An in vitro system for evaluating molecular targeted drugs using patient-derived tumor organoids

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Patient-derived tumor organoids (PDOs) represent a promising preclinical cancer model that better replicates disease, compared with traditional cell culture models. We have established a novel series of patient-derived tumor organoids (PDOs) from various types of tumor tissues in the Fukushima Translational Research Project, which are designated as Fukushima (F)-PDOs. F-PDOs could be cultured for >6 months and formed cell clusters with similar morphologies to their source tumors. Comparative histological and comprehensive gene-expression analyses also demonstrated that the characteristics of PDOs were similar to those of their source tumors, even following long-term expansion in culture. In addition, suitable high-throughput assay systems were constructed for each F-PDO in 96- and 384-well plate formats.

This presentation represents the structural features of F-PDOs and an in vitro evaluation of different classes of molecular targeted drugs, including small-molecule inhibitors, monoclonal antibodies, and an antibody-drug conjugate, using F-PDOs. The structural features of F-PDOs possessing various structure were accurately analyzed by performing 3D cell analysis. We evaluated epidermal growth factor receptor and human epidermal growth factor receptor 2 (HER2) inhibitors using a suitable high-throughput assay system. Next, the antibody-dependent cellular cytotoxicity (ADCC) activity of an anti-HER2 monoclonal antibody was evaluated to visualize the interactions of immune cells with F-PDOs during ADCC responses. Moreover, an evaluation system was developed for the immune checkpoint inhibitors, nivolumab and pembrolizumab, using F-PDOs. Our results demonstrate that the in vitro assay systems using F-PDOs were suitable for evaluating molecular targeted drugs under conditions that better reflect pathological conditions. In addition, our results indicated that F-PDOs have structural characteristics enabling the construction of an evaluation system for anticancer drugs, based on structural changes of F-PDO found with a 3D cell-analysis system, demonstrating that 3D cell analysis is a powerful tool for analyzing the characteristics of PDOs.

[References]

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