HIGH-THROUGHPUT SCREENING OF CANCER IMMUNOTHERAPY COMBINATIONS USING A HYDROGEL-BASED 3D IN VITRO TUMOR PLATFORM

Bin Xue*, Julia Schüler, Christopher Harrod, Kolin Hribar. Cypre, Inc., South San Francisco, CA, USA; Charles River Laboratories, Freiburg im Breisgau, Germany

Background Immunotherapies such as immune checkpoint inhibitors and CAR-T therapies have revolutionized cancer treatment in recent years. However, the success of the immunotherapies has been only limited to a small percentage of patients as primary and secondary resistance to single agent remains common and often results in treatment failure. Combination immunotherapies (e.g. combining multiple immune targets or different therapeutic modalities) have become a potential strategy to combat this drug resistance.

Methods Here we describe a 3D in vitro tumor model platform which can be used for assaying anti-tumor effects of novel immunotherapy combinations. The models incorporate tumor cells derived from patient-derived xenografts, fibroblasts and immune cells in a hydrogel matrix to recreate the complex TME. Tumor size reduction and tumor cell death were determined as endpoint readouts via high content imaging. The 96-well high-throughput format allows rapid screening for novel combinations and their additive or synergistic effects across multiple PDX types.

Results As a proof of concept, we tested the combination of anti-CTLA4 (Ipilimumab) and anti-PD1 (Nivolumab), both FDA approved treatments, to showcase their enhancement effect in several PDX models. We also observed that dosing kinetics and immune cell density dictated the degree of response for each agent compared to their combination.

Conclusions The Cypre 3D platform is a broadly encompassing tool capable of exploring novel combinations that alter multiple mechanisms of immune response.

REFERENCES

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