

# Evaluating Novel Cancer Therapeutic Strategies Using Living Tumor Biopsies



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Nearly half of all cancer patients are eligible for treatment with immune checkpoint blockade (ICB) cancer immunotherapy, but only about 10% of patients derive a durable clinical benefit. Hundreds of ICB-based therapeutic combinations have undergone clinical testing in recent years. However, the vast majority of these trials have failed to demonstrate meaningful benefit over established ICB agents. The lack of representative pre-clinical models of human tumor immunity has been cited as a key contributor to the failure of these therapeutic approaches and remains a major unmet need in the field.

My lab uses patient-derived organotypic tumor spheroids (PDOTS), a novel biomimetic technology platform to study tumor-immune system dynamics in a patient-specific manner (Jenkins et al. *Cancer Discovery* 2018). PDOTS are living tumor biopsies comprising patient-derived cancer cells and tumor-infiltrating immune cells that are grown in a 3D microfluidic culture device to closely mimic normal physiologic conditions.

PDOTS offer an opportunity to evaluate the sensitivity of a patient's tumor to existing ICB agents and/or novel therapeutic agents using clinically relevant biospecimens. We have confirmed the utility of dynamic PDOTS evaluation in examining novel therapeutic strategies to overcome ICB resistance (Sun et al. *Nature* 2023). We aim to expand our efforts to evaluate patient-specific sensitivity to existing, marketed ICB therapies for patients with ICB-responsive cancers (e.g., melanoma) in the next year.

In the near term, PDOTS offers clear value in pre-clinical drug testing to evaluate novel therapeutic strategies to overcome ICB resistance. Xsphaera Biosciences, a Boston-based startup, currently offers PDOTS testing for commercial partners. In addition, my lab is planning a clinical trial using PDOTS to test combinations of immunotherapies and inform rational drug combinations for future development. Our long-term vision is to develop PDOTS as a functional precision medicine platform to help oncologists optimize and prioritize therapies for their patients.