468 APPLICATION OF ORGANOID-BASED DISCOVERY PLATFORM FOR INNOVATIVE SCREENING, EVALUATION, AND IDENTIFICATION (ODISEI) IN IMMUNOTHERAPY

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Background Immuno-oncologic therapies are known to activate patients' endogenous immune system, resulting in the enhanced tumor-killing effects in cancer patients. These therapeutic strategies have been gradually preferred as a prior regimen to cure cancer patients due to relatively fewer side effects and prolonged efficacy. Although many new immunotherapeutic drugs have been developed, almost all new drugs failed in clinical trials, strongly necessitating the development of *in vitro* screening platform for pre-evaluating the efficacy of the immunotherapeutic drug candidates.

Methods Moreover, for the precise efficacy prediction of immunotherapy, *in vitro* platform in which the interaction between patient-specific Major Histocompatibility Complex (MHC) and T-cell receptor (TCR) could be mirrored is essentially required. MHC, an antigen molecular in the tumor cells, binds to the TCR of the T-cells, and T-cells can exhibit their tumor-killing effects via MHC and TCR matching. However, tumor cells can evade T-cell-mediated tumor killing effects through the interaction between immune checkpoint (ICP) in tumor cells and their receptors in T-cells.

Results Here we describe a robust and novel efficacy evaluation platform, namely "ODISEI" in which patient-specific immune system could be recapitulated using tumor organoids and PBMC from same donors. The improved performance of our ODISEI platform as an efficacy evaluation platform of immunotherapy drugs was carefully examined using PD-1/PD-L1 blocker antibodies. Moreover, we also developed a series of ODISEI platforms in which the specific interactions between tumor organoids and each immune sub-populations (T-cells, macrophages, regulatory T-cells, dendritic cells) were replicated. Indeed, we were able to validate our ODISEI platforms using multiple drug candidates by assessing their tumor-killing effects through the specific interaction of tumor and reactive immune cell types.

Conclusions In conclusion, we have successfully established novel and robust ODISEI platforms which could serve as a useful efficacy screening platform for the immunotherapeutic drug candidates.

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