

3D ProtoTissue™

in vivo-like cell cultures for toxicology studies and screening

Value proposition

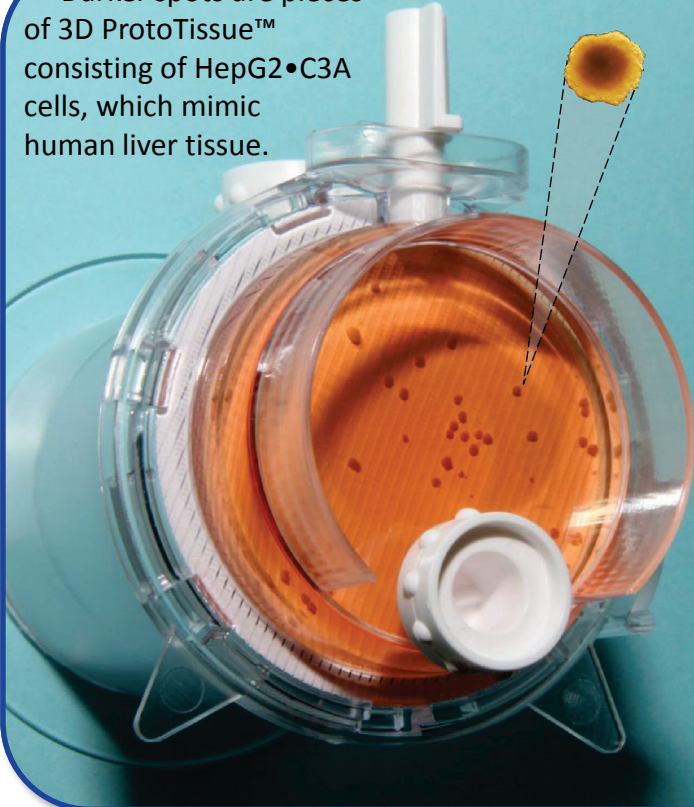
In a close collaboration between TCEL group at University of Southern Denmark and the private company MC2 biotek we offer:

- 3D ProtoTissue™ bioreactors and Multidrive Units.
- Professional training in growing and handling 3D ProtoTissue™.
- To perform compound screening (toxicology and efficacy) on a contract research basis.
- To engage in collaboration projects to further validate and expand 3D ProtoTissue™ applications.

Field of application

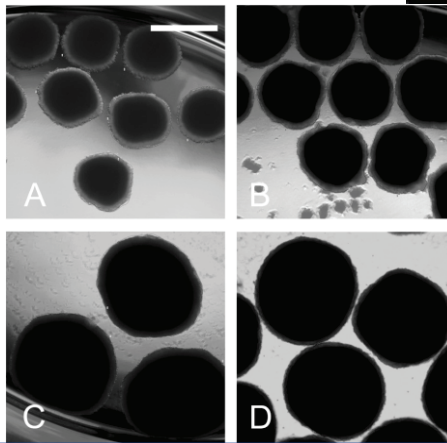
3D ProtoTissue™ is a robust and functional 3D cell culture system which can mimic human *in vivo* drug response *in vitro*. Our 3D ProtoTissue™ displays a tissue-like architecture and *in vivo* physiological functionality, which is equal or superior to primary cells in 2D culture. Thus 3D ProtoTissue™ can fill out the gap between 2D cell culture and animal studies. We primarily focus on the application of 3D ProtoTissue™ within the study of toxicity and biological efficacy profiling. However, the technology allows for expansion into almost any field where 2D cell studies are currently used.

Darker spots are pieces of 3D ProtoTissue™ consisting of HepG2•C3A cells, which mimic human liver tissue.



3D ProtoTissue™ system

Multidrive Unit in incubator rotates multiple 3D ProtoTissue™ bioreactors keeping optimum cultivating conditions independent of 3D ProtoTissue™ size



Growth of C3A spheroids. Photomicrographs of spheroid cultures at 21, 28, 35 and 42 days respectively. The bar in (A) indicates 1 mm.

Current state of technology

MC2 Biotek and TCEL have been developing 3D ProtoTissue™ system for the past 7 years. The technology is now mature and we provide equipment, disposables, technology transfer and trouble shooting to our customers.

Intellectual Property Rights

IP rights are held by the University of Southern Denmark and MC2 Biotek.

Business opportunity/potential products

We are looking for customers and collaborators who wish to use a system which mimics human tissue *in vivo*. We would welcome challenging projects involving stem cells, co-culture of different cell types or projects where existing technologies are inadequate.



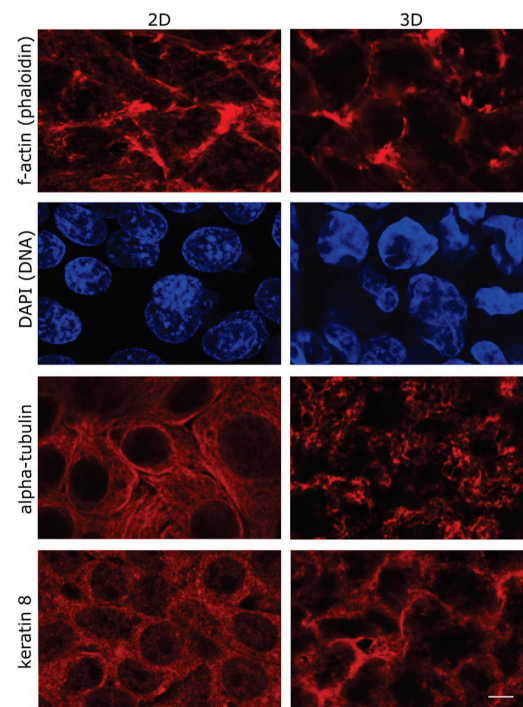
Unique 3D ProtoTissue™ solutions

Challenges	3D ProtoTissue™ solution
Optimal growth environment	<ul style="list-style-type: none"> • Rotating bioreactor • Humidified chamber with good gas exchange • Inert materials used: Non-toxic and low unspecific binding • Computer controlled multiple drive unit (wireless control, data logging) which fits standard CO₂ incubators.
Use different cell types	<ul style="list-style-type: none"> • Cells from any species can be used • Primary-, stem- and immortal cells can be used • ProtoTissue™ can be built from adherent and non-adherent cells
Easy sample access	<ul style="list-style-type: none"> • The bioreactor can be opened and provide a petri-dish like access to ProtoTissue™ and media • Repeated sampling possible by opening and closing the bioreactor.
Multiple samples	<ul style="list-style-type: none"> • Usable ProtoTissue™ from primary cells can be formed within 15 minutes • Bioreactor can cultivate up to 300 identical “biopsies” which can either be collected at once for multiple assays or at multiple time points for fewer assays.
Commercially justifiable	<ul style="list-style-type: none"> • Easy to operate and inexpensive • Low volume, inferring low culture medium to cell ratio • Easy to use, no advanced training required

Proof of Principle data

An optimized growth environment stimulates long term cell-cell interaction where cells reach a functional equilibrium for repetitive testing (over a month). This results in:

- *In vivo* physiology
Wrzesinski et al. Toxicology Research 2013 2(3) 163-172
- *In vivo* cellular ultrastructure
Wrzesinski and Fey. Toxicology Research 2013 2(2) 123-135
- Predictive toxicology better than primary hepatocytes
Fey and Wrzesinski Tox Sci 2012, 127(2) 403-411
- Cells recover to baseline after drug treatment
Fey and Wrzesinski, Valproic acid 2013 ISBN: 978-1-62417-952-5
- Dramatic improvements in molecular pathways and regulation (submitted manuscript – see right)



The inventors

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