A MICROFLUIDIC PLATFORM FOR PERSONALISED ONCOLOGY

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Dr Michele Zagnoni leads a multidisciplinary research group focussed on the development of microfluidic technologies for healthcare applications, including fundamental biological research, drug screening, personalized medicine therapy, organ-on-a-chip and synthetic biology (www.zagnonilab.com). Recently, he became the Chief Scientific Officer of ScreenIn3D (www.screenin3d.com)

Microfluidic technologies facilitate personalised oncology by enabling patient-derived tissue to be tested prior to treatment using biopsy-derived spheroid cancer models.

High-attrition rates during development of new cancer therapies persist despite several $BN investments are made per compound for discovery and validation of new anticancer molecules. Failure to translate promising preclinical drug candidates into clinical success exposes the limitations of our current drug discovery approaches, due in part to the lack of robust preclinical *ex vivo* models.

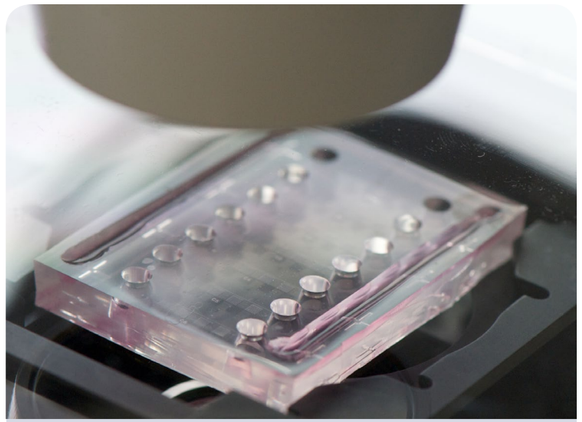

Figure 1.
Microfluidic platform for spheroid drug screening

Within this context, microfluidic and lab-on-a-chip technologies facilitate handling of small volumes of fluid containing chemicals and cell material and, therefore, have emerged as potentially highly relevant tools in cancer research.

Traditionally, drug discovery has relied upon 2D cell monolayer models, 3D clonogenic assays and small animal models, mostly utilizing cancer cell lines that do not recapitulate the complexity of *in vivo* tumours. It is now accepted that such preclinical models poorly predict clinical response. Therefore, development of more predictive, patient-specific models of human cancer are required for profiling novel anticancer drugs, as well as reconsider existing compounds in combinatorial studies. Additionally, technological advances in high-throughput and content phenotypic screening and 3D cell culture techniques provide new solutions for reshaping several key processes during drug discovery and development.

The unique combination of microfluidic and lab-on-a-chip technologies with physiologically relevant tumour models, based on 3D spheroids derived from primary human tissue, enables drug testing to be personalised. The ability to micro size drug-cell interactions will allow pharmaceutical and biotech companies do 100-fold more testing for the same money spent, increase productivity and access multiple readouts, concurrently.

We have developed a microfluidic, large-throughput 3D *ex vivo* system which provides a robust, customisable and cost-effective screening platform (Figure 1). The novel characteristics of this platform enable rapid decision making to prioritize the most promising drug candidates, as well as biomarkers and drug combination strategies for preclinical drug discovery and development. An advantage of the platform is the ability of cells to form a spheroid without the presence of exogenously added scaffolds. Thus, spheroids are formed using the endogenously produced extracellular matrices. This, together with the precise control of convective and diffusive mass transport, enables formation of human tissue derived spheroids in less than 3 days. Moreover, the system enables long-term culture as well as fractionated chemo- and targeted-therapy to study drug efficacy, as well as acquired drug resistance.

> *"Our microfluidic platform offers users the ability to reduce and replace animal models in cancer research and is targeted at improving anticancer drug treatment and accelerating development of new personalised medicine solutions using patient derived tissue."* - Michele Zagnoni

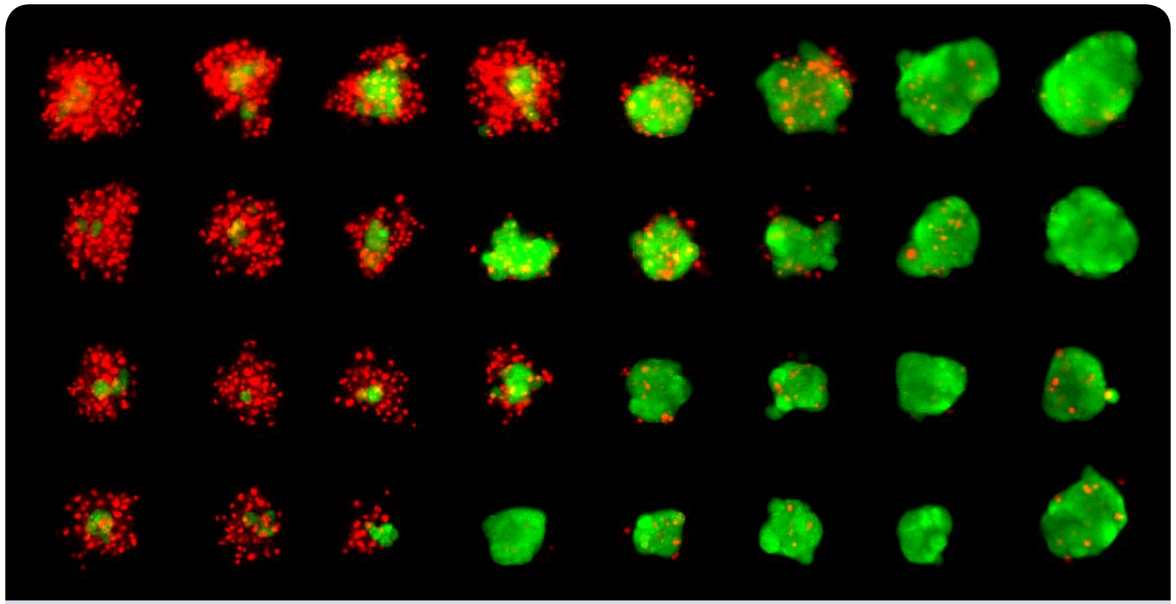

Figure 2.
Image of cancer spheroid responses (live/dead) exposed to a microfluidic concentration gradient of a compound

The platform has been validated by assessing spheroid formation and the efficacy of standard of care compounds against multiple cancer types including glioblastoma, prostate, ovarian, lung and pancreatic cancers. The platform, together with dedicated imaging software, provides multiparametric label-free and end-point measurements that include viability measurement (Figure 2), changes in spheroid size and shape, immunohistochemistry and assessment of the temporal evolution of spheroid response post drug treatment. Conveniently, the system also allows researchers to retrieve spheroids for proteomics and biomarker analysis post treatment. We are in the process of developing new models (aimed at immunotherapy testing and neuroscience).

Among other 3D *ex vivo* platforms available, our system provides a versatile tool well suited for cancer drug testing, particularly in the early development and profiling of a broad spectrum of molecules including small and targeted molecules, as well as facilitating development of personalised treatment. The technology has a variety of academic applications, as well as finding a commercial application with the provision of screening services via the University of Strathclyde spin out ScreenIn3D (www.screenin3d.com), commercialised through AMS Biotechnology (Europe) Ltd (AMSBIO).