Drug response prediction in precision oncology: a cancer organoids analysis

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Organoids have emerged as a powerful tool in cancer research due to their ability to recapitulate the architecture and function of native tissues. Organoids are aggregates of cells that grow in suspension and can reproduce some important characteristics of the original tumor, including its structure, heterogeneous cell compartment, cell interactions with the extracellular matrix, gene expression and drug sensitivity. This study aims to explore the effects of tumor inhibitor treatments on organoid cultures. Organoids were obtained from patient-derived tumor tissues using established protocols. Tissues were mechanically dissociated, and cells made to grow in a medium containing growth factors. The culture conditions were optimized to promote self-organization of the cells into organoids that mimic the histological and genetic characteristics of the original tumors. The growth and morphology of the organoids were monitored by imaging evaluations. To study the responsiveness of organoids to tumor inhibitors, a panel of 31 compounds targeting major oncogenic pathways was selected. These included kinase inhibitors (e.g. cetuximab), immune checkpoint inhibitors (e.g. atezolizumab), chemoterapeutics (e.g. oxaliplatino) and small molecules known to interfere with cancer cell proliferation and survival. A rigorous protocol for data acquisition was developed to ensure reproducibility and accuracy in measuring treatment outcomes. High throughput imaging techniques, including optical microscopy, were used to capture detailed morphological changes and cell viability over time. The results showed a differential sensitivity of tumor-derived organoids to various inhibitors, reflecting the heterogeneity observed in patient tumors. Kinase inhibitors showed a marked reduction in organoid growth and viability in specific subtypes, while immune checkpoint inhibitors elicited a robust apoptotic response in others. Combination treatments often resulted in enhanced efficacy, suggesting potential therapeutic strategies for overcoming drug resistance. In conclusion, this study underscores the utility of organoid cultures as a preclinical model for evaluating tumor inhibitor efficacy and tailoring personalized treatment strategies. The established data acquisition protocol provides a robust framework for systematic and reproducible analysis, facilitating the translation of these findings into clinical applications. The observed variability in treatment responses among organoids emphasizes the need for personalized approaches in cancer therapy, leveraging the predictive power of organoid models to optimize therapeutic outcomes. Future research will focus on quantitative image analysis for the extraction of features such as organoid size, shape, and density. To this end, the use of Machine Learning/Deep Learning models will serve to predict drug response based on organoid imaging, and develop a predictive system to anticipate the effect of one or a combination of two compounds and suggest a more effective treatment approach. Moreover, we will focus on expanding the organoid biobank and integrating multi-omics data to further elucidate the mechanisms underlying drug sensitivity and resistance.

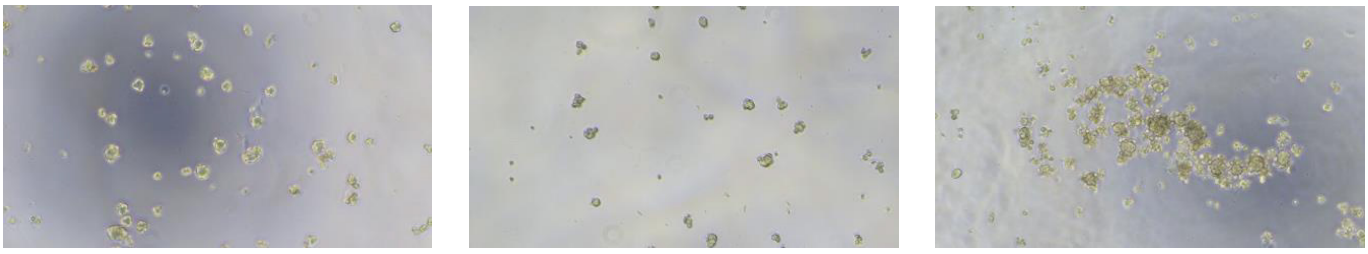

Figure 3: G605 treated with crizotinb at 24, 48 and 72h

SPOKE 3, TASK 4.3