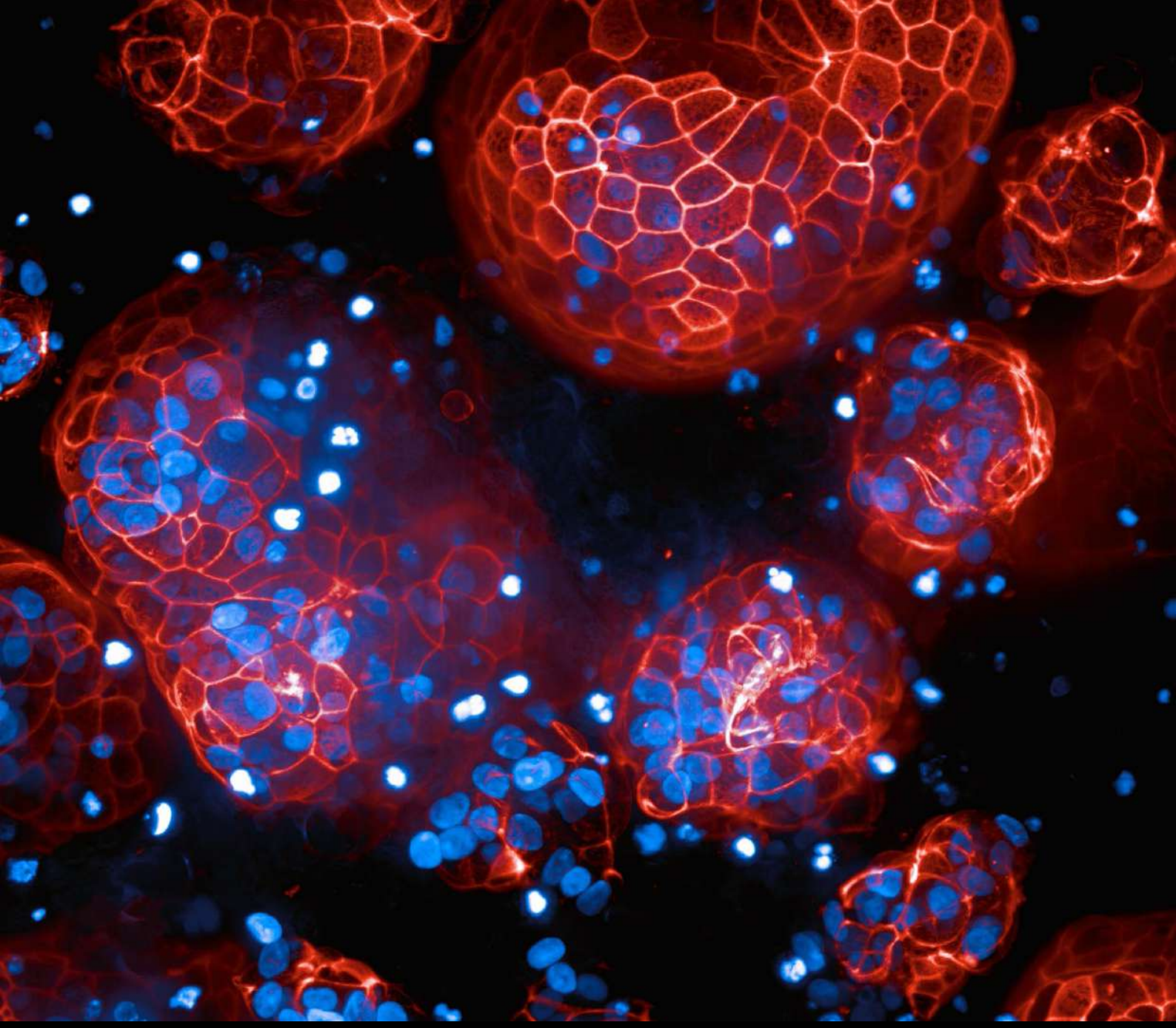


Introducing:

The ClinoStar System

Advance your 3D cell culture research using the ClinoStar system to grow cells and generate in vitro models that closely resemble real-world conditions.

Distributore ESCLUSIVO per l'Italia

CELVIVO
STRESS-FREE 3D™

CYTOSENS

cellular.cytosens.com

Breaking the Bias

At CelVivo, we collaborate closely with scientists to pioneer advancements in 3D cell culture research and in vitro models. We achieve this by creating physiologically relevant conditions that support active diffusion and eliminate shear stress.

Maybe you're working on how neural diseases affect the human brain and need to grow the perfect brain organoids in an effective and less time-consuming way? Perhaps you want to conduct long-term treatment of cells in an in vitro system? Or maybe you're looking for ways to expand blastoids for your developmental biology research?

Our patented ClinoStar system employs the clinostat principle, utilizing gentle rotation to uniformly distribute gravity vectors and encourage intercellular contact and communication. Consequently, it enables the generation of precise and reliable research outcomes.

Irrespective of your research area, we are dedicated to providing you with the finest tools and services to facilitate the development of fully functional multicellular constructs and to enhance your research with 3D cell culture and tissue technology.

We hope you find this brochure inspiring.

Sincerely,
The CelVivo Team

The Clinostat Principle

Have you ever considered how to unleash the hidden potential of cell communication and tissue formation? The ClinoStar system is at the forefront of this scientific pursuit, offering a solution that poses a provocative question: Why is it crucial for researchers to embrace the clinostat principle and eliminate shear stress in their work?

The majority of human cells never encounter shear stress

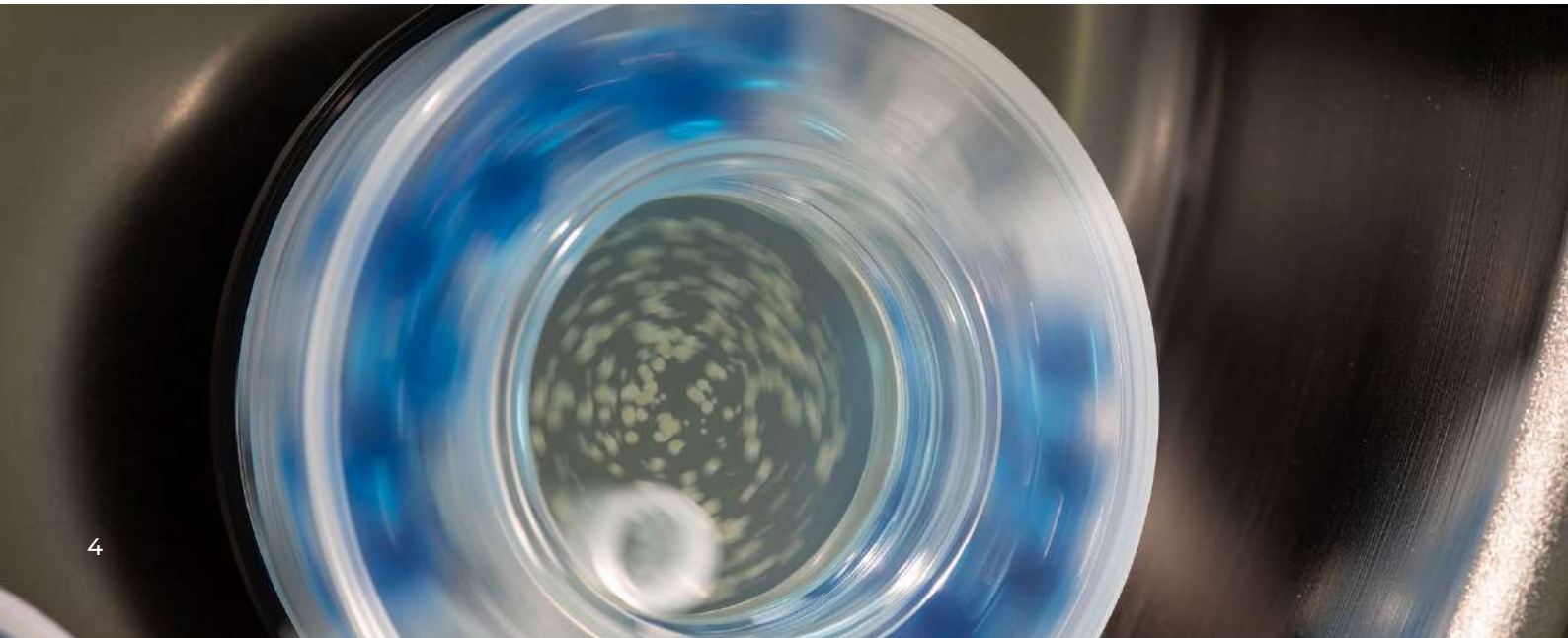
Shear stress is a mechanical force exerted by fluid flow on cells. When cells encounter excessive shear stress, they undergo mechanotransduction, triggering changes in gene expression and protein synthesis.

Excessive shear stress has been found to induce changes in expression of specific membrane proteins, such as adhesion molecules (e.g., selectins, integrins) and mechanosensors (e.g., ion channels). This can disrupt cellular functions and lead to adverse effects on cell health.

So, how do you liberate your cells from shear stress?

"*Critical/lethal shear stress for different mammalian cell types are in the range of 0.3–1.7 Pascal (Pa)".*[1]

"Mimetic tissue culture in a clinostat bioreactor provides very low shear forces (at 20 rpm, ca. 0.01 Pa on the suspended spheroids. Higher shear forces (and cellular effects) are seen for stirred suspension bioreactors (100–200 rpm, 0.3–0.66 Pa) and for orbital shakers (20–60 rpm, 0.6–1.6 Pa)".[2]



The technology behind the ClinoStar

The ClinoStar is a clinostat bioreactor, providing low shear forces within physiological levels.

The system promotes long term intercellular contact and communication allowing formation of organized and functional tissue constructs.

Passive diffusion vs. Active diffusion

When the media surrounding cells remains still (static conditions), cellular metabolism creates a depleted zone due to the consumption of nutrients and oxygen and production of metabolites.

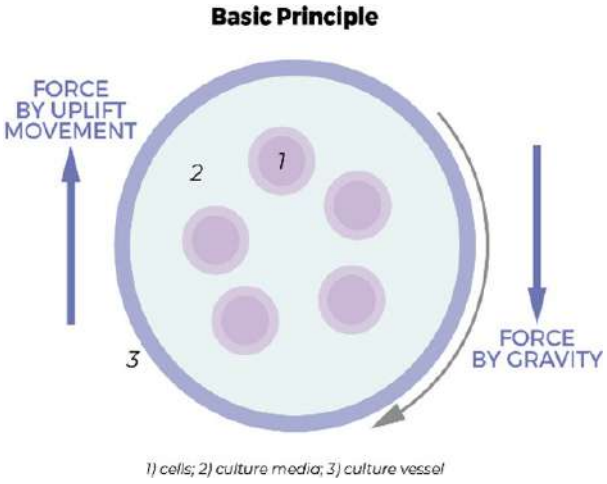
The rotation of the ClinoReactor generates a mild media flow (active conditions) that diminishes this depletion zone, leading to a notable enhancement in the lifespan, organization level and size of the constructs.

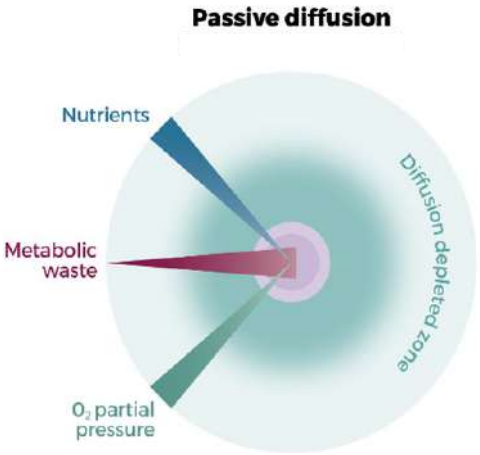
Clinostat principle in the ClinoStar:

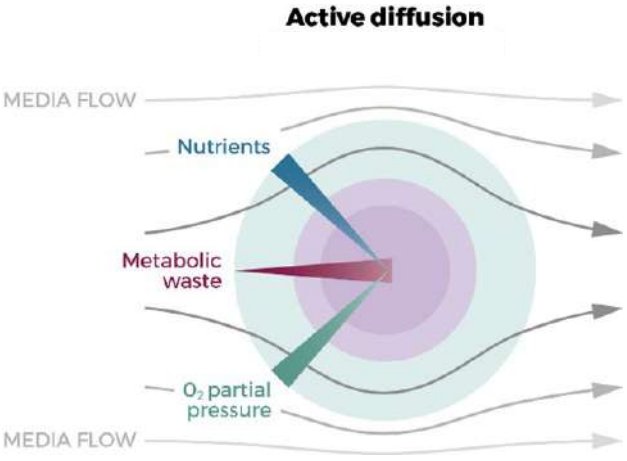
The ClinoStar system promotes tissue functionality.

Continuous gentle rotation generates a mild media flow that minimizes shear stress, maximizes the exchange of nutrients, gas, and metabolites, and prevents unwanted cellular attachment to the culture vessel.

Low shear/high diffusion environment allows cells to execute their natural programming. This results in the adoption of cell morphology and function, which mimics the same cells in the intact organism (in vivo).







1.: Croughan M. S., Wang D. I. Biotechnology 1991: 17:213-49. doi: 10.1016/b978-0-409-90123-8.50015-x
2.: Wrzesinski K., Fey S.J.; Bioengineering 2018 Mar 7;5(1):22. doi: 10.3390/bioengineering5010022

In Vivo just moved closer

CLINOSTAR ™

CONNECTING YOUR RESEARCH TO REALITY

You can control the temperature, CO_2, O_2 (optional), and individual rotational speed of the 6 clinostat axles.

You can monitor your constructions in each reactor through six live feed cameras

Integrated automatically adjusted fan ensures a uniform environment within the chamber.

CELVIVO CLOUD

CONNECT YOUR CLINOSTAR TO THE CLOUD

Access your ClinoStar through multiple devices from anywhere.

Keep an eye on your cultures and adjust individual rotational speeds as they progress.

Keep a register of changes and updates through the event-log.

CLINOREACTOR ™

CONNECT YOUR RESEARCH TO IN VIVO

4 to 6 times as much biomass per volume of media compared to traditional culture systems.

Multiple access ports allow easy access to constructs and media exchange.

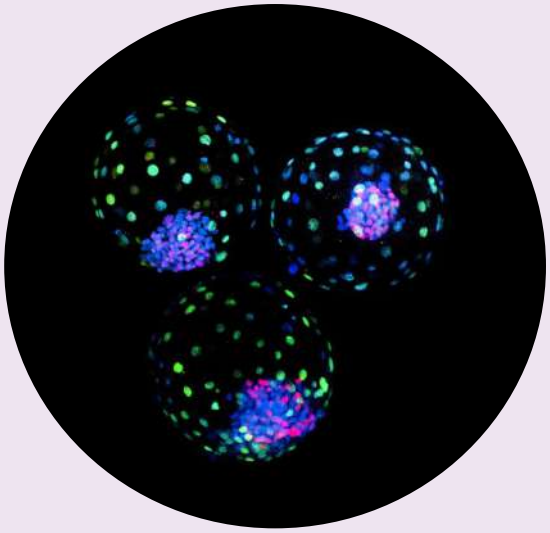
The inbuilt humidification system minimises the risk of infections and secures constant media volume.

See through design allows direct macro and micro observation.

Application areas

The ClinoStar allows the generation of uniform, reproducible and functional spheroids organoids and other constructs from one or more cell types (whether patient-derived, primary, stem cells or cell lines). The technology facilitates research by providing cell models with an unprecedented correlation between in vitro and in vivo functionality.

It is becoming an indispensable tool for an ever-increasing variety of research applications.



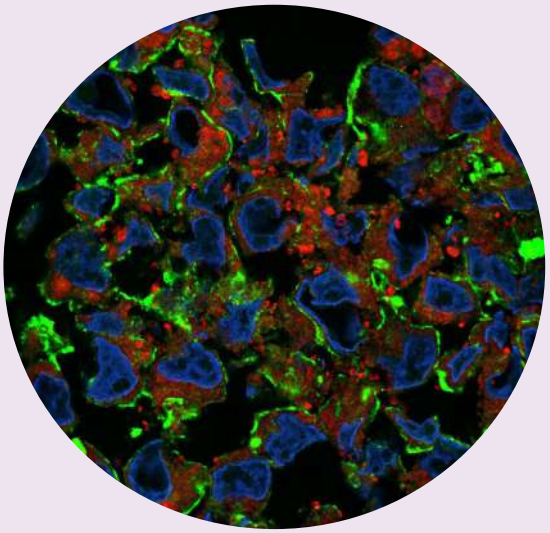
Liver[2]

The ClinoStar's precise control over rotational speed enables you to tailor the culture-conditions to your specific needs.

Hepatocytes constructs recover to a growth rate similar to hepatocytes in the liver, and can maintain advanced functions for months.

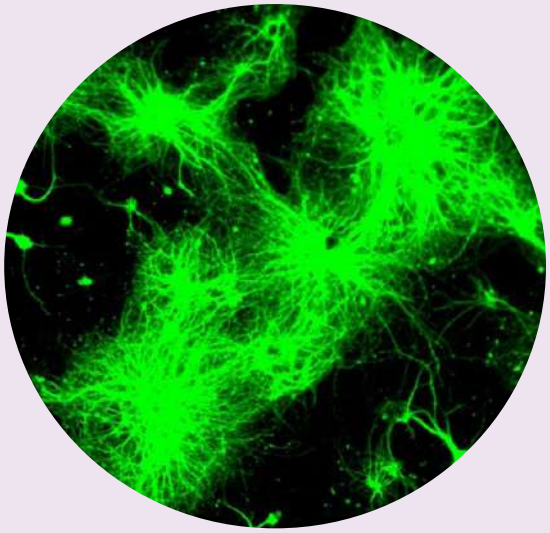
Developmental Biology[1]

By promoting cell-cell and cell-matrix interactions, the 3D culture system provides a more physiological environment for blastoid growth. This allows them to mimic developments which would occur in the Fallopian tubes and uterus.



1.: Pinzón-Arteaga C., Wang Y., Wei Y., Wu J. et al.;
Cell Stem Cell 2023, doi: 10.1016/j.stem.2023.04.003.

2.: Frandsen H.S., Rogowska-Wrzesinska A., et al.;
Cells 2022. doi: 10.3390/cells11203216

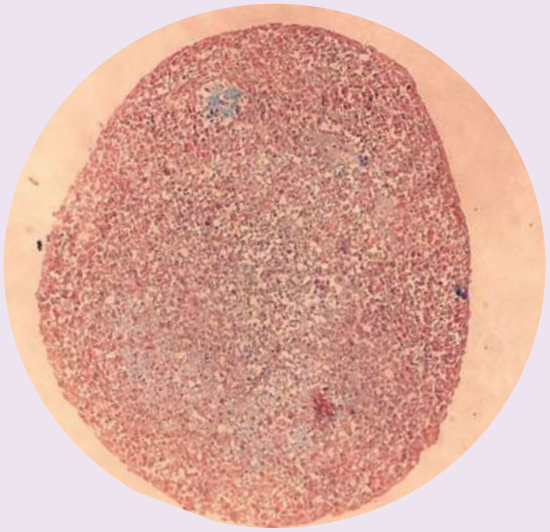


Neuroscience[3]

The system has been used to generate large numbers of neuronal (brain) organoids of a reproducible size and structure. This improves the reproducibility of experiments and facilitates higher-throughput drug screening.

Oncology[4]

Cancer tumoroids grown in the ClinoStar mimic the tumour microenvironment. This allows cultures to be maintained for very long terms (+1 year), providing a more accurate and informative platform for studying cancer cell behaviour and drug response.



3.: Harley-Troxell M.E., Dhar M.;
Int J Mol Sci 2023, doi: 10.3390/ijms241713506

4.: Van der Merwe L., Wrzesinski K., Gouws C., et al.;
Biotechnol Prog 2022, doi: 10.1002/btpr.3253

Using the ClinoStar for researching patient-derived organoids

Christophe Deben
Professor at the Center for Oncological Research, Antwerp University, Belgium

Research Area: Oncology

Reason for using the ClinoStar system

My research focuses on the field of oncology, where I aim to introduce the use of patient derived organoids in preclinical and clinical developments. I'm currently working on the development of high-througput drug screening assays, using patient drives organoids to support the drug development and also clinical decision making to find the right therapy for the right patients.

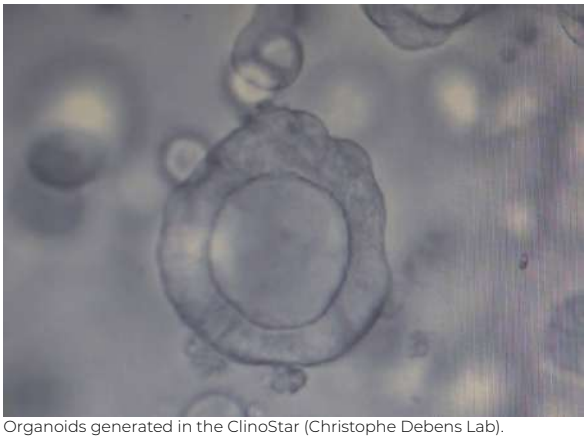
The ClinoStar enables us to enhance the success rates for certain tumor types by directly putting tumor fragments in the ClinoStar and letting them adapt to the in vitro cultures there, which allows us to culture large size organoids, which of course are more representative of what's happening in the patient.

Interesting Results

I really think the work we are doing here, or in general people doing work on organoids, can help oncologists in finding the right drug for the right patients.

So, with my research, I hope to achieve, helping patients and curing them by finding the right therapy. And this can be done in several ways. Like I said, it's the functional precision medicine approach. But also, really developing better models to study cancer, because 2D cell lines have been used for a very long time, but now we see that they don't represent the correct tumor microenvironment.

So, using these advanced clinical models, preclinical models, and new technologies like the ClinoStar can really help us recreate the tumor of the patients in an environment they they're happy to grow in. They can sustain for a long time. And where we can test therapies in a useful environment.



Organoids generated in the ClinoStar (Christophe Debens Lab).

"We are astonished how much faster organoids grow in the ClinoStar and by the ease of use for maintaining long-term cultures.

Learn more about how Christophe uses the ClinoStar for his work with patient-derived organoids.

Using the ClinoStar for pharmaceutical research on lung tissue

Chrisna Gouws
Professor at the Center for Pharmaceutical Research, North-West University, South Africa

Research Area: Drug Discovery

Reason for using the ClinoStar system

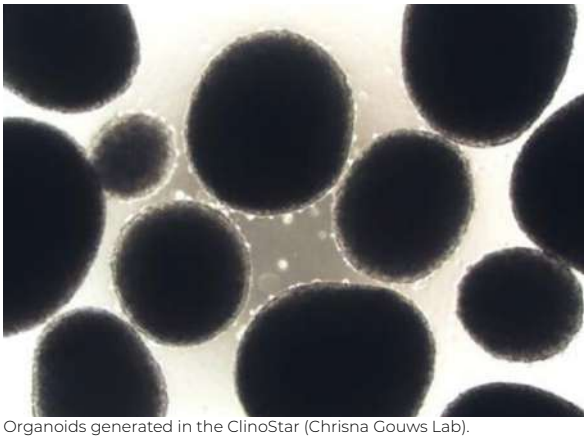
Working in the pharmaceutical research environment, being able to reduce the need for animal models in my research, while increasing the relevance of my research is very important. Using clinostat-based 3D cultures enables much longer treatment and experimental windows, in an in vitro format, while obtaining data with physiological relevance. Unlike with animal models, multiple daily samplings from the same bioreactor is possible, with no ethical implications. I believe this is an ideal approach.

Interesting Results

We compared 2D and 3D screening models to elucidate toxicity potential of herbal compounds, and the results suggested 3D cell culture models to be the superior model due to the lack of physiological relevance of the 2D models.

We saw some discrepancies in the data obtained from the 2D and 3D models, which suggested that the 2D model may result in initial false positive results and later in false negative results.

We proposed that this was due to different modes of DNA repair systems in the exponential growth phase where experiments with 2D models are executed, while in the 3D spheroid model the majority of the cells within the spheroid structure are predominantly non-dividing. In vivo and in intact organs cells are also at various stages of the cell cycle or non-dividing, suggesting that a 3D spheroid model will give a more accurate representation on how an organ, in this instance the liver, will respond to an herbal xenobiotic.



Organoids generated in the ClinoStar (Chrisna Gouws Lab).

“ Using clinostat-based 3D cultures enables much longer treatment and experimental windows, in an in vitro format

Learn more about how Chrisna uses the ClinoStar for her work with drug discovery.

CLINOSTAR® FEATURES & BENEFITS

The ClinoStar is a complete 3-dimensional (3D) cell and tissue culture system combining premium class CO_2 incubator with six independent clinostat axles, which each can hold a culture vessel (ClinoReactor). The system is operated using a cloud-based software system that permits control of the temperature, CO_2 and O_2* levels. Six camaras located opposite the axles enable live-stream video surveillance of the cultures without disturbing the environment.

Push to open
For convenient hands-free opening and reduced contamination risk.

Light illumination
Front and backlight can be provided to obtain crystal clear images.

Small footprint
Fits anywhere, even in your LAF-bench.

Uniform environment
The large heating element and automatically adjustable speed fan guarantee even distribution and rapid recovery of heat and CO_2 throughout the chamber.

Connectivity options
Wi-Fi and ethernet connection allows for direct internet access and to receive software updates via CelVivo Cloud.

Decontamination
Automatic UV-C decontamination cycles.

Hypoxia*
An add-on module lets you control the O_2 level in the ClinoStar

Wall Brackets*
An add-on tem that makes it possible for you to attach your ClinoStar(s) to the wall.

**Sold seperately*

A variable speed fan ensures rapid recovery and maintains chamber temperature, CO_2 and O_2 levels.

Backlighting makes it easier to monitor the movement and development of the cell constructs.

Hypoxia module in the ClinoStar.

CLINOREACTOR® FEATURES & BENEFITS

A ClinoReactor is an advanced cell culture vessel (bioreactor) with a fixed 10 ml culture chamber, that is supplied sterile in a sealed package. The humidification beads inside the ClinoReactor supply a humidified environment for the culture chamber, this eliminates the need for water in the incubator, greatly reducing the risk of infection. The beads and humidification zone help to maintain both the temperature and gas levels when the ClinoReactor is taken out of the ClinoStar (during for example a media change or microscopy observation).

The optically clear polystyrene enables microscopy of spheroids or organoids in a closed environment.

Fixed 10 mL cell culture chamber
Integral humidification system prevents water-loss from the culture chamber which can easily contain and maintain over 350 mature cell constructs (each with >80,000 cells).

Low bind surface
Polypropylene and polystyrene surfaces ensure a low adhesion and absorption of molecules.

Click-on
Simple click-on system for easy placement and removal of ClinoReactors in ClinoStar.

Unique airflow and membrane system
0.2 µm membrane protect the cultures from contaminants while gas exchange is maintained.

Multiple working positions
ClinoReactor design allows both vertical and horizontal stabile working positions with easy access to culture chamber via multiple access ports.

Petri-dish like accessibility with the front lid removed

Integral humidification system with hydratable beads prevents water-loss from the culture chamber. The rest of the ClinoStar can operate at ambient humidity: this reduces the contamination risk to the cultures.

Growth media exchange in a ClinoReactor takes just 30 seconds via the top access port.

CELVIVO CLOUD FEATURES & BENEFITS

CelVivo Cloud is an online software platform where you can remotely control and adjust the settings of your ClinoStar.

Remote Access
Access CelVivo Cloud from any internet enabled device anywhere in the world.

Individual control
Make specific ClinoStars units available to certain team members.

Live camera feed
Monitor your constructs in real-time and see the development in each reactor through the live feed.

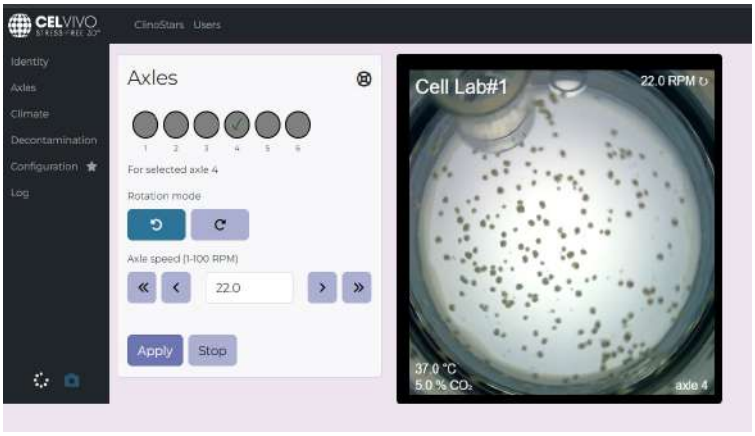
Climate adjustment
Adjust the climate settings in your ClinoStar through control of temperature, CO_2 and O_2 levels.

Decontamination
Automatic UV-C decontamination cycles can be remotely initiated.

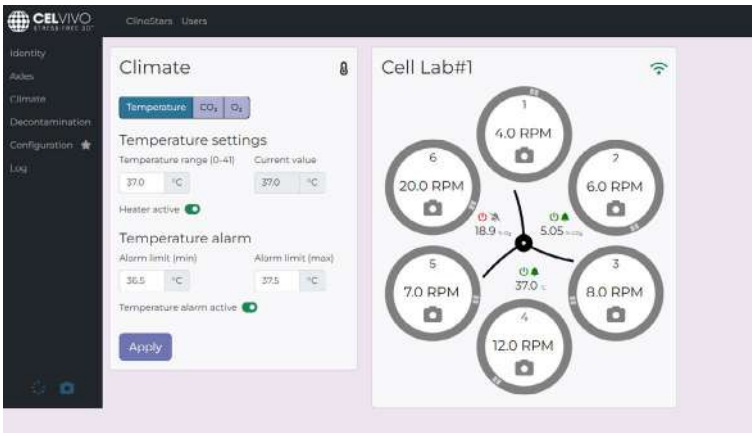
Speed control
Control the speed of each ClinoReactor individually.

Event log
Keep track of alerts, edits, adjustments etc. with the real-time automatically-updated event log.

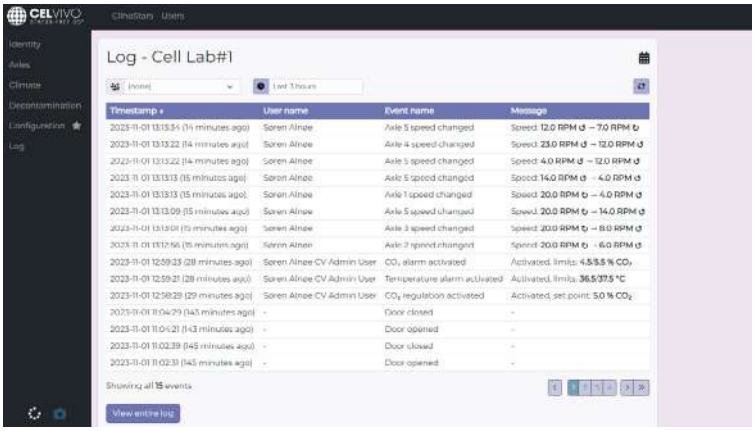
Password protected
You'll get your own password making sure, only you have access to your account.



Adjust speed and rotation direction in real time.



Monitor and adjust your climate settings.



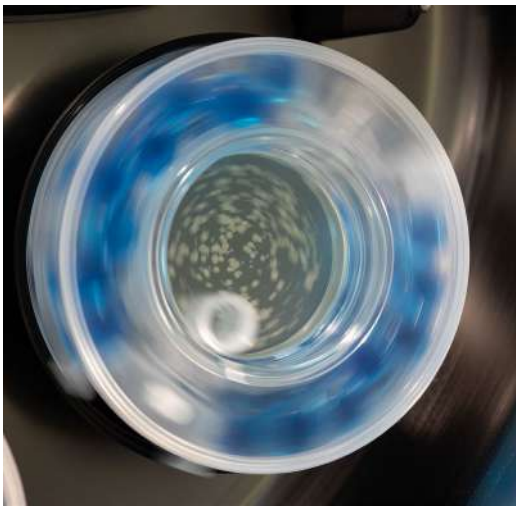
All changes are registered in the event log

ClinoStar Hypoxia Unit

Using hypoxia for 3D Cell Culture Research

Accurately establishing and monitoring oxygen levels during the culture period is crucial to mimic in vivo physiological conditions of tissues or organs. In the majority of traditional cell culture experiments, a standard cell culture incubator atmosphere of 5% CO_2 in air is used, resulting in approximately 19% oxygen and creating non-physiological conditions.

Oxygen concentrations in the human body vary, ranging from around 12% in the lungs to 5% in the brain, and as low as 0.1% in tumor tissues. The ClinoStar hypoxia unit enables the manipulation of in vitro atmospheric composition to tailor it to the specific physiological needs of tissues or organs.



Advantages of using hypoxia in the ClinoStar

- ◊ Ability to regulate level of oxygen from atmospheric to 2%.
- ◊ Rapid attainment of the media's oxygen level set point is achieved through active gas exchange between the ClinoStar and the ClinoReactor humidification chamber.
- ◊ The ClinoReactor semi-closed environment temporarily preserves hypoxic conditions for operations within a normal (21%) atmospheric oxygen environment. This simplifies short-term handling procedures, such as microscopy observation and documentation.

Distributore ESCLUSIVO per l'Italia

CYTOSENS

cellular.cytosens.com

CELVIVO STRESS-FREE 3D™

Working with the hypoxia module in the ClinoStar

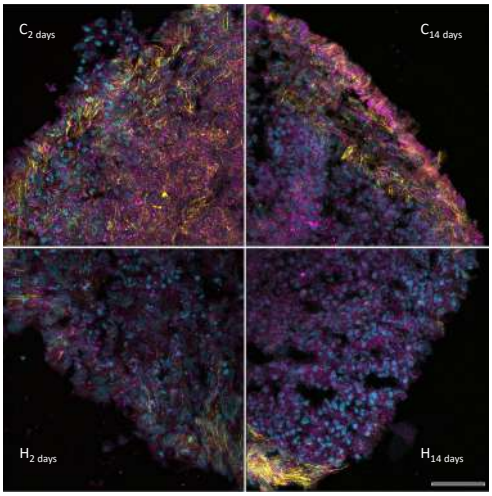
Anne Agger
Doctoral Fellow,
Centre of Functional Tissue Reconstruction, University of Oslo

When the ClinoStar met the FUTURE

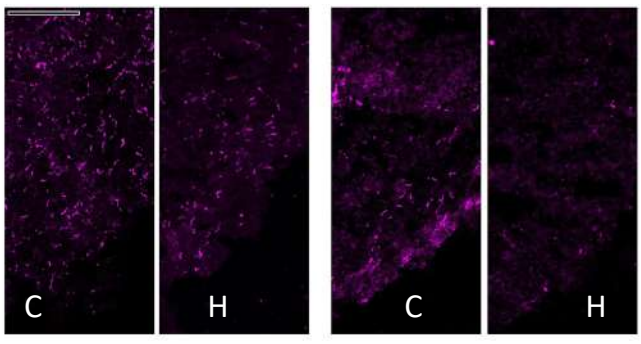
At the Centre of Functional Tissue Reconstruction (FUTURE) at the University of Oslo, Professor Reseland and Dr Samara have employed the ClinoStar platform and have been working towards several lineages of innovative models to study hypoxia.

Anne Agger, shares her preliminary findings, the structural changes in fibroblast spheroids cultivated for 14 days under both normoxic and hypoxic conditions. Through immunofluorescent labeling, the magenta-acetylated tubulin staining enables the visualization of reduced primary cilia,
suggesting downstream molecular effects of targeted hypoxia.

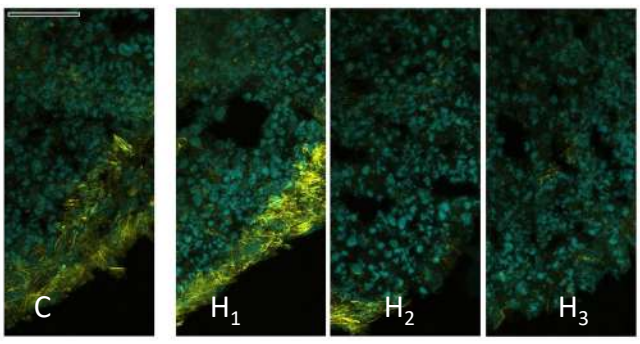
Meanwhile, actin in yellow vividly illustrates the heterogeneous morphological transformation of the rim of the spheroid.
Notably, hypoxia exerts significant effects on various cytokine profiles, underscoring its substantial impact on cellular responses and signaling pathways. This impact is particularly pronounced in the secretion of cytokines like VEGFa, MCP1, IL6, IL8, and more, as demonstrated in the graph where we monitored cytokine secretion over time.
These findings underscore the importance of valid in vitro models that can shed light on the intricate cellular responses to hypoxia.



C: Control; H: Hypoxia. All scale bars = 50 µm



2 DAYS 14 DAYS

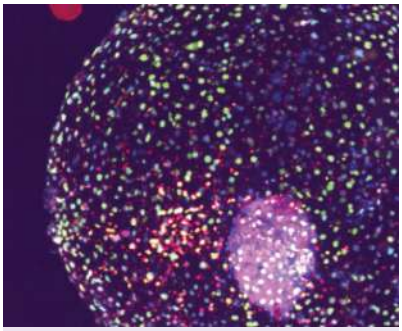


14 DAYS

future
center for functional tissue reconstruction

Want more?

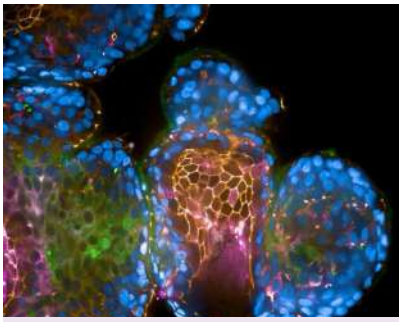
Immerse yourself in the endless research possibilities by reading some of the publications from our ClinoStar users at **cellular.cytosens.com/celvivo-clinostar2**



Bovine blastocyst-like structures derived from stem cell cultures

Authors: Carlos A. Pinzón-Arteaga, Yinjuan Wang, Yulei Wei, Jun Wu et al.

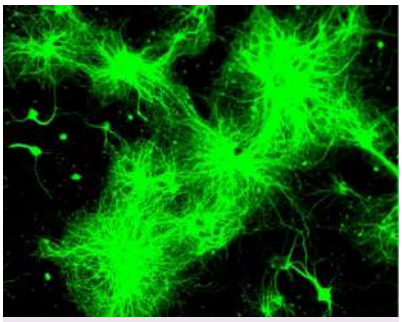
DOI: doi.org/10.1016/j.stem.2023.04.003



How to optimize respiratory models for SARS-CoV-2 research

Authors: Wilfried Posch, Stefanie Dichtl, Doris Wilflingseder et al.

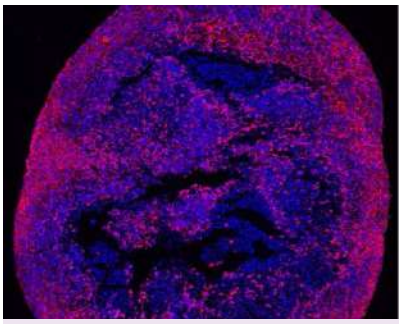
DOI: doi.org/10.26124/bec:2022-0009



Assembling Spheroids of Rat Primary Neurons Using a Stress-Free 3D Culture System

Authors: Meaghan E. Harley-Troxell and Madhu Dhar

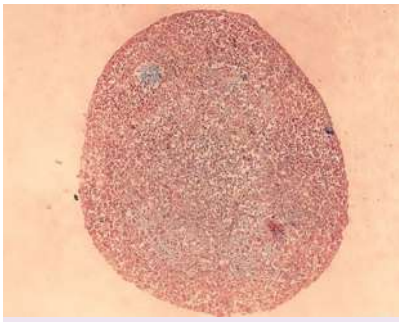
DOI: doi.org/10.3390/ijms241713506



Increased neurovirulence of omicron BA.5 and XBB variants over BA.I in KI8-hACE2 mice and humanbrain organoids

Authors: Romal Stewart, Kexin Ya, Andreas Suhrbier et al.

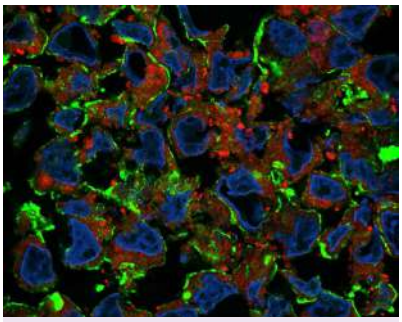
DOI: doi.org/10.1101/2022.12.22.521696



A novel NCI-H69V small cell lung cancer functional mini-tumor model for future treatment screening applications

Authors: Liezaan Van der Merwe, Krzysztof Wrzesinski, Chrisna Gouws et al.

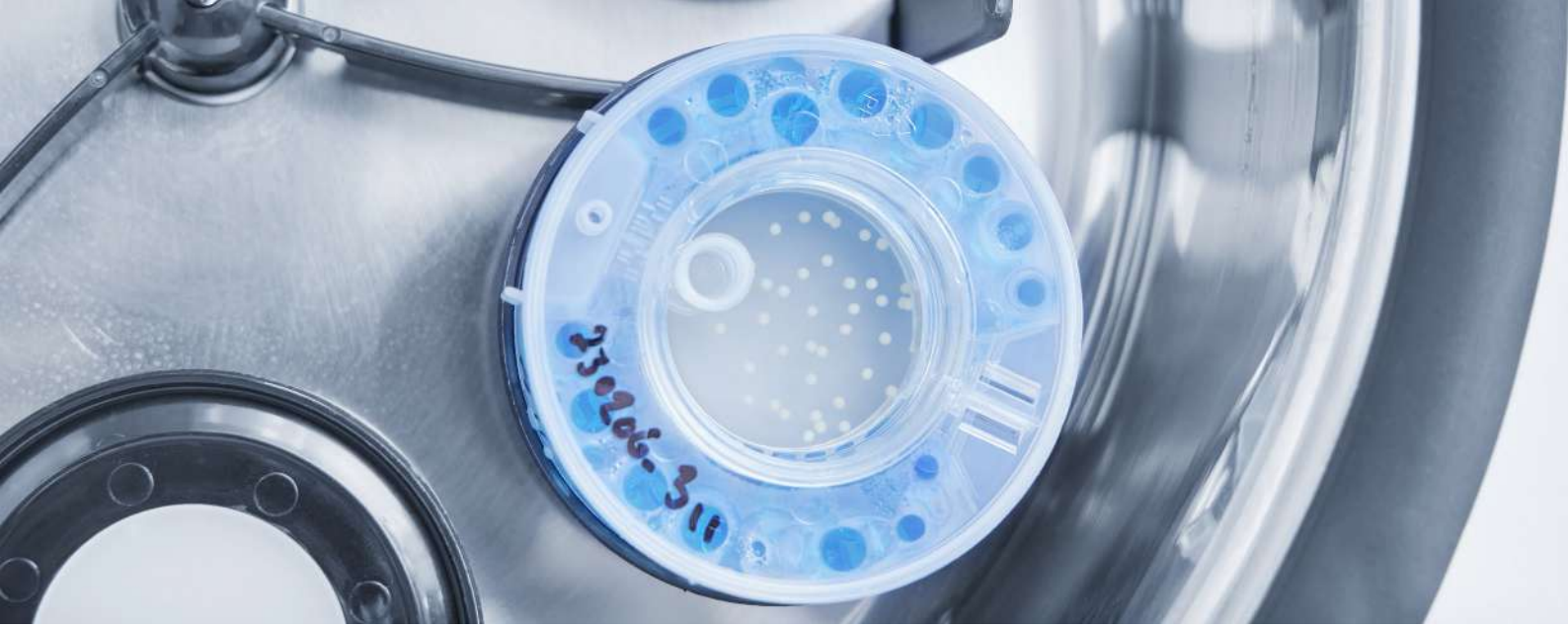
DOI: doi.org/10.1002/btpr.3253



Mapping Proteome and Lipidome Changes in Early-Onset Non-Alcoholic Fatty Liver Disease Using heptatic 3D Spheroids

Authors: Helle Sedighi Frandsen, Adelina Rogowska-Wrzesinska et al.

DOI: doi.org/10.3390/cells11203216



Get in touch

Are you interested in a demo or quote for the ClinoStar?

If you are curious about the benefits of integrating the ClinoStar in your lab, we suggest scheduling an informal meeting.

Distributore ESCLUSIVO per l'Italia

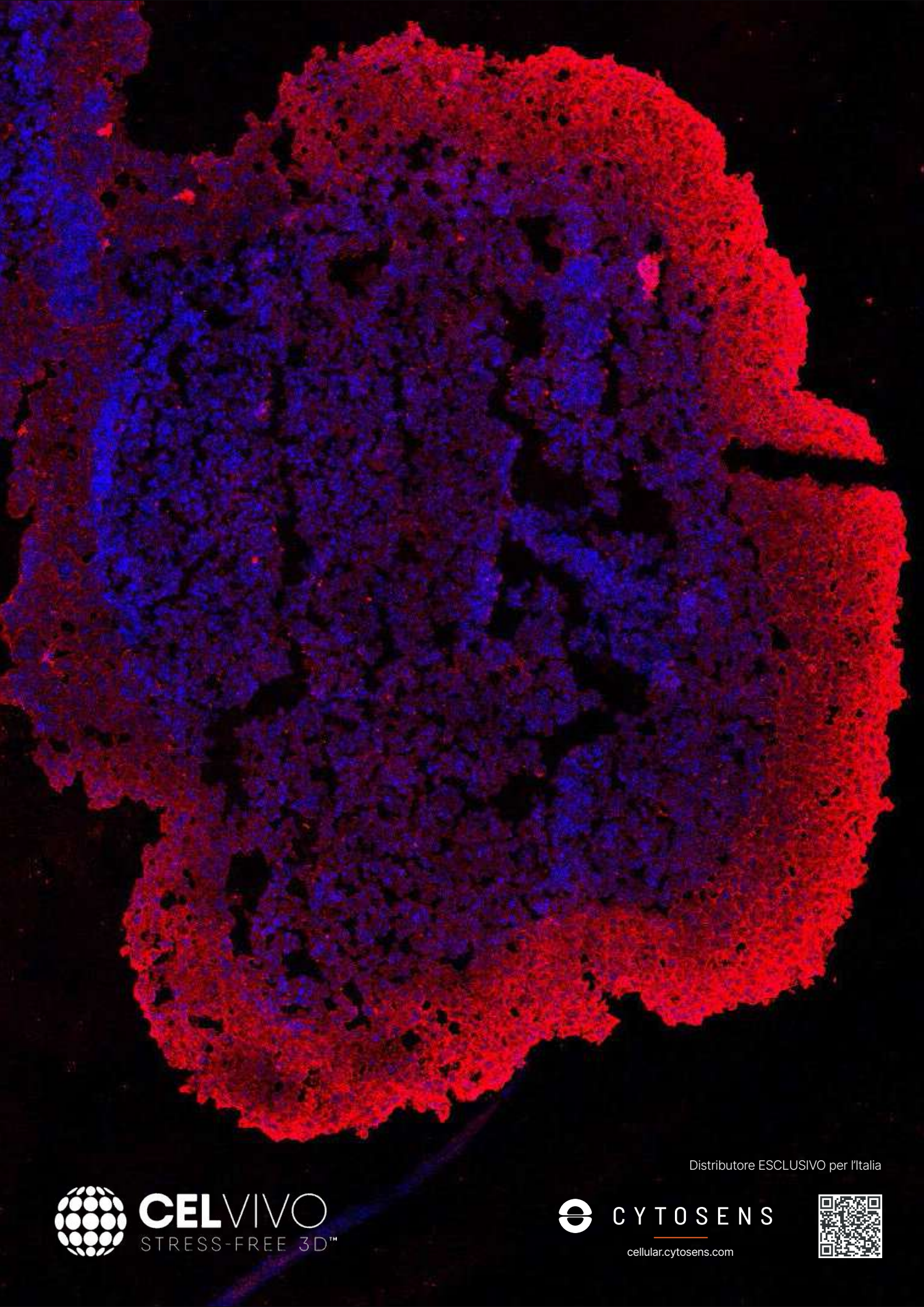
CYTOSENS

cellular.cytosens.com

cellular.cytosens.com

commerciale@cytosens.com

+39 02 947 51269



Distributore ESCLUSIVO per l'Italia

CELVIVO
STRESS-FREE 3D™

CYTOSENS

cellular.cytosens.com