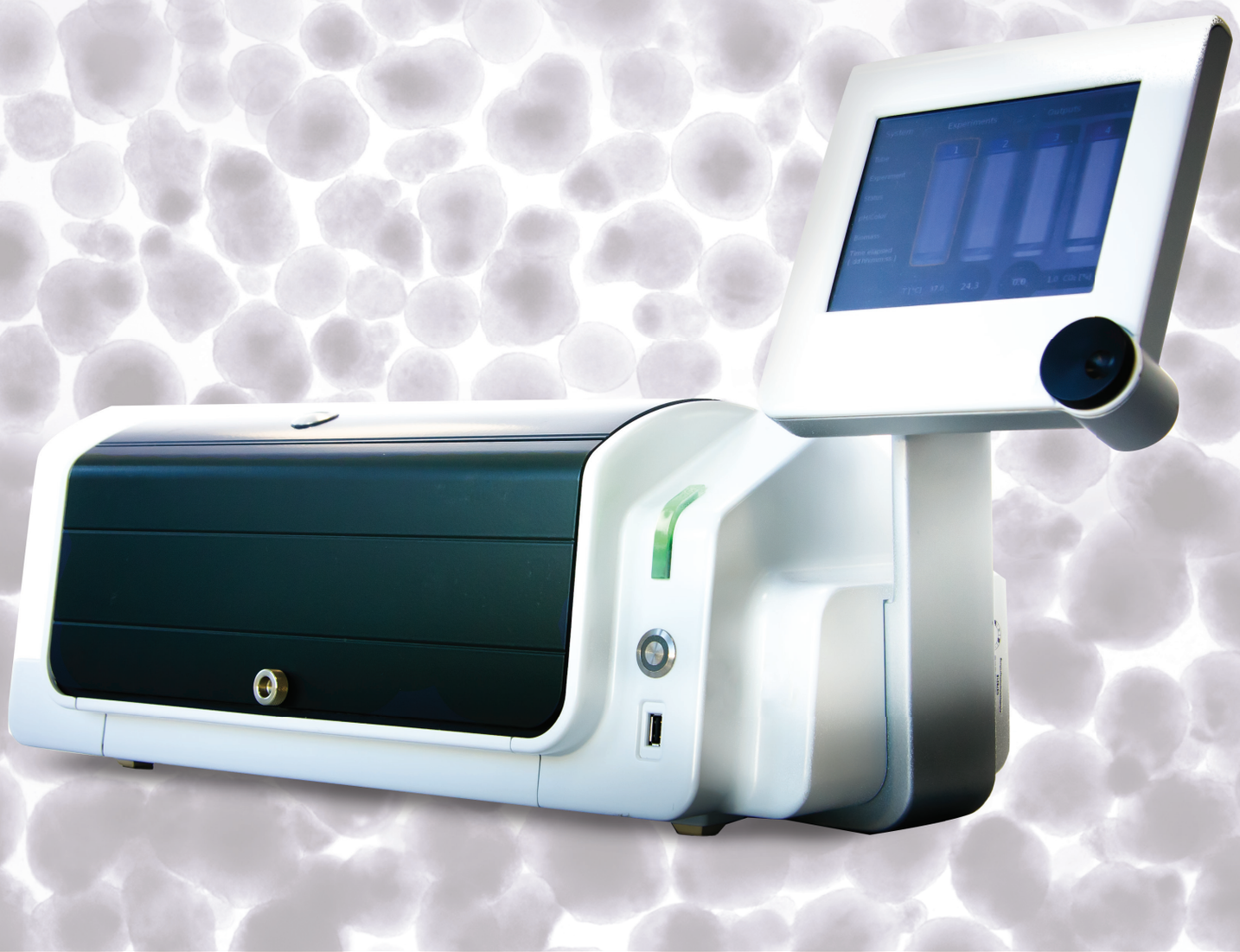
CELL Microsystems®

INNOVATING 3D CELL CULTURE

CERO 3D Incubator and Bioreactor



STEM CELLS | SPHEROIDS | ORGANOIDS | TISSUES

Break the Limits in 3D Cell Models

Stem Cells – Spheroids – Organoids – Tissues

The CERO 3D Incubator and Bioreactor offers a unique 3D cell culture technology to boost your research in stem cells, spheroids, organoids and tissues. The CERO 3D provides unmatched homogeneity and viability for long-term cultures.

Major benefits:

- Improved viability and maturation
- No embedding substrate required
- Low apoptosis & necrosis
- No shear forces
- Long-term cultivation for > 1 year
- Low running costs

CERO 3D Incubator and Bioreactor is a novel, standalone incubator that monitors and controls temperature, pH and CO_2 levels. 1- 4 individually controlled CEROtubes with a volume up to 50ml provide the highest biomass yields in a standardized way, with minimum handling requirements. The CEROtubes, with small fins and a flat bottom, are perfectly designed to reduce stress on your samples and create optimal culture conditions.

Pluripotent Stem Cells

The CERO 3D Incubator and Bioreactor provides a simple, cost-reducing scale-up and automation solution for stem cell expansion projects in biobanks, cell-based drug discovery, toxicity testing, and regenerative medicine.

Benefits:

- Microcarrier-free
- Stable pluripotency over many passages
- Easy to set-up and simple workflow
- Free-floating 3D aggregates
- Able to differentiate in 3 germ layers
- Homogeneous iPS cell and ES cell aggregates

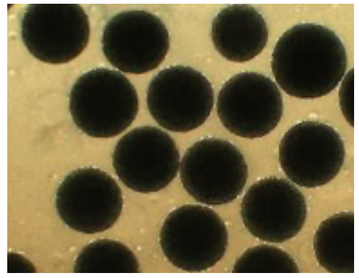


Fig 1: Human iPSC after expansion in CERO 3D Incubator and Bioreacactor

How it works

Pluripotent stem cells are directly inoculated as single cells into the CEROtube. They form homogeneous aggregates during a process called “autoadhesion”. Expansion continues for 5-9 days during which biomass increases significantly while only ~2min per day hands on time is required. The resulting stem cell aggregates can be used directly for differentiation in organoids.

Pluripotency

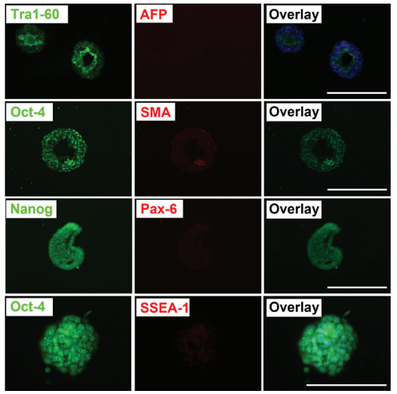


Fig. 2: Human iPSC after expansion in CERO 3D Incubator and Bioreactor tested for pluripotency

Differentiation

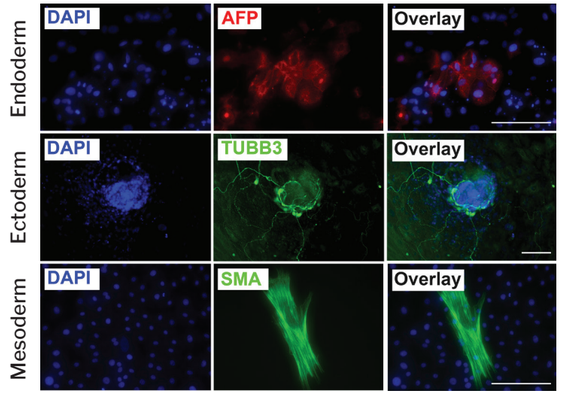


Fig. 3: Human iPSC after expansion in CERO 3D Incubator and Bioreactor tested for differentiation in different germ layers

Pluripotent stem cells expanded in CERO 3D will maintain pluripotency and can be differentiated into all 3 germ layers, as described by Elanzev et. al. 2015; Biotechnol. J. 2015, 10, 1589–1599.

Spheroids as Disease Models

Three-dimensional spheroids have great importance as in vitro disease models. They allow the ability to imitate in vivo microenvironments lacking in traditional 2D monolayer cultures. However, many scientist experience limitations when working with spheroids.

The CERO 3D Incubator and Bioreactor is the solution to many existing limitations and even enables scientists to perform experiments they were not able to do before.

Benefits
- Low apoptosis and necrosis
- Viability in long term culture > 80 days
- More than sufficient time for maturation
- Long-term proliferation
- High homogeneity
- High yield

Spheroids from a hepatocyte cell line were cultivated in CERO 3D for >80 days

Proliferation

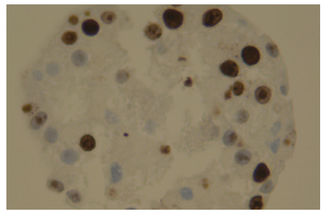


Fig. 4: Cells are positive for cell proliferation marker KI67

No Apoptosis

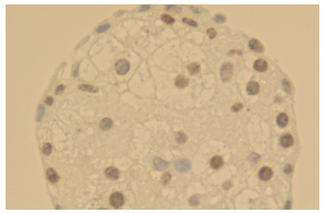


Fig. 5: Cells are negative for apoptosis marker Casp.cl.3

100% Albumin

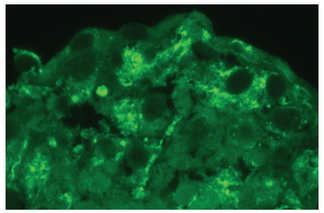


Fig. 6: Cells are positive for albumin marker

Virus Research

The CERO 3D Incubator and Bioreactor allows maturation of spheroids without necrosis and apoptosis while other technologies fail. Therefore, the CERO 3D allows the maintenance of state-of-the-art 3D cultures (see figure below). The disposable CEROtubes with HEPA filter allow for safe virus experiments.

24 hrs | 48 hrs | 72 hrs

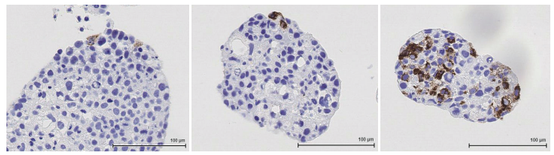


Fig. 7: Spheroid from a hepatocyte cell line was matured for 20 days prior to exposure to HCV. Spread of infection was controlled after 24, 48, and 72 hours (brown staining)

Prof. Dr. Heikenwälder, German Cancer Research Center (DKFZ), Heidelberg, Germany
"Our research takes advantage of healthy cells even from long-term cultures in CERO 3D. Moreover, we are now able to perform 3D long-term culture of human tissue specimen in CERO 3D – a paradigm shift."

Cardiac Bodies – a Complete Workflow

Stem cell derived cardiomyocytes are getting more and more attention in the field of cardiovascular science and therapies.

CERO 3D Incubator and Bioreactor enables scientists to start the workflow with stem cell expansion in homogeneous aggregates followed by direct induction and cultivation cardiac bodies. As a result, within a short time, a high number of beating cardiac bodies can be generated. Compared to induction and cultivation in orbital shakers, cardiac bodies in the CERO 3D have much higher quality, homogeneity, vitality, and yield.

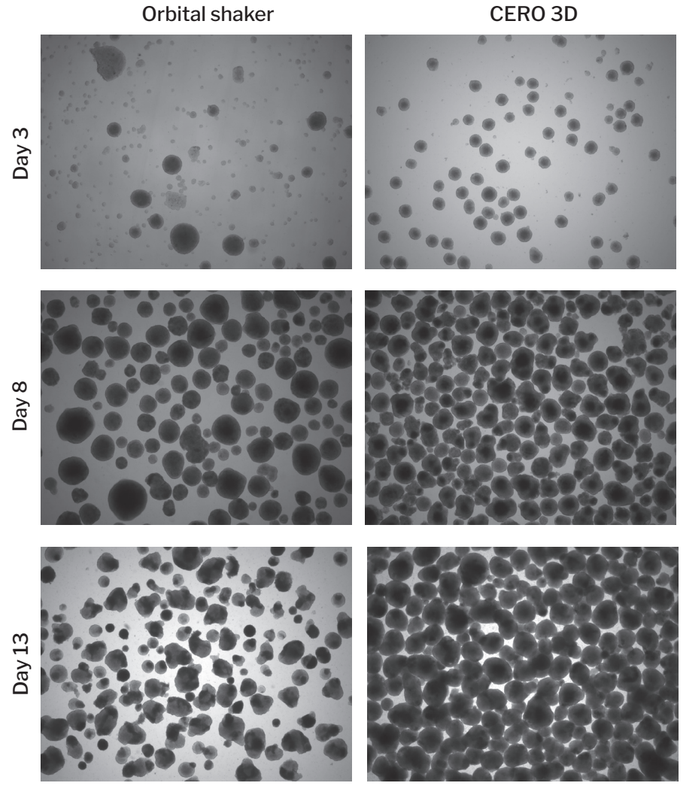


Fig. 8: CERO 3D versus Orbital shaker - cultivation of murine embryonic stem cell derived cardiomyocytes 3, 8, and 13 days after induction of differentiation

Benefits
- Homogeneous 3D aggregates in suspension
- Expansion and differentiation in the same CEROtube
- Easy to handle and standardize
- Highest yield
- No embedding substrate required
- Immediate reaction to drug treatment

Vital and homogeneous cardiac bodies generated in the CERO 3D Incubator and Bioreactor are perfect for drug testing as immediate reactions to drug treatments can be observed. Cells can also be used in 2D downstream monolayer applications.

Yvonne Eibach, Max Planck Institute, Bad Nauheim:
"This 3D cultivation system substantially improves viability, maturation and contractility, therefore provides a reliable tool for cardiovascular therapies."

From Adult Stem Cells to Organoids

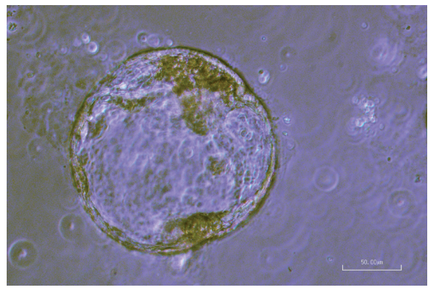
CERO 3D Bioreactor and Incubator provides a unique approach for lab scale-up production of organoids from pluripotent and adult stem cells. It offers an efficient, standardizable way to generate and maintain high yields of homogeneous organoids used as a tool in cancer research.

Benefits:
- Reduced cost and time
- Improved differentiation and polarity
- Standardizable workflows
- No stress
- High homegeneity and yield
- Long-term cultivation

Gastric Carcinogenesis Research

The generation of gastric organoids is a crucial step in the study of *Helicobacter pylori* infection and gastric carcinogenesis. The CERO 3D Incubator and Bioreactor allows generation in a much more efficient, reproducible, physiological, and cost efficient way compared to other approaches.

Day 7



Day 22

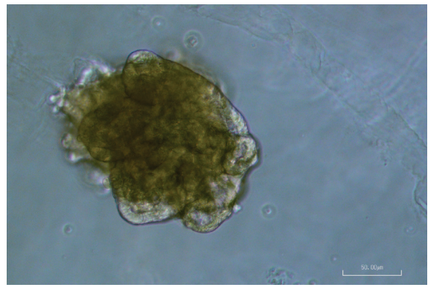


Fig. 9: Gastric organoids (bright field) at day 7 and after splitting on day 22 expanding from small cysts that expand to bigger spheres.

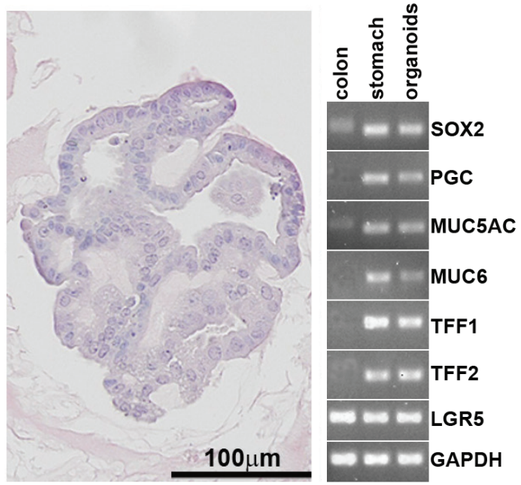


Fig. 10: HE staining of gastric organoids showing single layer of epithelia cells composed by the different cell types found in the stomach as seen in the PCR results: expression of gastric mucins MUC5AC and MUC6, trefoil factors and pepsinogen, for instance. There are also stem cells markers like Lgr5 and Sox2.

From Pluripotent Stem Cells to Organoids

The CERO 3D Incubator and Bioreactor offers the ability to combine expansion of pluripotent stem cells with the induction of differentiation and cultivation of organoids. Normally, this is a time and effort consuming, multistep process that is almost impossible to standardize. The CERO 3D Incubator & Bioreactor helps you to overcome these challenges.

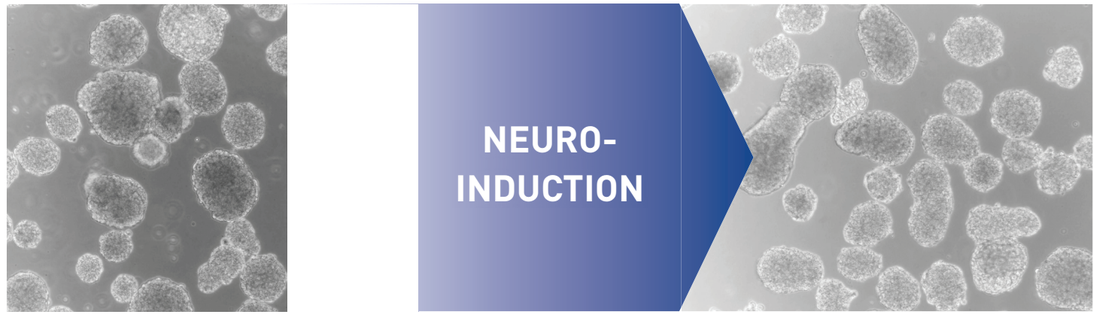


Fig. 11: Embryoid bodies before neuro induction.

Neurospheres (NSC) 5 days after induction. High density of homogeneous aggregates

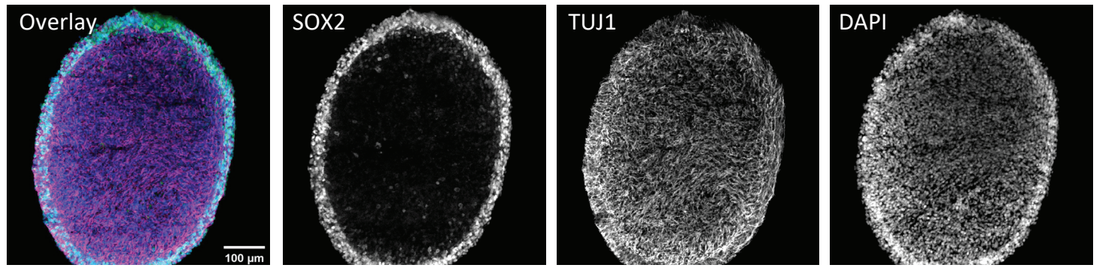


Fig. 12: Immunostaining of neurospheres 5 days after induction. The picture shows SOX2 as marker for proliferation at the outer layer of the spheroid while the signal of TUJ1 (pan-neural) and DAPI are equally spread. By Dr. Chong GAO, Dr. Kai LEI, School of Life Science, Westlake University, Hangzhou China.

The CERO 3D Incubator and Bioreactor is easy to operate and allows the generation of homogeneous aggregates NSC in high biomass (~1g per tube) in a short amount of time.

CERO 3D Incubator and Bioreactor
at a glance

Order information

- CERO 3D Incubator and Bioreactor
- CEROtubes (pack of 48)
- Convection Channel
- HEPA Filters (pack of 24)
- Adaptor Kit for CEROtubes (pack of 4)
- TYGON S3™ Tube E-3603, DEHP-free, 4,8 x 8,0 mm (price per meter)

For more information, visit cellmicrosystems.com/cero-3d

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