Realistic 3D Tumour Through Tissue Engineering Using Silk Scaffolds

National University of Singapore

A team of NUS researchers from the Departments of Bioengineering and Orthopaedic Surgery has developed a highly realistic three-dimensional (3D) tumour model. As it replicates the conditions in the body, it is able to track the effectiveness and progress of drug therapy. Their model has the potential to be a more effective method for studying tumours than in-vitro and even in-vivo methods.

The team comprised Professor James Goh, Associate Professor Toh Siew Lok and Dr Pamela Tan from the Department of Bioengineering at NUS Faculty of Engineering, and Associate Professor Saminathan Suresh Nathan from the Department of Orthopaedic Surgery at the NUS Yong Loo Lin School of Medicine, who carried out their study using osteosarcoma, which is the most prevalent form of paediatric primary bone cancer.

Reconstructing tumours in the laboratory has been a hot topic for research as current methods of testing have not been sufficient to yield concrete results.

Dr Tan, who has been researching on the 3D model for her PhD thesis, said: “Despite the urgent need to develop cancer therapeutics, little progress has been made due to the lack of good pre-clinical drug testing models. Current laboratory drug testing methods yield results that differ largely from animal testing because of the use of 2-D cell culture systems which cannot replicate the 3D properties of the tumour tissue.”

In in-vitro testing, cell culture systems are largely 2D, hence, lack the structural features of the 3D microenvironment. On the other hand, it is not feasible to carry

out large-scale molecular biology research using in-vivo experiments. Furthermore, society has become increasingly concerned about the use of animals in experimentation.

Prof Goh said that tissue engineering, a major focus of study at the Department of Bioengineering, can help bridge these gaps, thereby establishing a more physiological 3D in-vitro model. The team made use of techniques from tissue engineering to fabricate the 3D tumour model and reconstructed the tumour tissue into factors and cell types in order to form a clinically relevant tumour.

The team decided to use silk to fabricate the scaffolds onto which the osteosarcoma cells were grown because it has been demonstrated to have excellent properties for cell attachment and growth.

Their 3D tumour construct gives results that are much closer to those obtained from in-vivo studies, as compared to 2D in-vitro studies. When chemotherapeutic drugs (which target aggressively growing cells) were tested on the 3D tumour constructs, their effectiveness in killing cancer cells was greatly reduced, compared to testing the same drugs using the standard 2D system. Moreover, the therapeutic doses found using the 3D tumour constructs was within those measured in mice, indicating that the constructs have the potential to help bridge the gap between laboratory and animal testing, in order to improve the yield and quality of chemotherapeutic drug screening.

This is also the first time that a realistic 3D tumour has been constructed in a laboratory using silk scaffolds in a pressurised bioreactor. Their 3D bioreactor tumour model was able to express markers that indicate the ability of a tumour to initiate blood vessel growth at levels almost identical to that of the mouse model. The tumour constructs also responded to drugs that prevent blood vessel formation in a manner similar to that observed clinically.

“Our model also makes it possible to study how tumour cells interact with cells of the surrounding tissue, which results in more aggressive tumour behaviour,” added Dr Tan.

The team has been developing the concept of the tumour microenvironment as an important determinant of tumour behaviour over the last 10 years.

Said Assoc Prof Nathan, “Dr Tan’s recent contribution has shed remarkable insight into mechanisms of angiogenesis that were previously taken for granted and may now have to be re-addressed. Clinically this will have significant bearing on other drugs as well.”

“We will in future be expanding our findings to other cancers and incorporating other aspects of the tumour microenvironment like oxygen levels within the system to ultimately create a platform for testing that could save much in downstream applications of experimental drugs,” he added.

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