STEM-3D
Multi-Organs on a Chip: The next generation of biochips to test new drugs or chemicals

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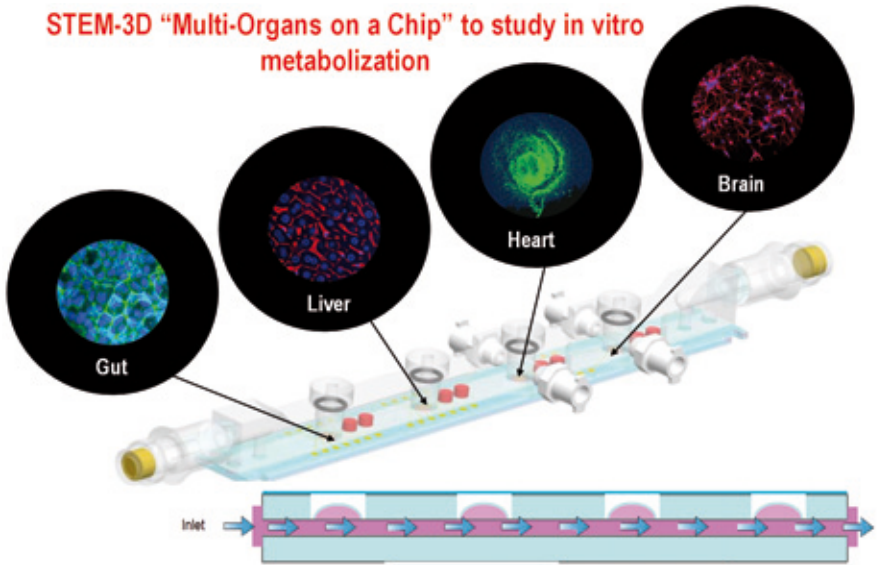
Descriptif

We have developed a small-volume *in vitro* system in which intestine-like cells, hepatocyte cells and 3D micro-organs derived from embryonic stem cells (cardiomyocytes and neural cells) were cultivated in 4 separate porous membrane micro-chambers connected by micro-channels with the presence of biosensors at different levels. A dedicated perfusion system based on air pressure was used to allow the circulation of the culture medium to the different micro-organs through a microfluidic system.

Points forts

Our technology will :

- Accelerate the evolution of the toxicity risks and hence dramatically shorten research cycles for the pharmaceutical and other industries.
- Improve the performance of toxicity testing systems and make a major contribution to safety pharmacology.
- Bring the potential of major time- and cost-saving factors for drug and chemical compound screening due to the automatic perfusion and sampling platform that allow testing several biochips in parallel, and hence increasing the testing throughput.

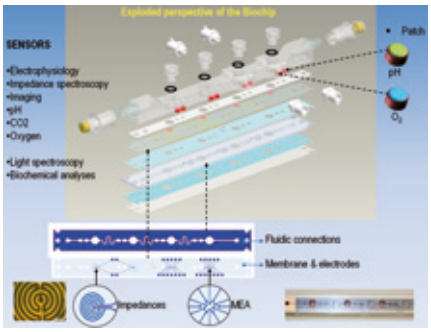


Micro-organs are placed within micro-chambers with bio-sensors connected through a microfludic system.

In vitro cell-based assays are often of limited predictive relevancy because they do not mimic with sufficient realism the complex environment to which a drug candidate is subjected within a living organism. Recent studies had showed that cell toxicity assays, and assay endpoints are useful for high-throughput cytotoxicity analysis in microfluidic devices, and had also concluded that 3D cell cultures that mimic the *in vivo* tissue are essential for obtaining results comparable to the *in vivo* response.

Based on these results, we have fabricated a small-volume *in vitro* system in which 3D micro-organs derived from embryonic stem cells or human cell line cells are cultivated in separate porous membrane microchambers connected by microchannels with the presence of biosensors at different levels. By selecting appropriate bio-mimic different human tissues in 3D we are reproducing *in vitro* some aspects of complex interactions occurring *in vivo.* While conventional culture plate models only measure the response of a single cell type, our "Multiorgans-on-a-Chip" system will allow us to capture the reactions of organ system as a whole ("organ interactions on-a-chip" concept). For example, metabolites resulting from a drug's influence on one organ can reach other organs and exert their positive or negative effect. These biochips will provide insight into inter-organ interactions resulting from exposure to pharmacological compounds, a capability which has not been previously demonstrated using *in vitro* systems. Therefore, we hope that this system will be a more predictive tool in experimental pharmaceutical screening for efficacy and toxicity.

Finally, in order to increase the throughput we are developing a semi-automatic platform which will allow us to screen molecules on up to 12 biochips in parallel.



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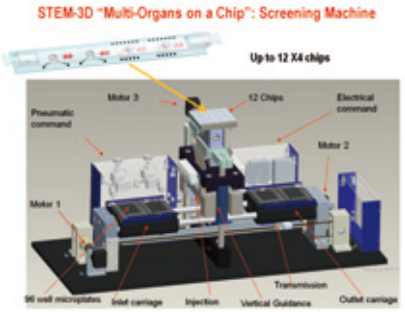

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Valorisation

- The development of our "MultiOrgans-on-a-Chip" will significantly contribute to the reduction and replacement (3R's) of animal experiments.
- The proliferation and the cell growth in three-dimensional structures will give us unique opportunities to observe selected cell behavior under normal or pathological conditions. This knowledge will likely enable meaningful advances in tissue engineering to design functional bionic systems that will be used in regenerative medicine.
- There is clearly a need for more predictive *in vitro* systems for the pharmacy industry (to decrease the attrition rate of new drugs), toxicology, and food companies. We have already received positive feed-back from our industrial partners to accept this kind of new technologies.
- In collaboration with Prof. KH Krause, we have created a start-up company Neurix S.A (a spin-out of the University of Geneva and hepia) that will offer services to pharmaceutical or food companies to assess the beneficial and detrimental effects of novel drugs or natural products (mandates).
- We have recently received a funding from the CTI to develop a specific assay that will open up new avenues for applied research as well as for the commercialization of this technology.

Légendes

1 - Visualization of the microfluidic system as well as the different biosensors integrated to the biochip.
2 - A semi-automatic system was developed where molecules to be tested are placed within standard microplates.