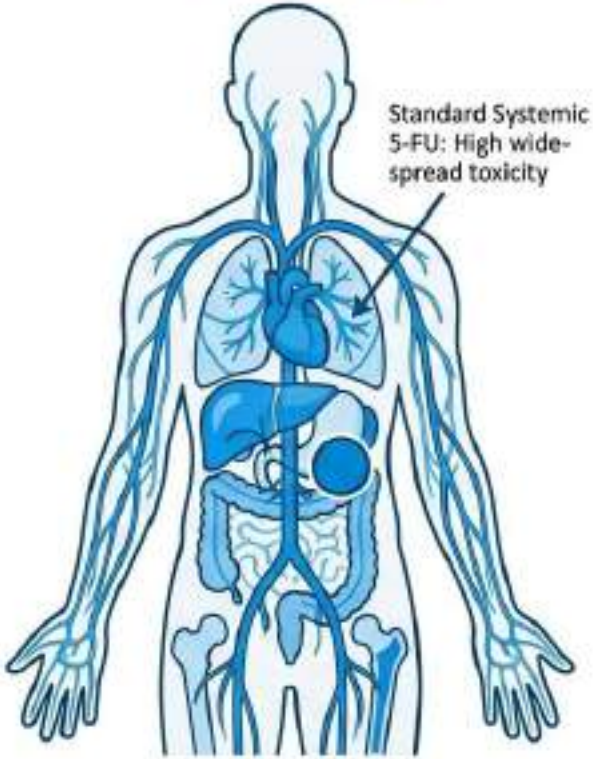
Physiological 3D Organization: Patient-derived CRC cells show natural aggregation and realistic 3D orientation.

Controlled Growth Dynamics: Tumors multiply and cluster together over time without invading the hepatic zone.

Enhanced Model Fidelity: Provides a highly relevant, tissue accurate environment for both cell types.

Targeted Intervention: Oncolytic Virus-Delivered Chemotherapy

The Challenge



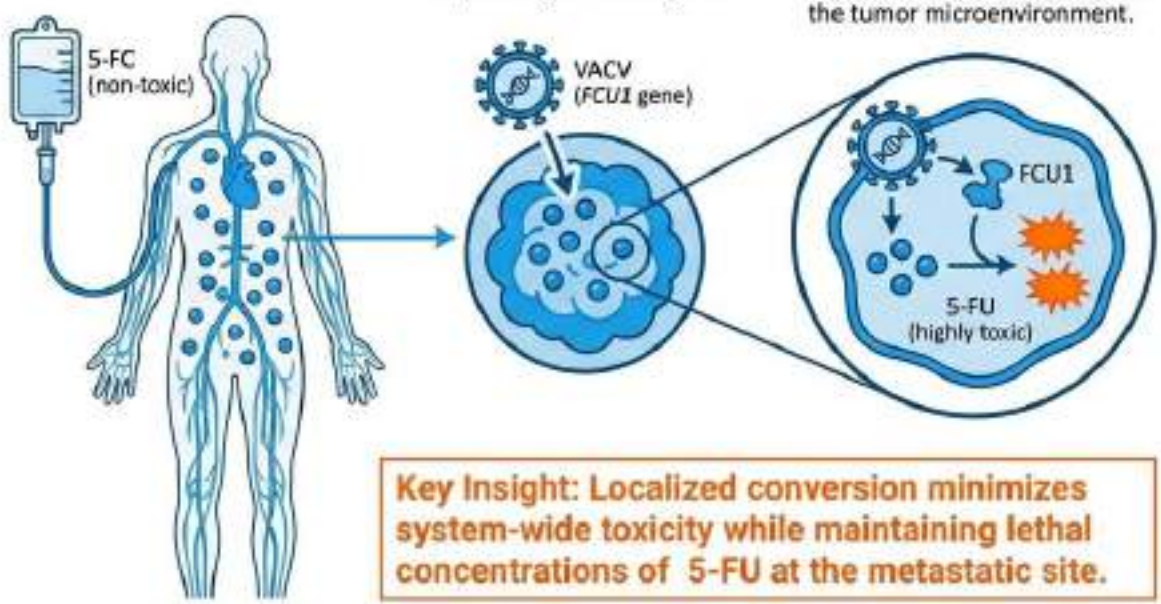
The Innovation

Annotated architectural flow for VVTG18168 Oncolytic Vaccinia Virus (VACV) system

Step 1: Systemic infusion of non-toxic 5-Fluorocytosine (5-FC).

Step 2: Localized tumor infection by VACV expressing the FCU1 gene.

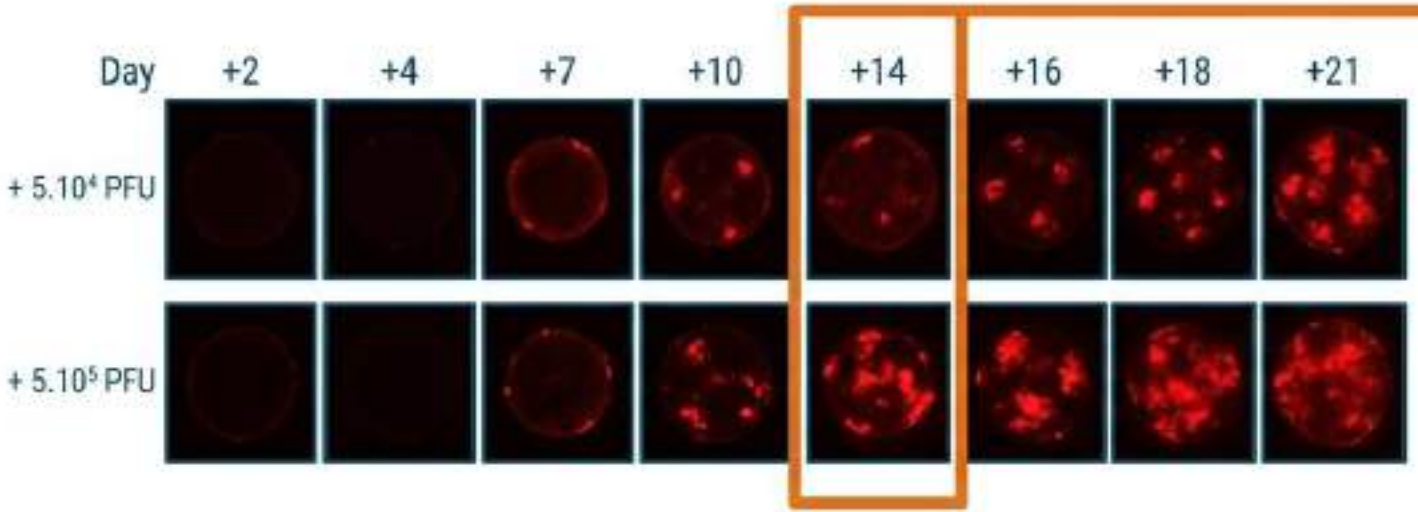
Step 3: FCU1 drives the local conversion of 5-FC into highly toxic 5-FU directly inside the tumor microenvironment.



Key Insight: Localized conversion minimizes system-wide toxicity while maintaining lethal concentrations of 5-FU at the metastatic site.

Results: Functional Screening of Advanced Biologics

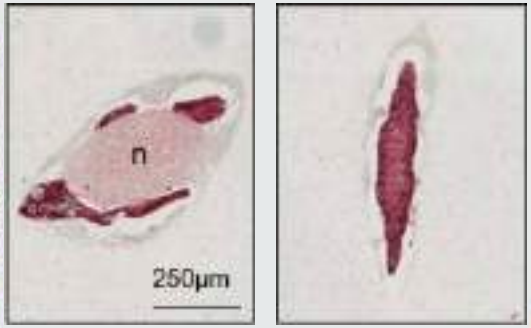
Advanced therapies frequently fail in clinical trials due to an inability to penetrate dense tumor microenvironments. This long-term model successfully proves deep viral penetration and active internal replication over multi-week timeframes.

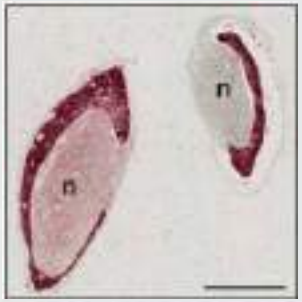


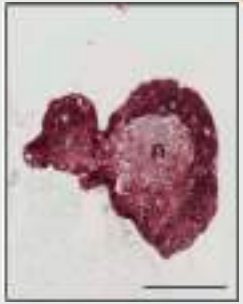
Results: Targeted Destruction via Viral Bystander Effect

Histology confirms the oncolytic virus successfully breached the tightly bound cellular system, replicated, and induced total tumor cell death through direct lysis and the chemotherapeutic bystander effect.

Control / Mock





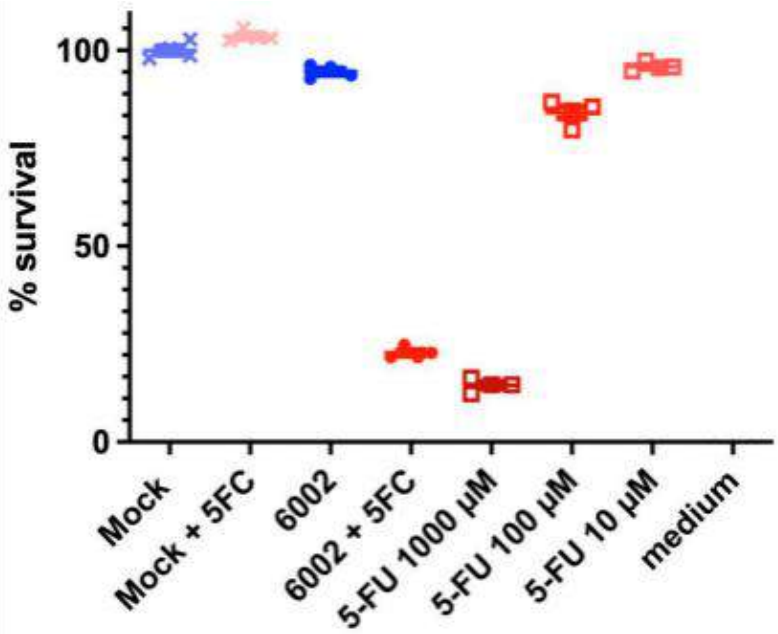


Dense living tumoral tissue wall

Treated (mCherry-OV 5x10^5 pfu, Day 25)

Total destruction of living cellular ring

Results: Stable, Measurable Viral Infection Kinetics



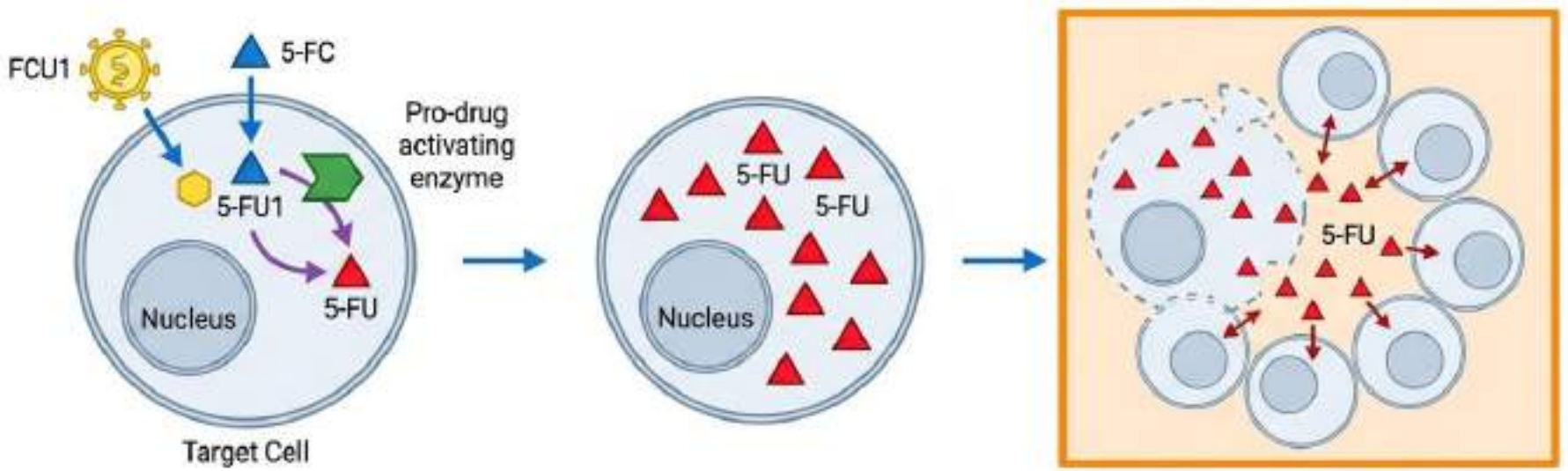
High Efficacy: OV + Prodrug slashes cell survival down to ~25%.

Proven Safety: 5-FC prodrug alone causes no cytotoxicity (targeted action).

Chemo-Level Power: Mimics high-dose 5-FU (1000 µM) to drive the bystander effect.

The 6002 + 5-FC therapy safely and efficiently drives cancer cell death, mimicking high-dose chemotherapy to trigger a powerful bystander effect.

Results: Mapping the localized Bystander Effect



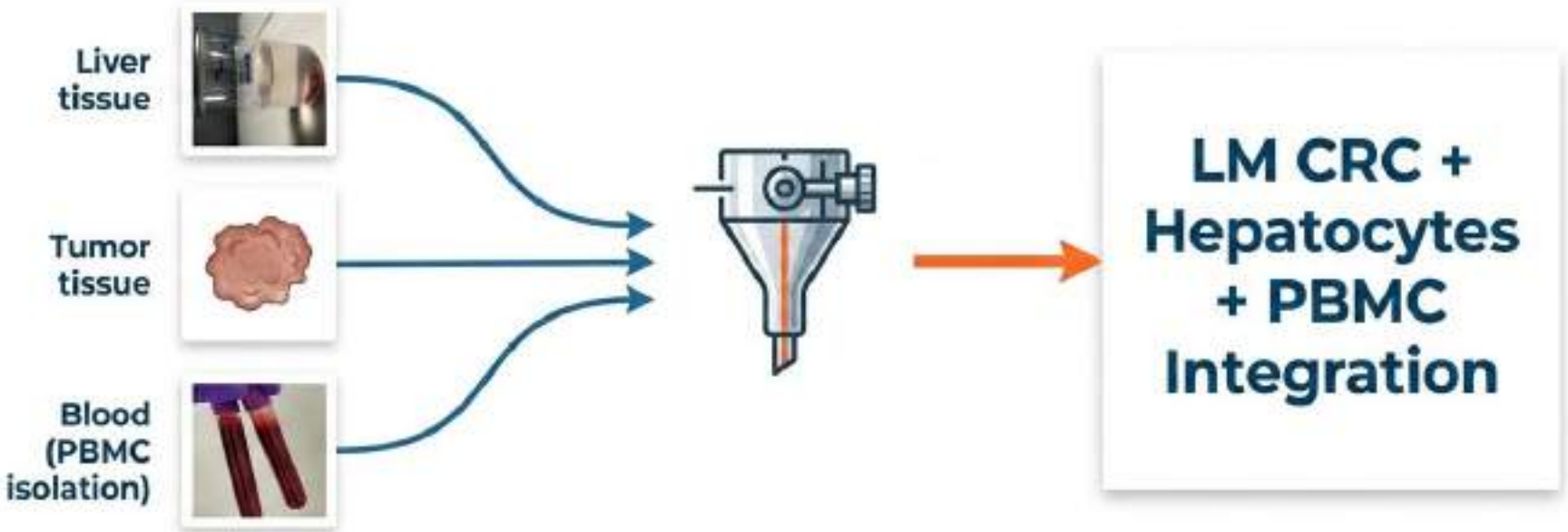
Step 1: Virus (FCU1) and non-toxic prodrug (5-FC) enter the target cell.

Step 2: Cell death triggered by localized production of toxic 5-FU.

Step 3: The Bystander Effect. Upon cell lysis, the toxic 5-FU diffuses into neighboring, uninfected tumor cells.

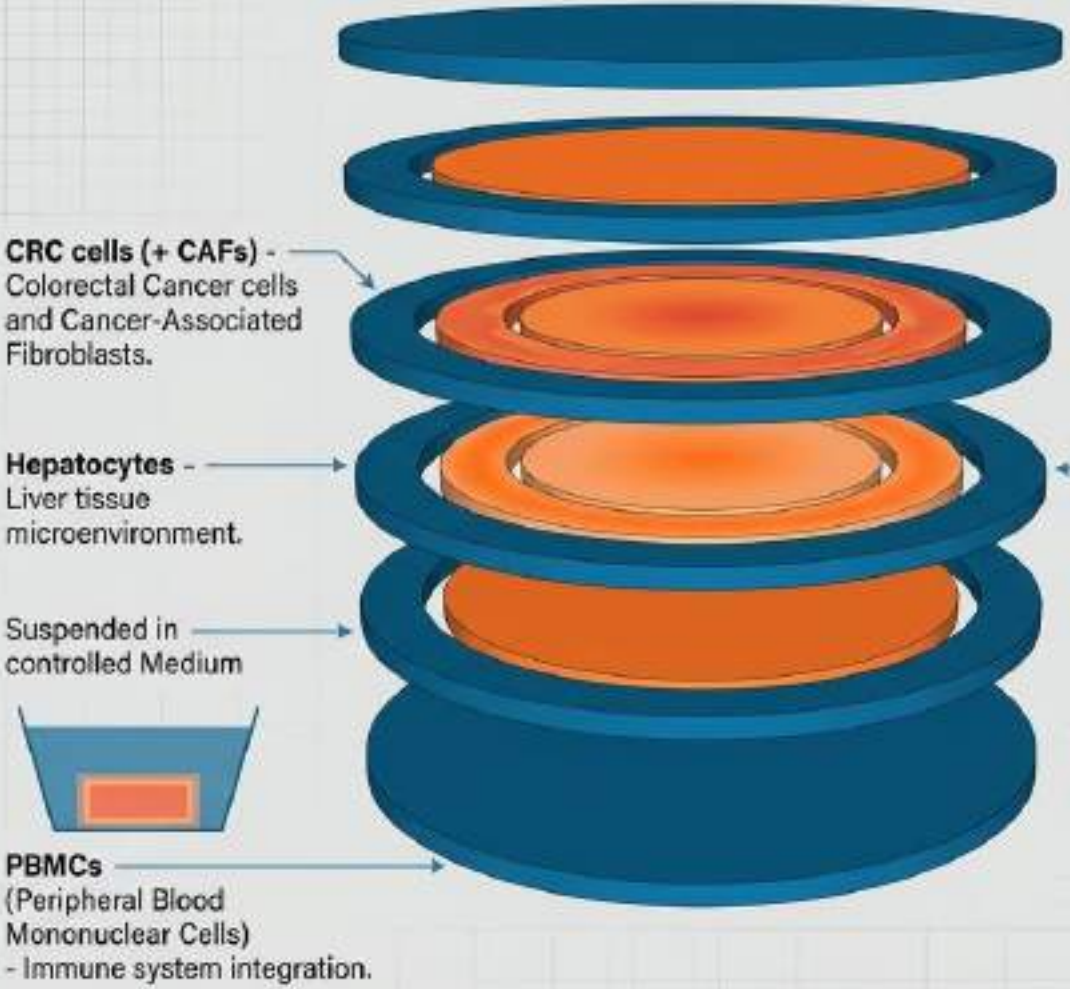
Clinical Implication: This cell-to-cell transfer overcomes the dense matrix of CRC tumors, allowing for significantly reduced viral and prodrug dosages while maintaining high localized lethality.

Expanding the Horizon: Complex Colorectal Models



The CTIBiotech platform scales beyond mono-cultures. By co-printing colorectal micro-tumors with functional hepatocytes and patient-specific peripheral blood mononuclear cells (PBMCs), we engineer fully integrated, immune-competent microenvironments.

Advancing Toward Complex 3D Models



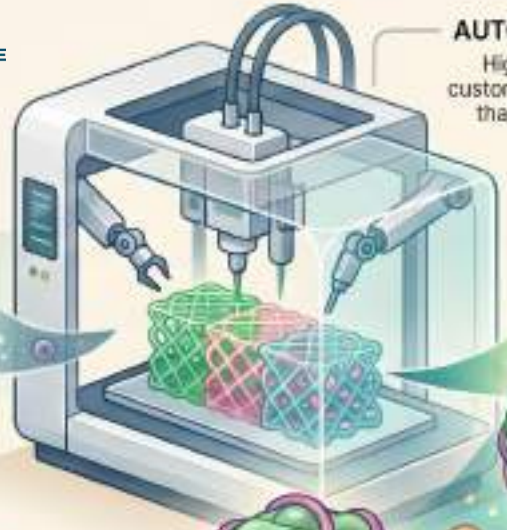
Complex Colorectal Cancer Models: Engineering precise multi-tissue spatial relationships to accurately model tumor/immune/hepatic interactions.

CTIONCOTEST™: The Future of Personalized 3D Bioprinted Cancer Research

cti BIOTECH™
VISIONARY SCIENCE

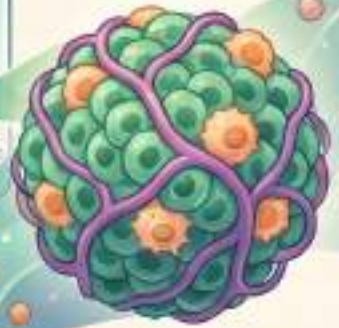
TISSUE COLLECTION & ISOLATION

Discarded human tissues are collected and processed into primary cells while preserving maximum viability.



AUTOMATED 3D BIOPRINTING

High-resolution printing creates customized 3D tissue structures faster than traditional manual methods.



LEVEL 3: ADVANCED MODEL

Includes immune and vascular cells, essential for testing modern immunotherapies.

LEVEL 1: STANDARD MODEL

Consists of 3D cancer cells only to analyze direct drug effects on tumors.

THREE LEVELS OF MODEL COMPLEXITY

SUPERIOR PREDICTIVE POWER

Realistic models increase preclinical accuracy, leading to higher success rates in human trials.

ETHICAL & ACCELERATED R&D

Provides a robust human-based alternative to animal testing while reducing drug discovery costs.

bpifrance

TOTAL FUNDING: **€2.46 MILLION** INNOVATION PROJECT

TIMELINE: **36**-MONTH INITIATIVE (2026-2029)

GOAL: ADVANCE FROM TRL 5 TO COMMERCIALIZED TRL 5 LEVEL

Thank you for your attention

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VISIONARY SCIENCE

cti BIOTECH USA™
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Towards True Personalized Medicine

By integrating patient clinical notes, histology, and tumor genomics into autologous 3D bioprinted models, CTIBiotech is not just accelerating drug discovery—we are engineering the future of patient-specific therapies.

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