A novel and rapid patient-derived organoid breast cancer platform for precision medicine

David Graham1, Gabrielle Rupprecht1,2, Eric Bankaitis1, Jeremy Force2, Wylie Watlington3, Steven Metzger4, David Hsu2, Xiling Shen1
1Xilis Inc., Durham, NC, 2Duke University, Duke Cancer Center, Durham, NC

Background

An increasing number of studies performing correlative drug screens on patient-derived organoids (PDO) are revealing enormous potential for these models in predicting patient response to therapy1,2. Despite this, their future use in a clinical setting is hindered by intrinsic limitations of traditional PDO models, namely low success rates in establishing growing cell cultures from tumor tissue samples and long return times for drug response data that fall outside timescales of clinical actionability.

We developed a novel emulsion-based microfluidic technology that generates PDOs from tissue samples within days to weeks as opposed to months. The core technology, known as MicroOrganoSpheres (MOS), relies on creating a microscale tumor environment containing a patient’s cells. MOS retain structural, cellular, and genetic properties of an individual patient’s diseased tissue and are amenable to liquid dispense.

Here, we tested the feasibility of generating MOS from breast cancer tissue biopsies across different subtypes of breast cancer. We performed dose response studies across standard-of-care chemotherapies, providing response data within 14-21 days from receiving a sample.

Method

A patient’s breast sample (primary or metastatic) is dissociated and packaged into MOS using our emulsion-based microfluidic device. MOS are established over a period of 1-2 weeks. Brightfield images showing established breast MOS growing over 4 days. Established samples are dosed using an automated workflow. Drug response is tracked and quantified using longitudinal imaging and viability measures.

Results

A total of 42 out of 50 breast PDO samples were established (84% success). Molecular subtypes (left) and tumor types (right) from the 42 PDOs are shown. IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, DCIS = ductal carcinoma in situ, MET = metastatic carcinoma, Other = largely Phyllodes and fibroadenoma tumors.

Conclusions

Our data demonstrate the feasibility of:

• Efficiently establishing PDO from breast cancer patient tumor samples from different subtypes using MOS.

• Performing drug dosing studies on MOS that results in improved turnaround times that are in line with clinical timescales.

Future directions

• Continue expanding our breast cancer PDO biobank, generating full dose response profiles across chemotherapies with rapid turnaround times

• Develop a predictive model using MOS to determine patient sensitivity to chemotherapy.

References
