New cell model to speed up development of brain tumour drugs

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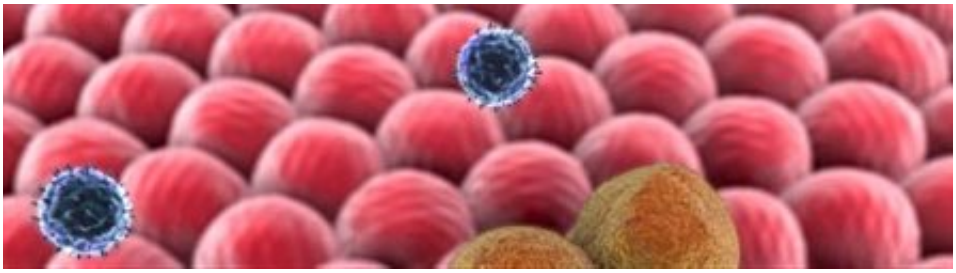

New research from The University of Nottingham looks set to improve screening for new cancer drugs and drug delivery systems specifically designed for children with brain tumours.

New cancer drugs are typically screened against cancer cells which are grown in culture dishes in labs (known as 2D culture) and are then compared with normal cells from animals. However, growing the human cancer and normal human cells in small balls (known as 3D culture) has been repeatedly shown to mimic more closely the conditions in the human body. Mainstream adoption of physiological 3D models has been stalled in the past 50 years due to high price, low speed and poor reproducibility.

In a new paper published in *PLOS One* , academics report a new methodology, which permits drug screening tests to be carried out

efficiently, accurately, conveniently and in high throughput in 3D cultures. Using a specially coated multi-well plate they were able to produce single ball-shaped (spheroid) cultures of human cancer and normal brain stem cells.

Prospective treatments can be quickly assessed in this test for their efficacy in killing tumours and safety to the developing brain. The growth or death of the cells are then determined after drug treatments by three different parameters including a novel measure of spheroid size. The spheroids are photographed with a camera-equipped microscope and their growth (expansion) and death (shrinkage) are determined using a specially written open-source image analysis program.

The first author of the paper, Delyan Ivanov, a PhD student at the School of Pharmacy at the University, said "The test has been specifically developed to use equipment and procedures which are readily available in all labs, so that this platform can be easily adopted by a range of laboratories in both academia and industry."

Senior author and principal supervisor Dr Martin Garnett has been developing new drug delivery systems to treat cancer together with Professor David Walker at the Children's Brain Tumour Research Centre (CBTRC) at Nottingham for some years. Dr Garnett said: "We needed to develop this test to investigate the properties of a nanoparticle drug delivery system we were working on. However, now we have developed this test we can see it has great potential for cancer drug screening in general, and could be applied to a wide range of situations."

Professor David Walker said: "This drug screening system will form a central part of our plans at CBTRC focussing research expertise to accelerate developments in drug delivery systems specifically designed for children with brain cancers. Brain cancers, constitute the biggest cancer killer in childhood and young adults up to age 40 years and

accounts for one in 50 of all deaths in people under 60 years of age."

A key contributor to this work was co-supervisor Dr Terry Parker, working within CBTRC, who was an expert in 3D brain cell culture, but who sadly died last October. The PhD project was part of the EPSRC AstraZeneca Centre for Doctoral Training on targeted therapeutics and next generation medicines, the UK's first pharmaceutical sciences Doctoral Training Centre jointly-funded by industry. Oncology is a key therapeutic area for AstraZeneca and the programme supports the company's pursuit of scientific leadership.

More information: Ivanov DP, Parker TL, Walker DA, Alexander C, Ashford MB, et al. (2014) "Multiplexing Spheroid Volume, Resazurin and Acid Phosphatase Viability Assays for High-Throughput Screening of Tumour Spheroids and Stem Cell Neurospheres." *PLoS ONE* 9(8): e103817. DOI: 10.1371/journal.pone.0103817

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