Dr. Christopher C.W. Hughes

Cancer accounts for 25% of US deaths, and the majority of patients die from metastatic disease that is refractory to the treatments they receive. The paucity of effective treatments in oncology can be attributed to two major issues: 1) that less than 10% of drugs entering clinical trials ultimately receive FDA approval, with most failing in clinical studies despite showing promise during preclinical studies; and, 2) treatments are not tailored to an *individual's* own tumor. Both limitations suggest the need for improved screening platforms.

The Hughes lab and collaborators have addressed this need by designing and validating a microfluidic device that supports the formation of a perfused, vascularized micro-tumor (VMT) through co-culture of multiple cell types (fibroblasts, endothelial cells (EC), and cancer cells) in an extracellular matrix. Growth and survival of the tumor and stromal cells is entirely dependent on flow of tissue culture medium through the microvascular network, such that cessation of flow leads to tumor death. This novel platform more accurately mimics the in vivo tumor microenvironment than standard monoculture, monolayer drug screening modalities. As such, the VMT represents a major breakthrough in drug screening. The platform is low cost, composed entirely of human cells, optically compatible for fluorescent image analysis, and arrayed for high-throughput experiments. Physiologic flow rates through the microvascular bed formed within the device are maintained by a gravity-driven pressure differential, obviating the need for expensive and cumbersome external pumps and valves. Importantly, the VMTs form within days, require very few cells for establishment, and allow for rapid testing of anti-cancer and anti-angiogenic drugs. These features will be critical in developing the platform for personalized medicine applications.

Currently, personalized medicine involves comparing a single patient's molecular signature to a large cohort of patients and treatment is then based on the sub-cohort with which the patient most segregates. In contrast, we propose to test how an individual patient's tumor cells respond to combinations of FDA-approved anti-cancer drugs – a truly personal drug screening methodology. Working with UCI physicians we will address two key questions: 1) Does the VMT platform accurately model patient tumors; and, 2) can findings in the VMT translate to clinical practice. To answer these questions primary VMTs (pVMTs) will be established from patient-derived colon cancer samples collected in excess of clinical need as part of a prospective clinical study (already approved by the IRB), and then analyzed for responsiveness to multiple drug combinations. Findings will then be correlated to patient outcomes based on the drug combinations they actually received. The translational infrastructure providing real-time information from patient-derived tumor cells in our VMT will support efforts to improve patient outcomes.