Establishment of Tumor-On-Chip System to Study the Role of Tumor Microenvironment on Cancer Progression in a Patient-Specific Manner

Samaneh Kamali*, Mara Gilardi, Abhay Andar, Karin Abara Heidemann, Michael Ritchie, Maria Mancini. Champions Oncology, Hackensack, NJ, USA

Background Cancer research has traditionally relied on two-dimensional (2D) cell culture, focusing mainly on cancer epithelial cells and their abnormal genetics. However, over the past decade, the contribution of tumor stroma as well as its complex microenvironment in cancer progression has been highly appreciated. Limitations remain with traditional preclinical cancer models including a lack of ex vivo model systems that imitate human physiology and the inability of animal experiments to fully recapitulate and tune human organ microenvironments. Recent advances with engineered co-culture systems, such as microfluidic organ-on-chips, have overcome some of these limitations to better model cell-cell and cell-extracellular matrix (ECM) interactions. The microfluidic nature of these systems sustains longer-term experiments and allows for continuous effluent collection to monitor byproducts as an indirect measure of tissue function and viability. These novel systems are also designed to recapitulate organ-level structure, function, and physical forces that mimic in vivo cyclic strain and fluid shear stress.

Methods Here, we use the Tumor-on-Chip (TOC) platform to develop a complex co-culture system of our previously established TumorGraft3D (CTG3Ds) biobank at Champions Oncology. Notably, CTG3Ds feature the phenotype of their original tumor tissue and may be used as a powerful tool to study the effect of microenvironmental factors such as immune cell recruitment in cancer therapy. To this end, we established TOCs by coating the microfluidic channels with ECM of choice and optimized cell seeding conditions in both top (seeded with epithelial cells) and bottom (seeded with endothelial cells) channels. Next, we applied the established TOCs to introduce the autologous tumor-infiltrating lymphocytes (TILs) for a defined amount of time and study TILs migration from the vascular endothelial to epithelial cells.

Results Furthermore, key readouts included measurements of epithelial barrier permeability, imaging of recruited TILs in the epithelial channel, and Luminex analyses of cytokines in the effluent collected from the epithelial channel. Our initial focus on colorectal cancer proved the feasibility of forming a non-leaky epithelial barrier by CTG3Ds and establishment of a robust TOC system. We also confirmed a high level of consistency in between replicate chips in terms of epithelial barrier integrity and cytokine secretion panels.

Conclusions This makes the TOC platform an advanced tool for potential downstream applications such as immunotherapy and drug testing.

References

Ethics Approval All human biological samples utilized for the research described in this abstract have been procured or collected after an Informed Consent form has been issued according to the current local legislation. All animals studies described in this abstract have been conducted under Champions’ approved IACUC.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0025