New technology to speed up testing of cancer drugs

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Credit: University of Nottingham

A new technology that could speed up the testing of drugs and reduce the use of animals in the lab has been developed by scientists at The University of Nottingham.

The researchers in the University's Division of Cancer and Stem Cells have designed a device that allows dozens of tiny balls of cells, called spheroids, to be sliced simultaneously to examine their structure and function.

The method, which is detailed in the academic journal *Scientific Reports*, will enable other scientists to more rapidly assess whether new therapies and tissue engineering are likely to work in the real world, and could be up to 11 times more efficient than current methods.

Dr Delyan Ivanov said: "When I started exploring spheroids by slicing them, I was frustrated by the slow and gruelling nature of the process. I had to cut spheroids cultured in many different drugs and it was taking me months, there were many manual steps.

"Inspired by the principle of 3D printing, I decided to design my own tool for arranging all spheroids from an experiment in the same plane in a microchip-like pattern in a gel."

Overcoming limitations

Dr Ivanov, who designed the device during his EPSRC-funded doctoral prize fellowship (Engineering and Physical Sciences Research Council), was able to refine the design after enlisting the help of Joseph White, a research technician in the University's Additive Manufacturing group, who printed 20 different versions of the prototype for testing.

The team will now be sharing the design files and methodology openly with the scientific community to ensure that everyone can immediately benefit from the technology.

New drugs for cancer and strategies to build tissues from stem cells have historically been tested in the laboratory in human cells grown as a 'carpet' on plastic. In contrast to the natural behaviour in the human body, the cells in these two-dimensional cultures have limited interaction with each other and produce little of the natural 'glue' called extracellular matrix.

To overcome these limitations, tiny three-dimensional balls of cells (spheroids) which are smaller than a pinhead, interact more closely with one another and behave more like their natural counterparts in the human body are now being used.

Scientists are growing spheroids derived from tumour and normal tissues and have even developed improved, more organised structures which resemble organs, called organoids.

The catch was that, while two-dimensional structures can be examined just by looking down the microscope, the 3D spheroids need to be sliced into hundreds of thin slices just 0.005mm (5 µm) thick in order to get a reliable picture of their structure and function.

Reducing animal testing

The Nottingham invention allows researchers to arrange 66 spheroids grown in the presence of different drugs and molecules and slice simultaneously and more quickly, allowing scientists to answer more questions using the same set of laboratory-grown tissues.

Many experiments currently done in animals could be done in these spheroid and organoid cultures reducing and ultimately replacing some animal testing in cancer research and tissue engineering.

Dr Anna Grabowska, who mentored Dr Ivanov at Nottingham during his post-doc, added: "We would like to create cell-based models in the laboratory which closely mimic the natural behaviour of cells in the human body. We are doing this not only by culturing cells as spheroids but by including multiple cell types and the right extracellular matrix. Delyan's technology would allow us to monitor the behaviour of laboratory models of human tissues and organs in a faster, more efficient way."

The paper being published in *Scientific Reports* includes the blueprints of the device, demonstration of the possibilities of the new technology and offers an instructional video to show researchers how to make their own spheroid microarrays.

More information: Delyan P. Ivanov et al. Spheroid arrays for high-throughput single-cell analysis of spatial patterns and biomarker expression in 3D, *Scientific Reports* (2017). DOI: 10.1038/srep41160

Provided by University of Nottingham