An automated standardized screening workflow for assessing combination therapies in human pancreatic cancer organoids

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Precision medicine for cancer patients promises the tailoring of targeted therapies to specific genetic alterations. Currently, alterations in 43 oncogenes can be targeted based on Level 1 clinical evidence. Still, the majority of cancer patients lack efficient targeted therapy options with lasting benefit.[1]

Ex vivo assays, such as tumor tissue explants, hold the promise to directly measure the impact of anticancer compounds and their combinations. However, a significant challenge for *ex vivo* drug testing lies in the efficient establishment of fresh primary cell cultures for testing, within clinically actionable timeframe, and in the available tumor volume.[2]

To this end, patient-derived organoids (PDOs) have been proposed as viable and efficient alternatives for ex vivo testing. PDOs show long-term expansion potential while retaining tumor histopathology as well as cancer gene mutations.[3]

We have shown how homogenous reproducible PDOs based on Gri3D® hydrogel microwell arrays could be generated for high-throughput drug testing of single and combination therapies.[4]

Here we demonstrate on human pancreatic cancer organoids how amalgamation of anti-cancer drugs could enhance efficacy compared to mono-therapy approaches. By targeting pathways in a characteristically synergistic or an additive manner, a lower therapeutic dosage of each individual drug is required, potentially also reducing toxic side effects.

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