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Insights from the Network

How 3D bioprinting can generate complex cancer models

By Darya Alcock, Vaidehi Patel, Milena Restan-Perez, Lennard Shopperly and Dr. Stephanie Willerth

Glioblastoma multiforme (GBM) is an aggressive type of brain cancer that can quickly spread to several areas of the brain, leading to disability or death. According to the Brain Tumour Registry of Canada, this devastating disease affects 4 in 100,000 Canadians. The invasive and proliferative nature of cancer cells within healthy neural tissue can commonly cause headaches, disorientation, memory loss, personality changes, and seizures. The current treatments for GBM include tumour removal in combination with radiotherapy or chemotherapy, which have remained the standard of care for the past 30 years. However, these options have limited success as GBM often recurs in an aggressive fashion.


100μm
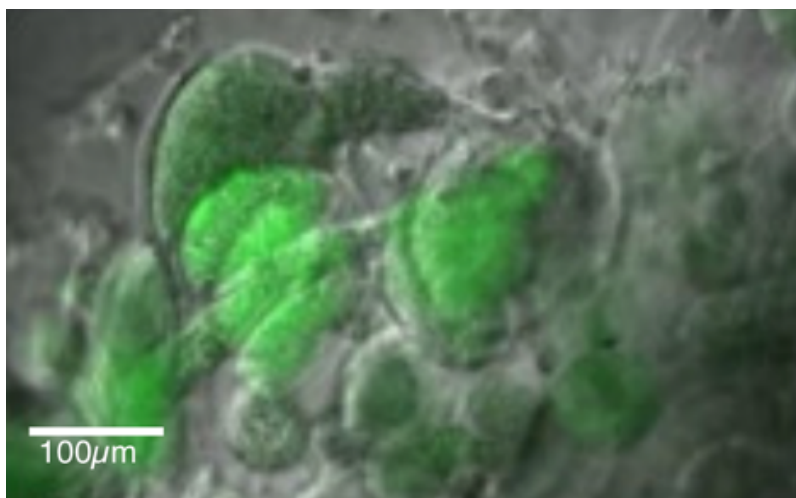
A bioprinted tissue containing brain cancer cells (shown in green) printed alongside healthy brain tissue. As tissues grow, the brain cancer cells infiltrate the surrounding environment.

One of the reasons for the lack of advances in treating this type of brain cancer is the inaccuracy of the animal models used to investigate potential cancer treatments. These animal models often require implanting human tumour tissues into animals lacking the ability to fight off disease. These systems are highly artificial and do not replicate the conditions found when tumours occur in humans.

To solve this problem, the Willerth Lab, located at the University of Victoria, uses 3D bioprinting to generate models of human neural tissues. These models are ideal tools for studying and developing treatments for various neurological diseases such as Alzheimer's disease, Parkinson's disease, and GBM. 3D bioprinting, a subset of 3D printing, uses "bioinks" laden with human cells to fabricate complex structures that can mimic the extracellular matrix of the human body. Using specifications contained in a digital file, the bioprinting process can generate tissues with multiple cell types, meaning it can print brain cancer tissue alongside healthy tissue, allowing us to understand how the disease progresses over time.

3D bioprinted tissue models can mimic the three-dimensionality of the human body and therefore can better represent how potential cancer treatments affect it. These models can be used as a tool to screen potential drugs alongside existing 2D cell culture models and reduce and replace animal models. A recent publication from our lab successfully utilized bioprinting techniques to create a comprehensive model of GBM, incorporating both healthy glial cells — non-neuronal cells found in the nervous system — and cancerous glioblastoma cells.
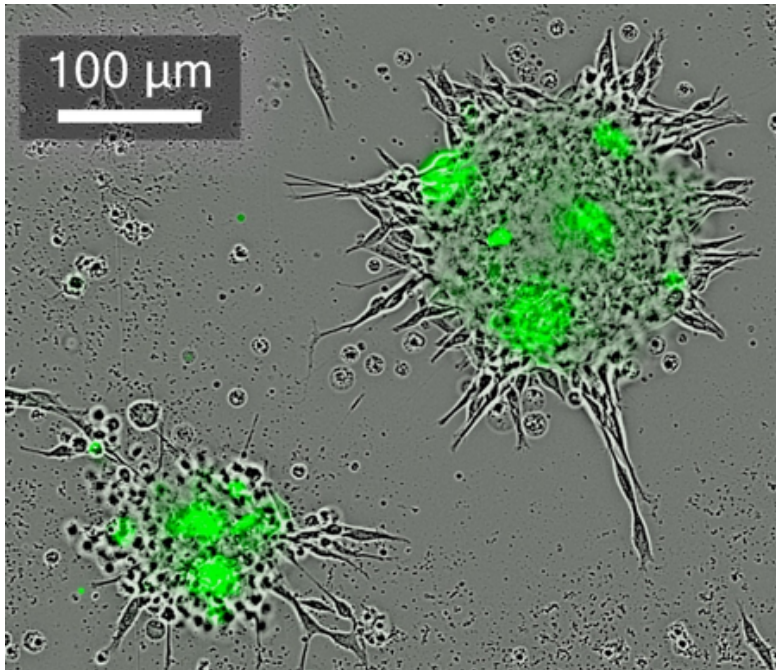
GBM Neurospheres derived from cancer patients after transfection with GFP using nanofibers.

This bioprinted GBM model was highly advantageous in demonstrating the selective efficacy of novel anticancer drugs, selectively targeting and eliminating cancer cells while promoting the survival of healthy cells. The Willerth lab used the 3D bioprinted GBM cancer model to identify a potential drug that could shrink the tumours present in these tissues without being toxic to healthy brain cells.

Besides developing disease models, the Willerth Lab also investigates nanotherapeutic approaches for treating GBM. Lennard Shopperly, a current visiting graduate research student, has been investigating a novel type of nanofibre for the treatment of GBM in collaboration with the Manners Lab at the University of Victoria. Nanofibers are nanoscale fibre composites loaded with therapeutic agents, like chemotherapeutic drugs, and can efficiently deliver their cargo to brain cells. These therapeutic agents are often difficult to administer due to the protective nature of the blood-brain barrier (BBB), which is extremely selective as to which molecules can enter the brain's environment. Farnoosh Kalantarnia, a PhD student at the Willerth lab, is currently conducting research on developing a microfluidic lab-on-a-chip device to model the BBB, thus aiding in advancements for therapeutic drug delivery to the brain.

By anchoring the power of 3D bioprinting and nanotechnology, our research aims to advance the approaches for GBM treatment and provide new insights into the development of targeted therapeutic approaches. Overall, utilizing 3D bioprinting in the study of GBM holds great potential; through the creation of accurate and reliable bioprinted models of GBM, researchers can evaluate the efficacy and potential adverse effects of drug candidates, paving the way for more personalized and effective future treatment strategies. The ongoing efforts of the Willerth Lab and its collaborators highlight the power of 3D bioprinting in the fight against GBM and other neurological diseases.