3D-Bioprinted cancer models for target discovery, drug development, and personalized therapy

Prof. Ronit Satchi-Fainaro, Ph.D.

Department of Physiology and Pharmacology, Faculty of Medicine; and Sagol School of Neuroscience, Tel Aviv University
Tel Aviv 6997801, Israel

ronitsf@tauex.tau.ac.il

Many drugs show promising results in laboratory research, but eventually fail in clinical trials. We hypothesize that one main reason for this translational gap is that the cancer models used are inadequate. Most models lack the complex tumor-stromal cell interactions with their microenvironment which are required for tumor progression. Conventional 2D cultures, where cells grow on rigid plastic plates mainly as mono-cultures of a single type of cells, are not able to recapitulate the complex settings of such interactions. Therefore, there is a need to develop a 3D model that better mimics the tumor microenvironment[1]. Hence, we developed a vascularized, hydrogel-based 3D-bioprinted tumor model consisting of patient-derived tumor and microenvironmental cells[2]. Our 3D-bioprinted models are based on a library of hydrogels that we developed as scaffolds for different tumor types, designed according to the mechanical properties of the tissue/organ of origin. The patient-derived models consist of cells from a biopsy, constructed based on CT/MRI scans, and include functional vessels that allow serum and peripheral blood mononuclear cells (PBMC) to flow when connected to a pump. Using this unique model platform, we identified P-selectin as a novel immune checkpoint in the brain regulating cancer-microglia-tumor-associated macrophages (TAMs) interactions[3]. Based on this finding, we have begun an investigator-initiated clinical trial, testing the efficacy of the anti-SELP antibody, Crizanlizumab, alone or in combination with anti-PD-1 antibody, Nivolumab, for GB and melanoma brain metastasis patients (NCT05909618). Moreover, we are currently validating our 3D platform for its ability to mimic patient-specific tumors and their microenvironment in order to predict patient response to different treatments (such as chemotherapy, immunotherapy, and targeted therapies). In addition, we exploit this platform to identify unique biomarkers, which can be used as targets for our Turn-ON chemiluminescent probes for image-guided surgery, early detection, and/or companion diagnostics. Hence, we are currently conducting an 80-patient "basket" clinical trial testing different treatments on patient samples to validate the ability of our model to predict patient outcomes covering 7 different cancer types. These unique 3D-bioprinted models have the potential to facilitate target discovery and drug development, as well as to serve as a reliable system for precision medicine.

References

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