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Non-destructive technique measures oxygen levels in 3-D cells used for toxicity testing

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A non-destructive technique which can measure the concentration and consumption of oxygen in 3D models of biological cells has been developed by Plymouth University in partnership with pharmaceutical company AstraZeneca.

Using Electron Paramagnetic Resonance (EPR) oximetry, scientists assessed the gradient of oxygen concentration within spheroids, 3D cell cultures typically used for testing the chemical toxicity within liver and tumour models.

It had previously been suggested that the centre of spheroid cultures becomes devoid of oxygen leading to cell death that may limit their use, but until now there has been no way of measuring the precise levels.

Work by PhD researcher Laura Langan and Senior Research Fellow Dr Nicholas Dodd demonstrated smaller spheroids with a diameter of less than 120 micrometres (μm), and containing fewer than 2,500 cells, lose less than 12% of their oxygen concentration after one week decreasing to less than 50% two weeks after their creation.

Overall, the study recommends the use of smaller spheroids to allow comparable oxygen concentrations to native tissues, with scientists believing the research provides further evidence of the appropriateness of these in vivo studies as a tool to elucidate fundamental biological processes in the spheroid systems and aid in the reduction of whole animal experiments.

The study was led by Professor Awadhesh Jha, from the School of Biological Sciences, and Professor Simon Jackson, from the School of Biomedical and Healthcare Sciences, at Plymouth University.

They said: "It is widely accepted that the biological activities present in spheroids more closely reflect key characteristics of the living organism, and as such may offer a more relevant alternative to in vivo exposure in biological research. EPR oximetry has provided insights into the size and cell seeding densities at which oxygen gradients play a confounding role in subsequent exposure applications and thus enable the wider use of the spheroid model to non-tumour based biological studies."

Over the past three decades, the use of three dimensional cell culture has gained increased recognition as an important tool in biological research and pre-clinical trials over conventional organs and animal models.

Spheroids are one example of these, and are typically used to assess the chemical toxicity and evaluation of environmental samples in biological and ecotoxological studies.

Plymouth University has previously perfected the technique of coaxing cells from the liver of rainbow trout and then manipulating them to form a three-dimensional spheroid.

This ball of cells behaves much more like normal animal tissue than cells grown in traditional ways in the lab and so can give researchers a more accurate picture of how an animal's body would respond to a chemical in the environment.

The current study is published in the *PLOS ONE* scientific journal.

More information: *PLOS ONE*, dx.doi.org/10.1371/journal.pone.0149492

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