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HEALTH ICT

‘Body-on-a-chip’ set to accelerate drug discovery

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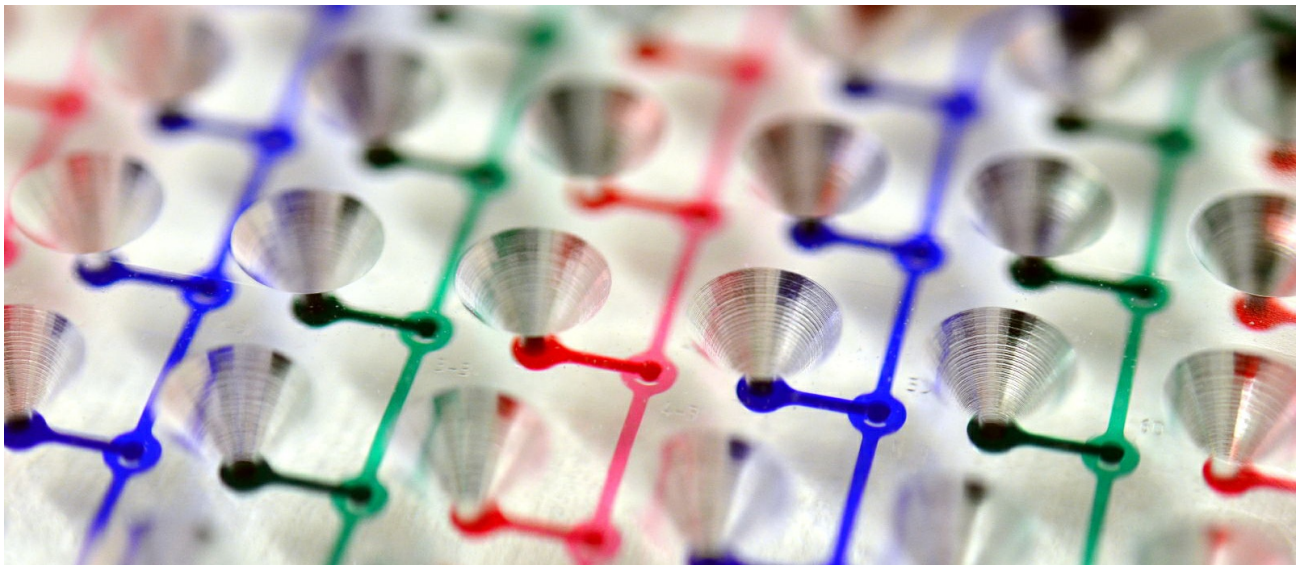

Body-on-a-chip technology could test if drugs work before going to human trials without the need to test on animals. Image courtesy of InSphero

Testing new medicines on miniature samples of human tissue, known as organ-on-a-chip or – in the case of multiple tissues – body-on-a-chip technology, promises to make medical research faster while reducing the use of lab animals.

If you were among the millions of people who tipped cold water over their heads during the Ice Bucket Challenge craze in 2014, you might already be familiar with amyotrophic lateral sclerosis (ALS). Sadly, despite the surge in awareness and donations, this progressive neurodegenerative disease is still fatal and there is no treatment.

Many would-be drugs have worked in animal models only to fail in human trials. This has been bitterly disappointing for patients and scientists, as well as costing millions of euros in research funding. However, a new approach to studying the mechanisms that cause disease could allow researchers to test potential drugs much more quickly using so-called chips that mimic the human body.

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Scientists at the University of Crete, Greece, are studying human brain cells to understand what goes wrong in ALS patients and how it can be fixed. They say a human brain-on-a-chip could pave the way for a new era in research.

Professor Achilleas Gravanis leads the EU-funded ALS-on-a-chip project. His team and Dr Dimitris Tzeranis, a Marie Skłodowska-Curie fellow, working with colleagues at the Massachusetts Institute of Technology and the Harvard Stem Cell Institute, US, are developing a 3D chip loaded with motor neurons and myocytes – cells essential for movement – and star-shaped brain cells known as astrocytes.

'These cells are playing a pivotal role in ALS,' he said. 'We are comparing the cells of ALS patients and healthy people to identify differences, combining state-of-the-art systems pharmacology and imaging techniques.'

The chip is constructed using three-dimensional scaffolds made of collagen, a human protein, lying in glass micro-wells.

Using it, the scientists can run studies to define the cause of the disease and test new drugs to see if they improve how the human brain cells work. The benefit of using a 3D chip is that it can mimic human tissue more accurately than tests on animals or 2D cell culture.

Petri dish and chips

For one thing, the tissues are human; for another, the next generation of chips will have a system that mimics the blood supply, using microfluidics. This is a key difference to looking at isolated cells in a petri dish, as it offers a more realistic simulation of how a drug would perform in the dynamic environment of the body.

It may not mean an end to animal research altogether, but it would reduce the use of animals and, by weeding out drugs that are likely to fail, increase the success rate for potential medicines that make it to human trials.

Prof. Gravanis says the chip could be an intermediate step between initial safety and efficacy tests in animals and expensive trials in human volunteers.

'This would enormously reduce the number of animals used,' he said. 'And it allows us to test many more compounds from a chemical library. If the ALS chips with human neuronal cells confirm that a compound works, we will have a better chance of success in humans.'

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>
> *Professor Achilleas Gravanis, University of Crete, Greece*

For diseases like ALS and Alzheimer's Disease – where new treatments are desperately needed – this will make research more efficient. 'It is very disappointing that none of the ALS drugs tested on animals worked well in humans, but you cannot simulate the human body by looking only at animal cells in a dish,' Prof Gravanis said. 'We need something in between.'

It may take another two to three years to evaluate the ALS chip containing human tissues, but the team in Crete is already looking to apply their tool to Alzheimer's and other diseases.

The brain is not the only organ being mimicked on a chip. InSphero, a biotech start-up based in Switzerland, is set to produce a 3D microtissue chip that allows researchers to study how drugs interact with the liver, heart and other body parts at the same time.

Holistic view

Dr Jan Lichtenberg, InSphero's chief executive, says combining several tissues types in one microfluid chip gives a more holistic view of what's happening inside the body.

'Some existing drugs are only activated when they are chopped into smaller pieces by the liver,' he explained. 'One of these smaller fragments is the active drug that affects the body, so we need to have liver tissues as part of the chip along with the tissues you expect the drug to act upon.

Not only do drug developers need to know whether a molecule is an effective treatment, they want to know that it's safe. To test a cancer drug, for example, researchers might need liver cells to activate the molecule, tumour cells to test whether it kills cancer, and other cells to check whether the drug is toxic.

'You could have an anti-cancer drug that, once it is metabolised in the liver, becomes toxic (to) heart muscle,' explained Dr Lichtenberg, who leads the EU-funded BOC project.

Dr Olivier Frey, also from InSphero, is working towards commercialising the technology to meet the needs of the market. 'A prototype had been developed as part of a proof-of-concept study but we have redesigned it to make it compatible with industry standards,' he said. It could be of major interest not only to medical researchers but also to the chemical and cosmetic industries.

The chip, which could be on the market at the end of 2017, will be flexible enough to meet the needs of researchers. 'Labs will be able to create different systems by choosing to add different combinations of tissues in the chip,' Dr Frey said. This new era of research is fast approaching.

More info

BOC

ALS-on-a-chip