APPLICATION NOTE

A Tumor-on-a-Chip System with Bioprinted Blood and Lymphatic Vessel Pair

OVERVIEW

A 2D model cannot accurately replicate the intricacies of tumor microenvironments, leading to difficulty in identifying effective anticancer drugs. In this study, researchers mimicked a 3D tumor microenvironment using a bioprinted hollow blood vessel and lymphatic vessel pair. This tumor-on-a-chip *in vitro* model has the capacity to simulate the complex transport mechanism of biomolecules and anticancer drugs within the tumor microenvironment.

MATERIALS AND METHODS

Bioink

- 7% w/v gelatin methacryloyl (GelMA)
- Photoinitiator (PI)
- 3% w/v alginate
- 4% w/v PEG diacrylate (PEGDA) - for blood vessel analog
- 4% w/v 8-arm polyethylene glycol-octaacrylate (PEGOA) - for lymph vessel analog

Hollow microfibers were printed using an Allevi 2 fitted with a custom triaxial nozzle. The innermost and outmost layers of the triaxial nozzle contained CaCl2 to physically crosslink the bioink being extruded through the middle layer. The final construct was photocrosslinked under UV light. Finally, MCF-7 human breast cancer cells cultured in a 3D GelMA matrix were added into the chamber to form the completed system.

RESULTS

The researchers investigated interactions between several different combinations of blood and lymphatic vessel and tumor cell arrangements. The hydrogels showed enhanced mechanical properties which remained self-supporting under internal and external pressures. Permeability of the hollow tubes was measured using fluorescein isothiocyanate-BSA diffusions and was found to be tunable according to the composition of the bioink. By altering the ink's proportions, they were able to tune the density of the hydrogel and therefore the rate of diffusion for various biomolecules and drugs. They also found that diffusion from the blood vessel to the lymphatic vessel occurred, and that drugs delivered to the embedded cells via this diffusion interacted with the cells as expected.

CONCLUSION

This model reproduces the microcirculation using both delivery and drainage routes to mimic the transport of drugs. Though this is not high throughput, the permeability parameters of the bioprinted blood and lymphatic vessels were regulated by tuning the composition of the bioink which could accommodate for different biological needs of the tumor microenvironments.

REFERENCE:

Cao, X., Ashfaq, R., Cheng, F., Maharjan, S., Li, J., Ying, G., Hassan, S., Xiao, H., Yue, K., Zhang, Y. S., A Tumor-on-a-Chip System with Bioprinted Blood and Lymphatic Vessel Pair. Adv. Funct. Mater. 2019, 29, 1807173. https://doi.org/10.1002/adfm.201807173

Advantages of using 3D BIOPRINTING

- 3D bioprinting offers the most precise yet convenient control over the deposition of hydrogel biomaterials for tissue biofabrication. In this case, the channel design was highly customizable
- The multilayered coaxial, concentric nozzle and adjustable flow rates of bioinks offer control over fabrication of complex biomimetic patterns. That tunability gives you effective representation of supply and drainage around a tumor to see how a drug gets delivered and affects the tumor
- The Allevi 2 bioprinter can be used as a valuable tool to create 3D cell culture and organ-on-a-chip models