

Patient in the lab[®]: downscaling patient-derived organoid screening for diagnostic purposes

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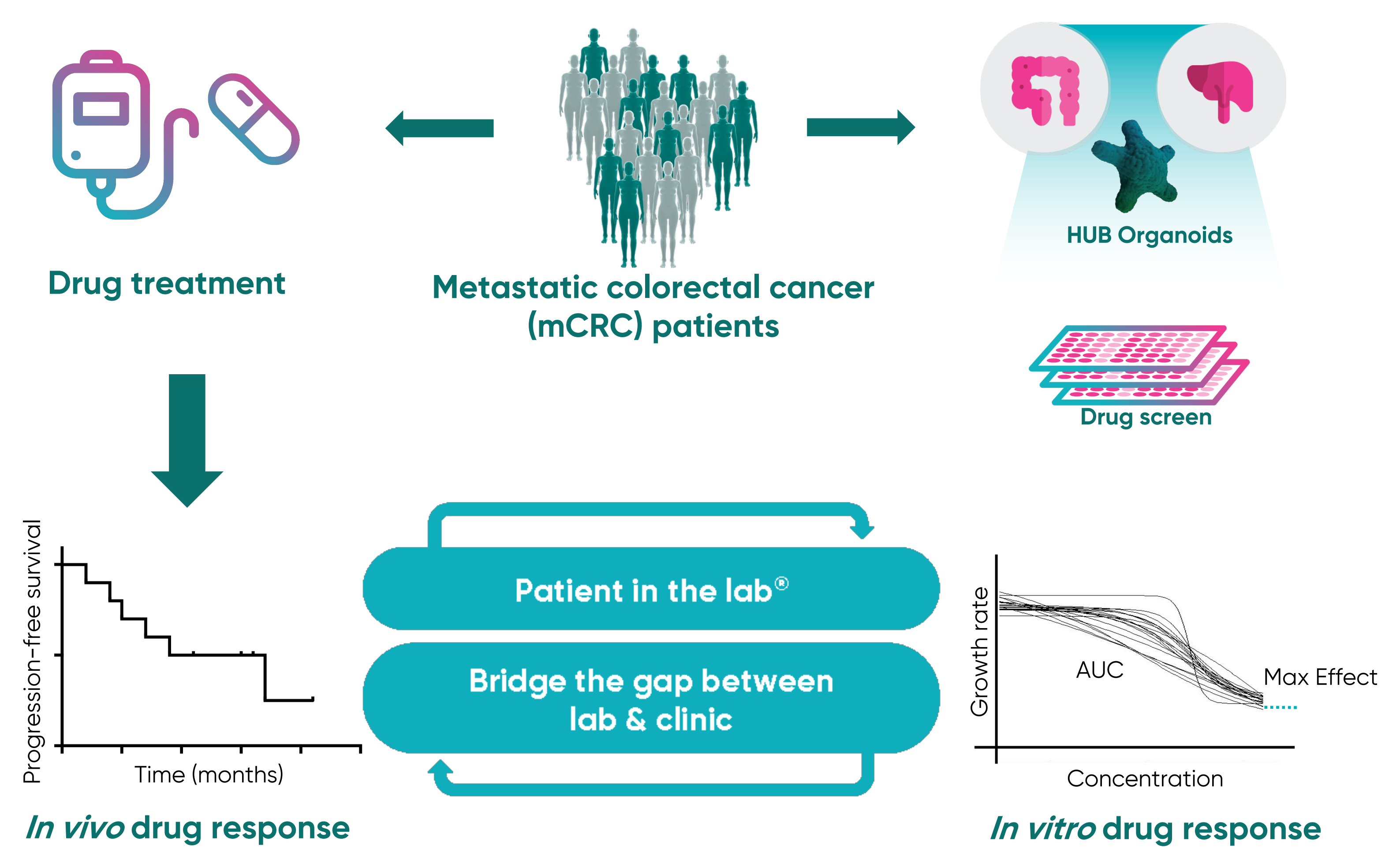
Introduction

Colorectal cancer (CRC) is the third leading cause of cancer and cancer-related deaths. A large fraction of CRC patients diagnosed with *de novo* metastatic disease does not benefit from standard medical care and experience substantial side effects. Therefore, there is an urgent need for preclinical models that help predict patient response in the clinic. Patient-derived organoids (PDOs or HUB Organoids[®]) represent a significant breakthrough in preclinical modelling of human disease as they are directly established from patient tissue and accurately recapitulate patient disease. HUB Organoid Technology has already demonstrated promising outcomes in preclinical drug screening. However, to provide direct patient benefit, the turnaround time between patient diagnosis and PDO-based drug response results must be shortened. In collaboration with Yamaha Motor, the YAMAHA CELL HANDLER[™] has been optimized and validated to automatically pick-and-place with high accuracy a significantly reduced number of organoids per screening plate.

Methods

- Informed consent was obtained from all patients prior to inclusion in the study and samples were obtained under HUB Biobank and/or OPTIC clinical trial protocols.
- Patient material for the study was acquired and the procedure to establish PDOs from mCRC small needle biopsies was optimized (Figure 1).
- Automated and accurate organoid seeding in screening screening plates was achieved using the YAMAHA CELL HANDLER to reduce the number of organoids/well (Figure 2).

Figure 1. HUB Organoids for clinical predictivity



Results

The YAMAHA CELL HANDLER showed a significant increase in organoid transfer efficiency and accuracy using the single organoid picking software. The latest software update for picking multiple organoids within the same tip accelerated transfer time. Moreover, Yamaha 6-well and CORNING Elplasia source plates showed comparable and enhanced performance over transferring from ECM droplets. The optimum organoid number and size were selected, and a fluorescent-based readout was validated using YAMAHA CELL HANDLER. Furthermore, the optimized assay set-up successfully detected the sensitivity profiles of Panitumumab towards *KRAS/BRAF* mutation status.

Figure 2. YAMAHA CELL HANDLER: an automated system for selecting, picking and seeding organoids on screening plates



Figure 3. Optimization of input material characteristics and transfer protocol

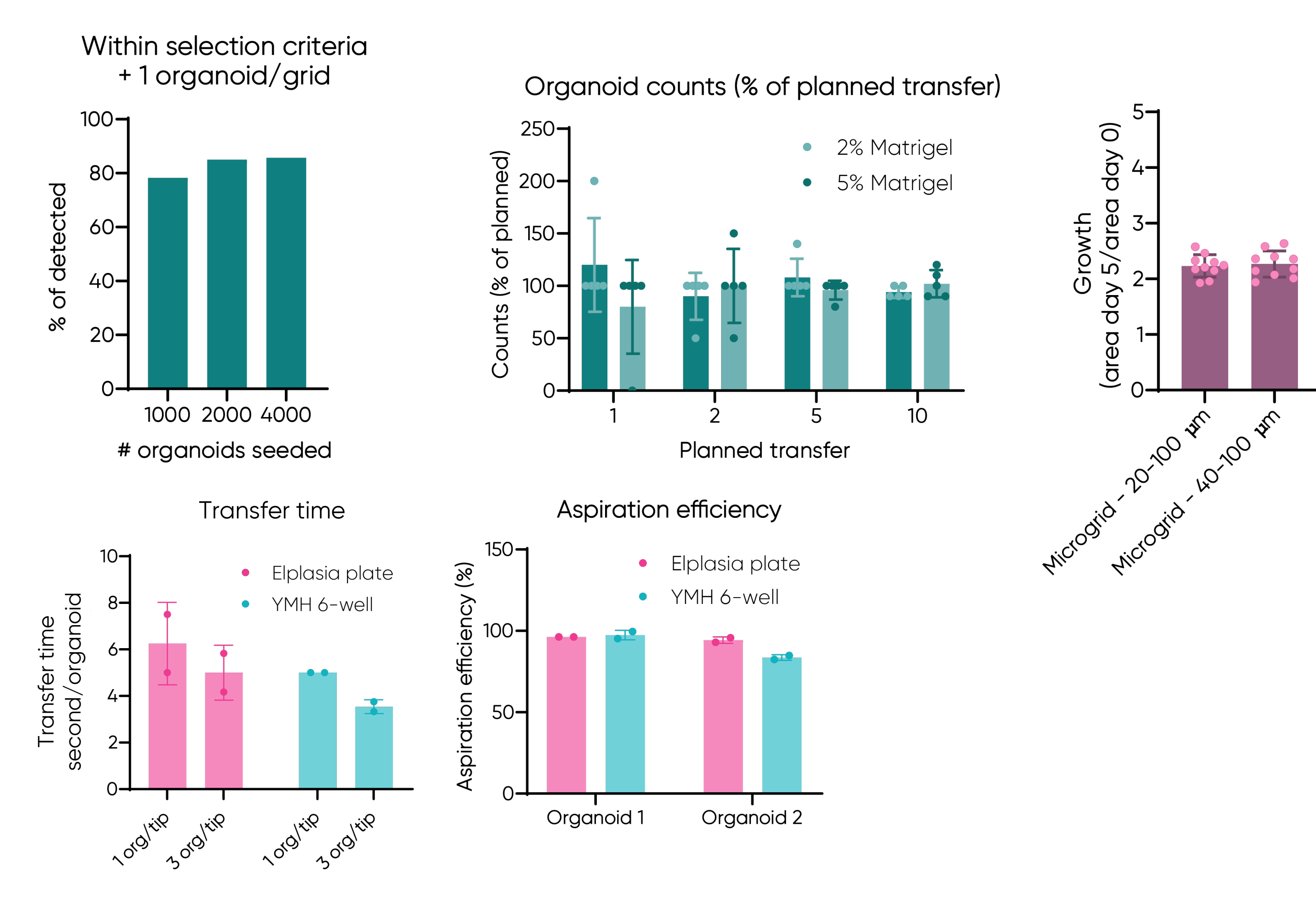


Figure 4. Comparison of single and multiple organoid picking protocols

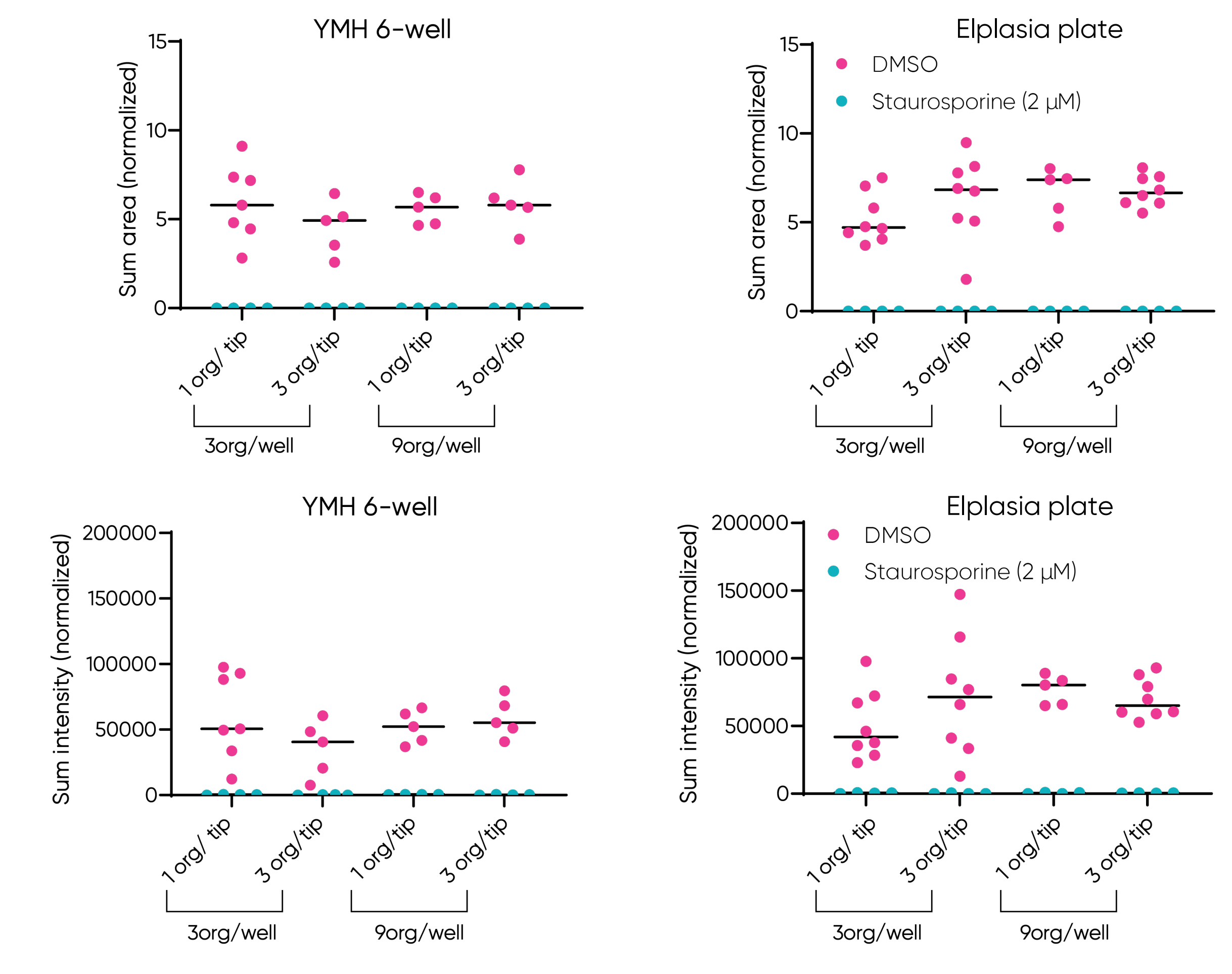


Figure 5. Source plate comparison for 5-FU and Oxaliplatin compound treatment

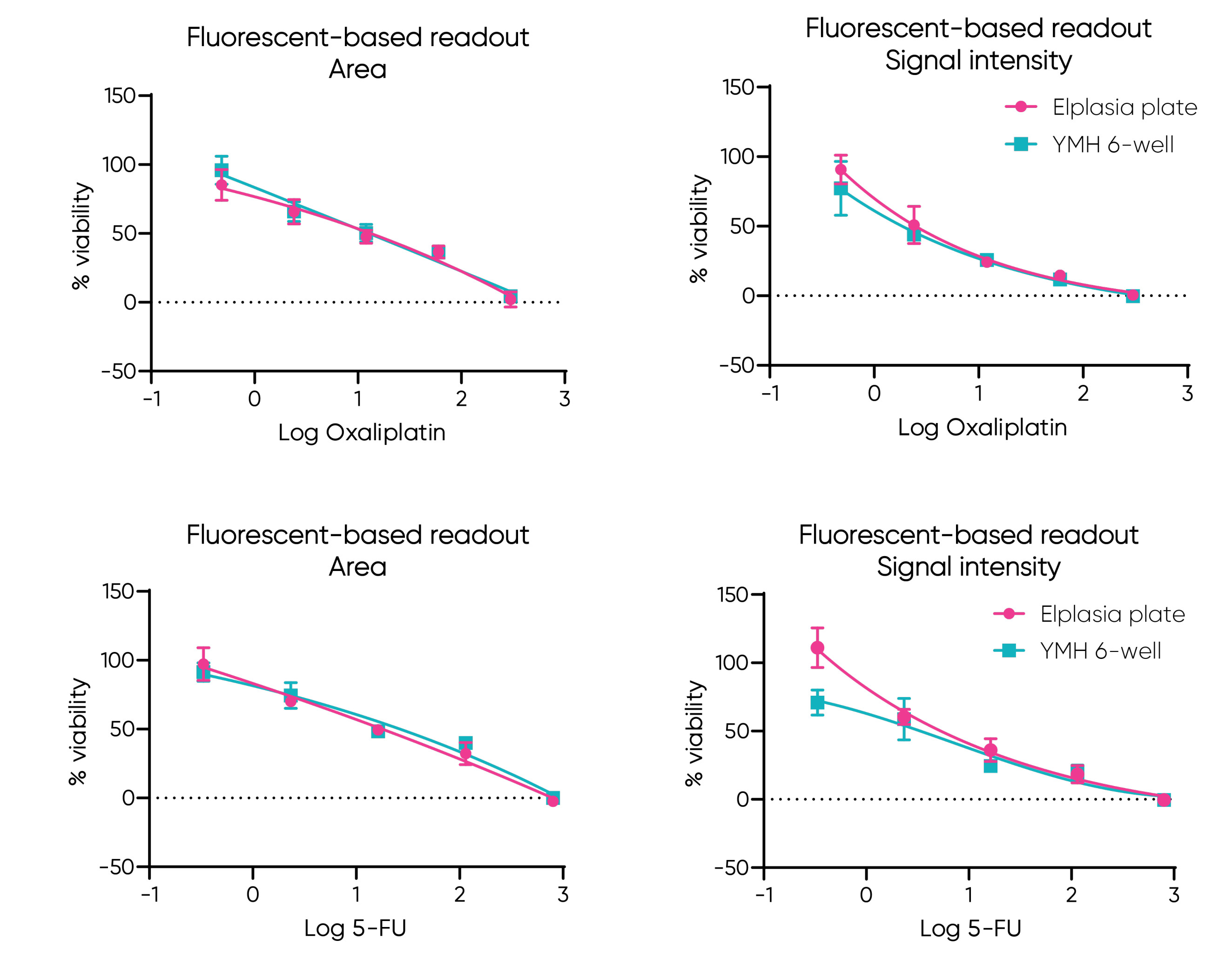
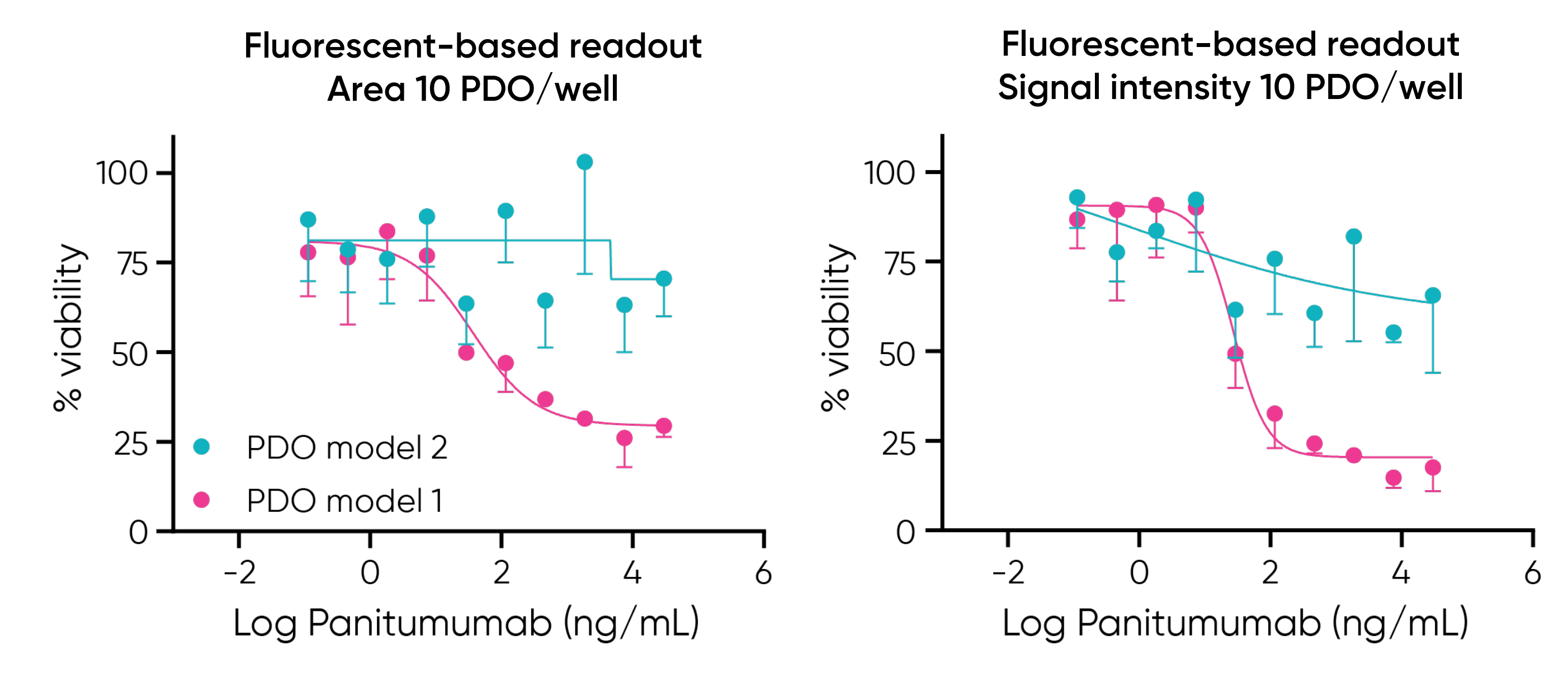


Figure 6. Organoid responses towards Panitumumab



Summary

- The most recent YAMAHA CELL HANDLER transfer software updates allow to transfer multiple organoids within the same tip, which significantly reduces the number of organoids needed to obtain robust data and accelerates the assay duration.
- In this study we were able to reduce the amount of input material in the source plates independently from the amount of ECM in the screening plate (Figure 3).
- Yamaha 6-well and CORNING Elplasia source plates show better transfer efficiency and accuracy over ECM droplets.
- Organoid transfer speed and efficiency were improved using CORNING Elplasia or YMH 6-well source plates by implementing multiple organoids picking protocol (Figure 4).
- Organoid response to 5-FU and Oxaliplatin compound treatment was compared using the different source plates with no significant difference between the two types of source plate tested (Figure 5)
- Using the YAMAHA CELL HANDLER, we were able to compare drug response between two different PDO lines with different genetic profiles (Figure 6 and data not shown)

