Development of a Novel Microfluidic Device for Anti-Cancer Drug Screening.

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Acquired resistance to conventional cancer therapeutics remains a confounding issue in patient management. The tumour microenvironment (TME) plays a critical role in protecting solid tumours from therapeutic interventions. Functional interactions between tumour cells and the adjacent stroma results in decreased drug penetration, induction of epithelial to mesenchymal transition and increased tumour heterogeneity. As a result, the efficacy of otherwise effective treatment regimens including combination and targeted therapeutics is inherently compromised. Drug screening regimes have demonstrated limited clinical success due to poor translation between bench and bedside. This can be attributed to inferior recapitulation of the TME and 3D tumour architecture in conventional cell culture methods, as well as limited availability of patient samples. Microfluidic devices offer salient advantages as drug screening platforms. Notably, they are scalable to allow for high-throughput, consume less reagents and samples than conventional culture methods and are of relevant biological scale. Here we propose a novel microfluidic platform capable of culturing patient-derived microtumours in a physiologically-relevant environment. Features of the platform include gradient generation, fluid flow with continuous perfusion and application of shear stress as well as the accommodation of a range of sensors. A computational fluid dynamic model with multiphysics simulation was used to guide the design of the device and a first prototype was fabricated using soft-lithography against 3D printed master moulds. The proposed workflow is compatible with standard laboratory equipment and can be modified to suit a breadth of applications including assay automation. We anticipate that this unique platform for chemo- and immunotherapeutic drug screening offers a more streamlined and clinically relevant approach than current commercially available devices.