62 APPLYING MACHINE VISION TO EMPOWER PRECLINICAL DEVELOPMENT OF CELL ENGAGER AND ADOPTIVE CELL THERAPEUTICS IN PATIENT-DERIVED ORGANOID MODELS OF SOLID TUMORS

Sonal Khare*, Chi-Sing Ho, Madhavi Kannan, Brian Larsen, Brandon Mapes, Jenna Shaxted, Jagadish Venkataraman, Ameen Salahudeen. *Tempus Labs, Chicago, IL, USA*

Background Cell engager and adoptive cell therapeutics have emerged as efficacious and durable treatments in patients with B-cell malignancies. Though many analogous strategies are under development in solid tumors, none have received approval. Preclinical development of these therapies requires cell labeling of immortalized cell lines and/or primary expanded T cells to distinguish target and effector cells. However, cell engager and adoptive cell therapies have had limited evidence of reproducibility in primary patient-derived models such as tumor organoid cultures thus far. Here, we build upon our tumor organoid platform[1] to measure organoid specific responses to these therapies. Utilizing machine vision coupled with time-lapse-microscopy, we obtain multiparameter kinetic readouts of patient-derived tumor organoid cell killing and allogeneic MHC-matched primary peripheral blood mononuclear cells (PBMCs).

Methods The patient-derived tumor organoids were co-cultured with PBMCs in the presence of engagers/activators and vital dyes and incubated for 96 hrs. Cell death was measured by quantifying the caspase 3/7 vital dye pixel intensities at different time points using high throughput imaging. As a first step, a fully convolutional neural network was trained to segment out organoids from brightfield images comprised of organoids, immune cells and potential background artifacts. This segmentation mask was then transferred over to registered caspase 3/7 images to quantify tumor cell specific phenotypes in a rapid and automated manner.

Results The time-lapse imaging assay allowed for both the tracking of the organoid growth over time as well as the quantification of the kinetics of engagers/activators in comparison to controls resulting in accurate and precise technical reproducibility. Further, this assay allowed for the co-localization of the organoids and the immune cells over time, thus, enabling a spatiotemporal summary of dose dependent efficacy of candidate therapeutics.

Conclusions We demonstrate the scalability and throughput of a machine vision tumor organoid immune co-culture platform across multiple unique patient-derived tumor organoid lines bearing a target of interest, enabling future discovery of biomarkers of therapeutic response and resistance.

REFERENCE

1. Larsen B, Kannan M, Langer LF, Khan AA, Salahudeen AA, A pan-cancer organoid platform for precision medicine. *Cell Reports* 2021; **36**:109429

http://dx.doi.org/10.1136/jitc-2021-SITC2021.062