A NOVEL TUMORGRAFT3D IMMUNE CO-CULTURE PLATFORM FOR HIGH THROUGHPUT IMMUNE-ONCOLOGY SCREENING

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Background
The complexity of the tumor immune microenvironment (TIME) plays a critical role in immunotherapy treatment response, and this requires robust preclinical research models recapitulating patient-specific tumor-immune interactions. Immune oncology research has highlighted the need to model TIME complexity at the level of a single patient. Rapid progress has been made, yet there are still challenges while developing rigorous ex vivo models mimicking the hierarchical architecture and cellular synergy within TIME.

Although patient-derived 3D cultures overcome the limitation of standard 2D methods allowing for proliferating cells and high throughput drug screening, these systems still lack functional immune components to successfully test the effect of therapeutic agents in modulating the TIME.

Methods
The challenge of replicating functional features of immune populations in vitro lies in the immune cells’ limited stability and on the limited availability of autologous patient immune cells. To provide a solution to this challenge, Champions Oncology generated a bank of autologous ex vivo models, which combines clinically relevant patient-derived TumorGraft3D models with immune cells from the same patient.

Results
The characterization of the platform showed proliferation of the cancer cells, while immune profiling by flow cytometry confirmed representation and functionality of different immune cell populations. The molecular profile of the TumorGraft3D models showed a tight overlap with the original tumor, highlighting their clinical relevance.

To establish autologous TumorGraft3D co-cultures, surgical resections from patients were used to generate TumorGraft3D models and TILs were expanded using the standard Rapid Expansion protocol. 3D confocal analysis allowed for a deep evaluation of cancer-immune cellular interaction at the single cell level. The development of our proprietary staining system allowed assessment of cancer-immune cell spatial distribution and cellular death. Our proprietary pipeline of image analyses enabled the evaluation of tumor infiltration and drug cytotoxicity.

The novel co-culture platform has been tested across various indications allowing the evaluation of drug response to several ICIs including pembrolizumab, nivolumab, durvalumab, and ipilimumab. The quantitative image analysis results demonstrated varying degrees of TIL infiltration and cytotoxicity with different ICIs. Our findings corroborate emerging clinical results.

Conclusions
In summary, this novel platform allows high throughput screening of novel immune-modulating agents to determine impacts on immune cells infiltration and tumor cytotoxicity on therapeutic response. TumorGraft3D is a versatile platform and can be used to test a variety of therapeutic modalities, alone or in combination, including but not limited to allogeneic, innate cell therapies, engineered immune cells as well as therapeutics targeting proliferation mechanisms.

REFERENCES

Ethics Approval
All human biological samples utilized for the research described in this abstract have been procured or collected after an Informed Consent form has been issued according to the current local legislation. All animals studies described in this abstract have been conducted under Champions’ approved IACUC.

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