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Conference Report

Disease Cell models – Their Use in Industry
TEDD Workshop in Sion on 27 March 2014

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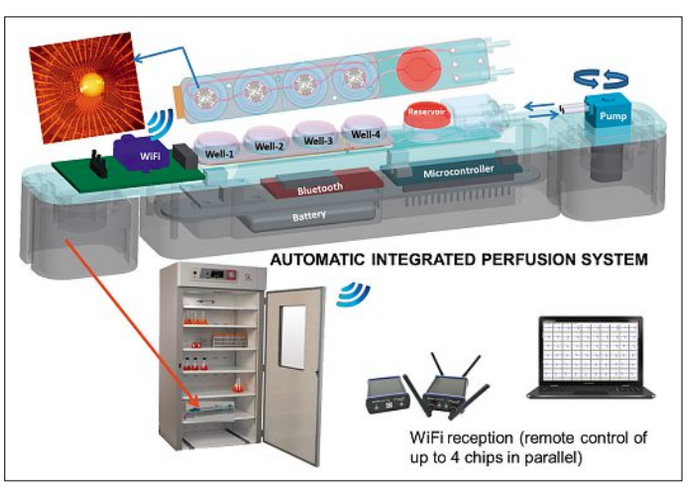
Abstract: On 27 March 2014, experts met at the first TEDD Workshop 2014, held at the HES-SO Valais/Wallis in Sion, to present innovative cell models for industrial applications. This was the first time that a TEDD event had been organized in French-speaking Switzerland and it offered local network partners an opportunity to showcase their research activities.

Keywords: Disease cell models · Idiopathic pulmonary fibrosis · Molecular ageing profiles · Toxicological screening

In vitro Models for Neurotoxicity Studies

How can we recreate the complexity of the human body, in which various organs interact and in which one type of tissue affects the ability of another type to function? The *in vitro* tools developed by ***Luc Stoppini***, Professor of Biotechnology at the HES-SO Tissue Engineering Laboratory in Geneva, in collaboration with his colleague Prof. ***Dominique Müller***, represent one approach to this task.



Scheme of the stand-alone BioChip showing the different parts of the integrated system. A miniature peristaltic pump allows the perfusion of the culture medium from the reservoir to the different wells through a Bluetooth remote control. The insert shows a 3D neural culture derived from hESCs placed onto the multi-electrode array. Recordings of electrical signals are sent to the acquisition software through a WiFi transmission. Image: Luc Stoppini.

Luc Stoppini is analyzing the effect of therapeutic agents or chemicals on brain tissue in order to develop real alternatives to animal-based experiments. This work produces sections of rodent brain, which he grows in air-liquid cultures on porous and transparent membranes. "We are studying communication between neurons by recording the level of synapse responses in various areas of the hippocampus in the brain," Stoppini explains. He uses human embryonic stem cells to create tissue *in vitro* which then form a basis for toxicological screening. "3D tissue has a complex biological structure that fills the gap between classic 2D cell culture and animal tissue," he continues. "We are creating a stable and durable *in vitro* culture-based environment in 3D as a model for *in vitro* neurotoxicity testing." This '21st century petri dish' provides alternatives for testing new medicines and for gaining a better understanding of why an organism reacts and adapts when it is exposed to xenobiotics.

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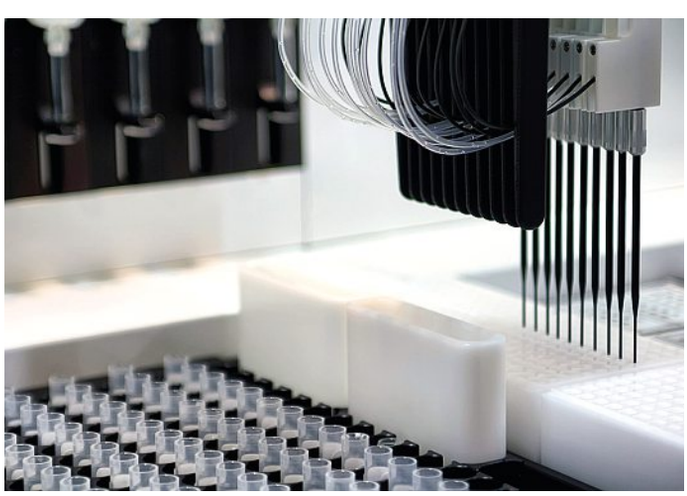
Anti-ageing as a Research Topic

"The molecular mechanisms of ageing are difficult to elucidate, but they seem to be divided into four groups," explains ***Peter J. Girling***, founder of CELLnTEC Advanced Cell Systems AG in Berne. *Signalling pathways* provide access for many intrinsic and extrinsic factors that modify cell behaviour and facilitate the ageing process. The *mitochondrial electron transport system* is known to be the cell's energy generator. Disruption of these mechanisms can boost the production of ROS (reactive oxygen species), leading to greater damage to the DNA and membranes and reduced stem cell function. *Apoptosis* and *senescence* are important mechanisms that selectively eliminate damaged or defective cells and protect against cancer. They are regulated by the p53 protein. However, activation of p53 may promote ageing, for example if stem cell function is reduced as a result of impaired mitochondrial functioning. Recent studies have documented the *critical role played by DNA repair mechanisms* in maintaining stem cell differentiation and delaying the ageing process. "The latest information about molecular ageing mechanisms combined with innovative, stem cell-based *in vitro* models is now enabling us to produce comprehensive molecular ageing profiles of cells with and without cosmetic substances in just 2–3 weeks," explains Peter Girling, who coordinates research and development at



Focusing on anti-ageing: CELLnTEC worked with Biognosys, the leader in multiplex proteomics, to develop a powerful MRM-based process capable of quantifying over 100 proteins rapidly and precisely in a single sample. Image: CELLnTEC.

CELLnTEC. "This lets us identify the potential and impact of cosmetic ingredients more accurately and to respond much more effectively to the needs of the cosmetic industry."

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The Fight against Pulmonary Fibrosis

Idiopathic pulmonary fibrosis is a relatively rare lung disease whose cause has not been researched in detail. It usually affects men over 50. They suffer from increasing breathlessness caused by scarring of the lung structure due to the formation of excess connective tissue in the lungs. This could be due to miniscule injuries to the alveolar epithelium. ***Marcel Felder***, who works at the ARTORG Centre for Biomedical Engineering at the University of Berne, and Prof. ***Thomas Geier*** and his research team at the Inselspital hospital in Berne are focusing their attention on microlesions of this kind. In order to better understand the mechanisms involved in idiopathic pulmonary fibrosis, they have developed a microplatform for culturing epithelial alveolar epithelial cells and subsequently damaging them by means of hydrodynamic focusing. Injuries of tiny dimensions can be created very accurately, something that is not possible with the traditional approach. Moreover, this technique in no way damages the cells at the wound margin. This type of microfluidic platform allows *in vivo* conditions to be recreated more accurately *in vitro*, thus substantially enlarging our understanding of epithelial repair mechanisms. "Microfluidic wound healing systems allow us to adjust the conditions for regeneration more precisely and are an interesting alternative to existing systems," comments Felder, who has an MSc in biomedicine and works in the Lung Regeneration Technologies group under Professor Olivier T. Guenat. "Microsystems of this type are especially well suited to use in personalized healthcare since these tests require only a very small amount of patient material."

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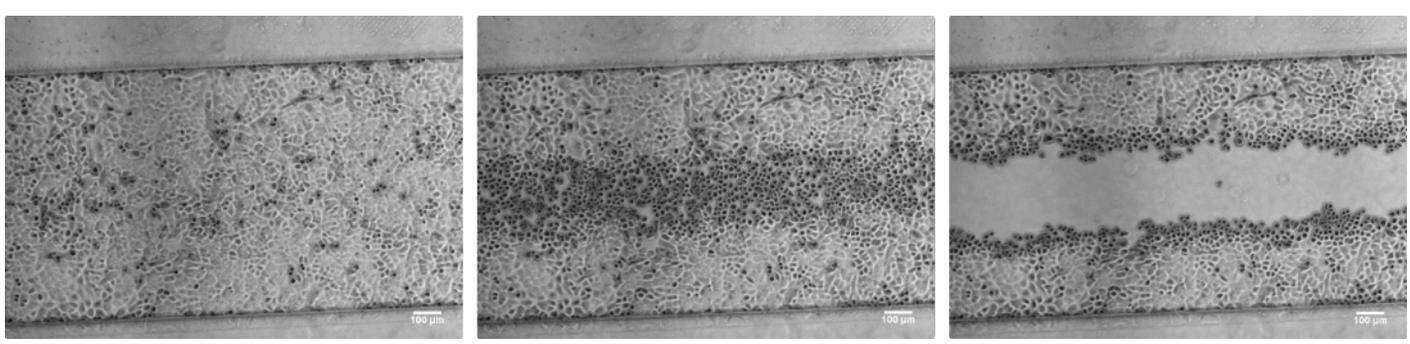
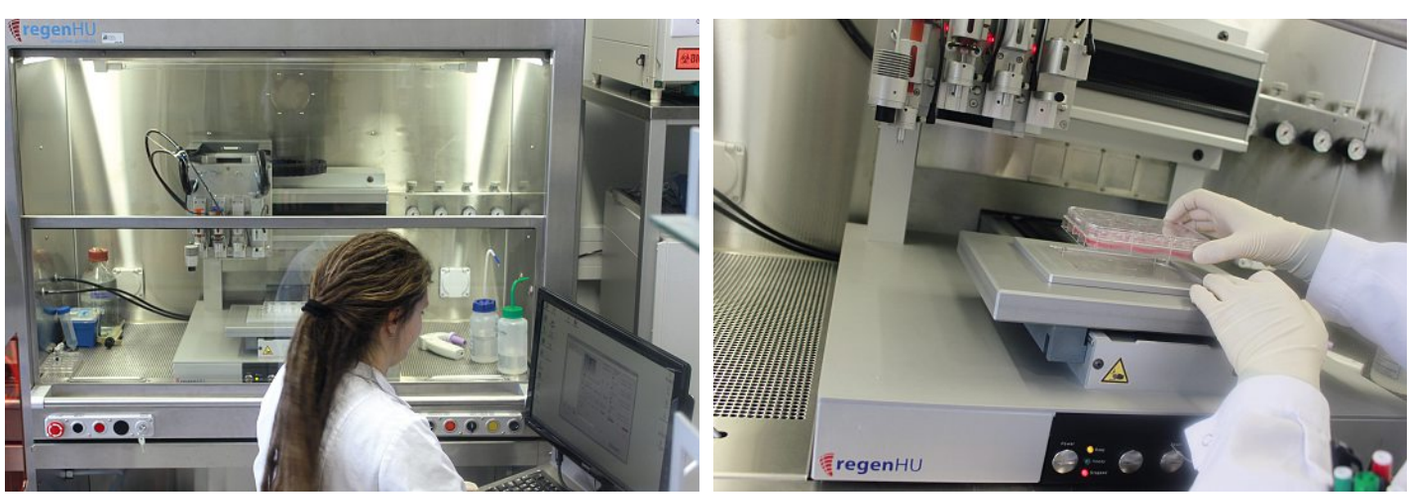
TEDD on the Road to Success

The TEDD network continues to launch new activities with its customary élan. In January it submitted a proposal for a National Research Programme to the State Secretariat for Education, Research and Innovation. A small selection from the 69 proposals received was submitted to the Swiss National Science Foundation for a feasibility study. The TEDD proposal, which integrates two further initiatives, was one of the selected few. The proposal focuses on organ-like tissue models for medicine and animal welfare. Members of the TEDD Advisory Board and the management team produced a special theme edition featuring 19 reviews of 3D tissue models. It appeared in the April 2014 issue of *Advanced Drug Delivery Reviews*.[1]

The TEDD management team is currently preparing for the international *3D cell culture* symposium that is due to take place in Freiburg im Breisgau from June 24–27, 2014. TEDD is represented on the Scientific Board and is organizing the workshop on *Advanced in vitro liver models for toxicological profiling*.[2] In addition, the TEDD Annual Meeting will be taking place in Wädenswil on October 9, 2014. It is part of the *European Biotech Week* organized by the National Thematic Network NTN Swiss Biotech. In keeping with the *biotechnet Switzerland*



Creation of an alveolar microlesion using hydrodynamic focusing in a microplatform. Time-lapse images of the alveolar epithelial cells before, during and after experimental injury. Image: ARTORG Center.



3D bioprinting of skin models: Layer-by-layer production of skin enables dermis and epidermis to be created rapidly and precisely, with an OCT camera ensuring *in situ* quality control. Images: Stephanie Mathes.

Representatives of the TEDD network and the HES-SO with speakers at the meeting organized by Prof. Bruno Schnyder and Marc Pfeifer at the HES-SO in Sion. Image: HES-SO Sion.

strategy, TEDD is seeking to bring representatives from industry and research together with the aim of developing innovative 3D tissue cultures and promoting their use. Events like this create shared fertile ground on which to develop new ideas and initiate network projects.

Information: *www.icbc.zhaw.ch/tedd*

The TEDD Competence Center (Tissue Engineering and Drug Development) is part of the technology platform biotechnet Switzerland.

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[1] Innovative tissue models for drug discovery and development, 'Advanced Drug Reviews', volumes 69-70, pp 1-270 (20. April, 2014), *http://www.sciencedirect.com/science/journal/0169409X/69-70*

[2] *http://events.dechema.de/en/3DCC2014*