Applying machine vision to empower preclinical development of immunotherapies in patient-derived organoid models of solid tumors

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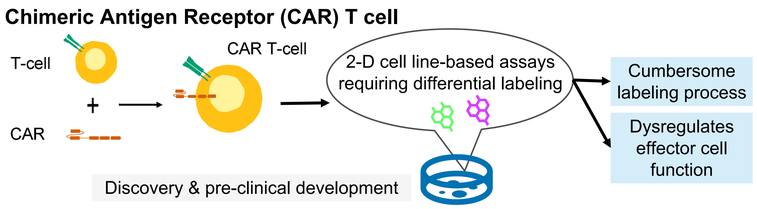
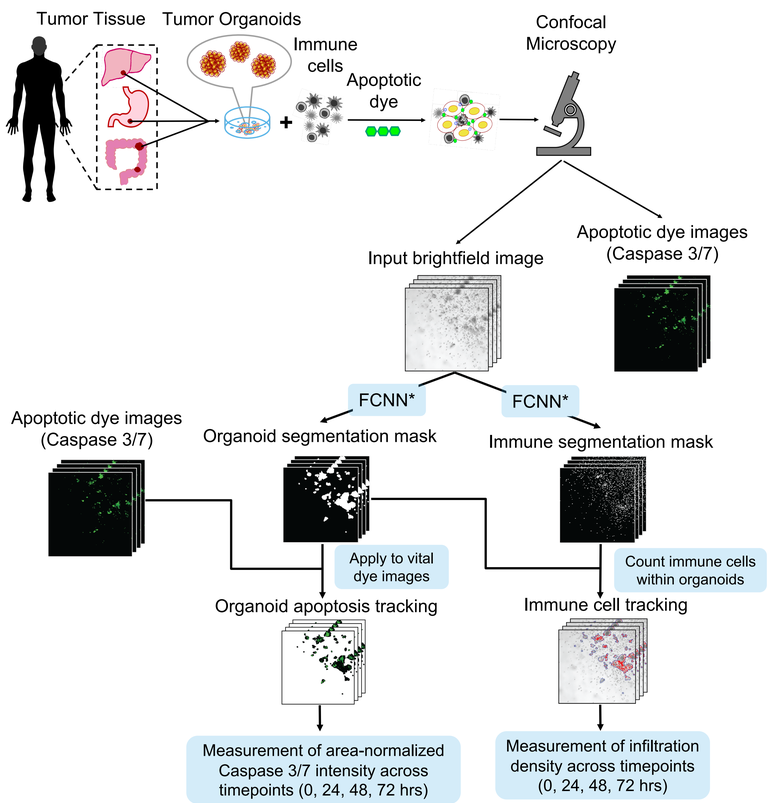
INTRODUCTION



- Conventional approaches to preclinical development of cellular therapies face challenges with fluorescent labeling
- We build upon our patient-derived tumor organoid (TO) platform to measure TO-specific responses to next-gen immunotherapies using brightfield-only deep learning segmentation models

METHODS

We utilize machine vision on time-lapse microscopy to obtain multiparameter kinetic readouts of tumor apoptosis, enabling dissection of mechanisms of CAR-T cells.



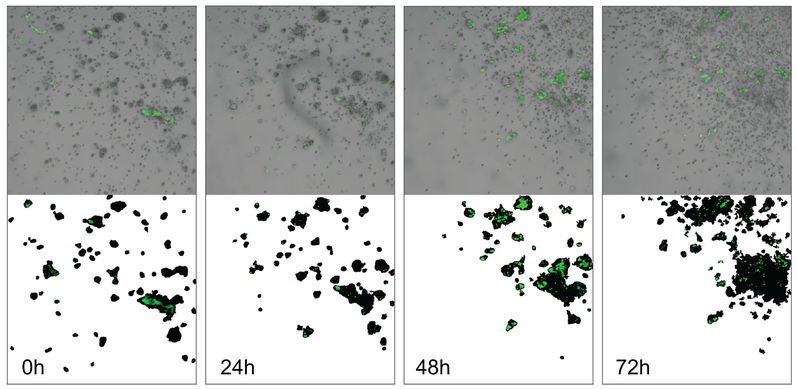
*Fully Connected Neural Networks

SUMMARY

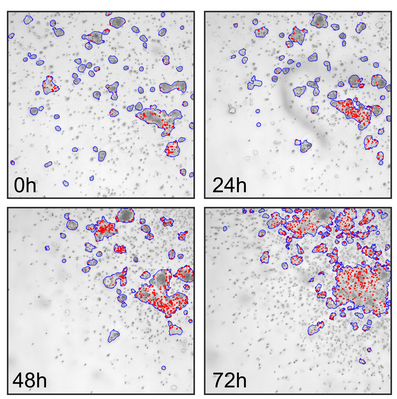
- We present an effective solution for **scalable, label-free quantification of TOs and immune cells from brightfield images** to understand their dynamics in time-lapse imaging.
- Our machine vision platform enables **high-throughput immune oncology preclinical studies to screen and mechanistically probe therapeutic candidates** across hundreds of unique TO models, accelerating their evaluation as immuno-oncology therapeutic candidates in cancer patients.

RESULTS

We find that the rate of immune cell infiltration is correlated with TO apoptosis over time, lending strong biological interpretability to the effectiveness of immunotherapies. We observe a differentiation of response between HER2-targeted and untargeted CAR-T lines, where targeted CAR-T lines exhibit higher infiltration rates with higher corresponding cell death rates. These correlations generate label-free insights into the pharmacokinetics and mechanisms for specific immune therapies.

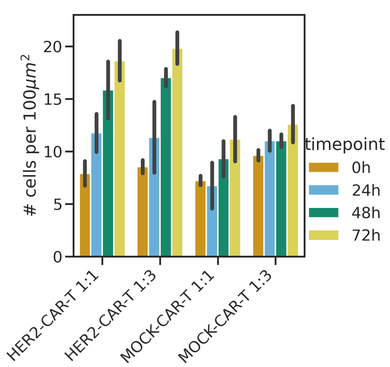


Top: overlaid Caspase 3/7 (green) and brightfield images. Bottom: Caspase 3/7 signal within organoid segmentations



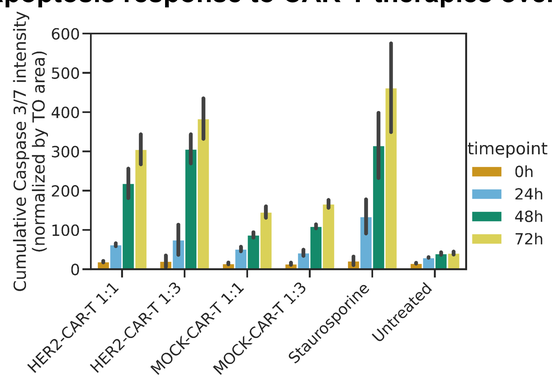
Organoid segmentations (blue) and immune detections (red)

Immune FCNN infiltration



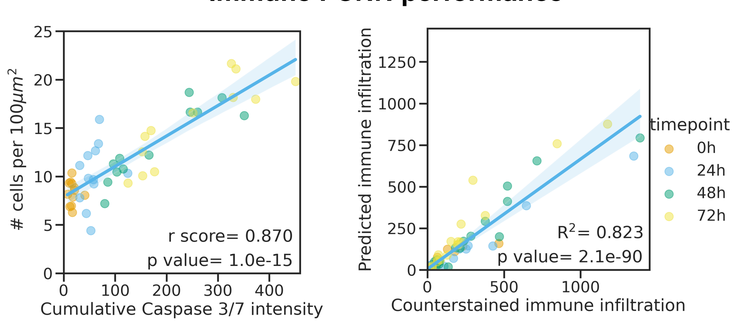
Higher infiltration is observed in HER-2 targeted CAR-Ts

TO apoptosis response to CAR-T therapies over time



HER-2 targeted CAR-Ts generate a stronger apoptotic response compared to untargeted CAR-Ts.

Immune FCNN performance



Predicted immune infiltration correlates well with both TO response and counterstained ground truth

Acknowledgements: We thank Amrita A. Iyer, Ph.D, for poster preparation & review.

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