



A game-changing technique to screen for novel cancer drugs

Biotech business Celleste aims to revolutionise cancer drug discovery by using 3D human-derived organoids and state-of-the-art imaging techniques to accurately predict the efficacy of novel compounds for further clinical development.

Celleste, which is based at the Medicentre on the Cardiff University Hospital of Wales campus, is addressing the urgent medical need to speed up drug discovery, reduce costly late-stage drug failure and reduce animal use.

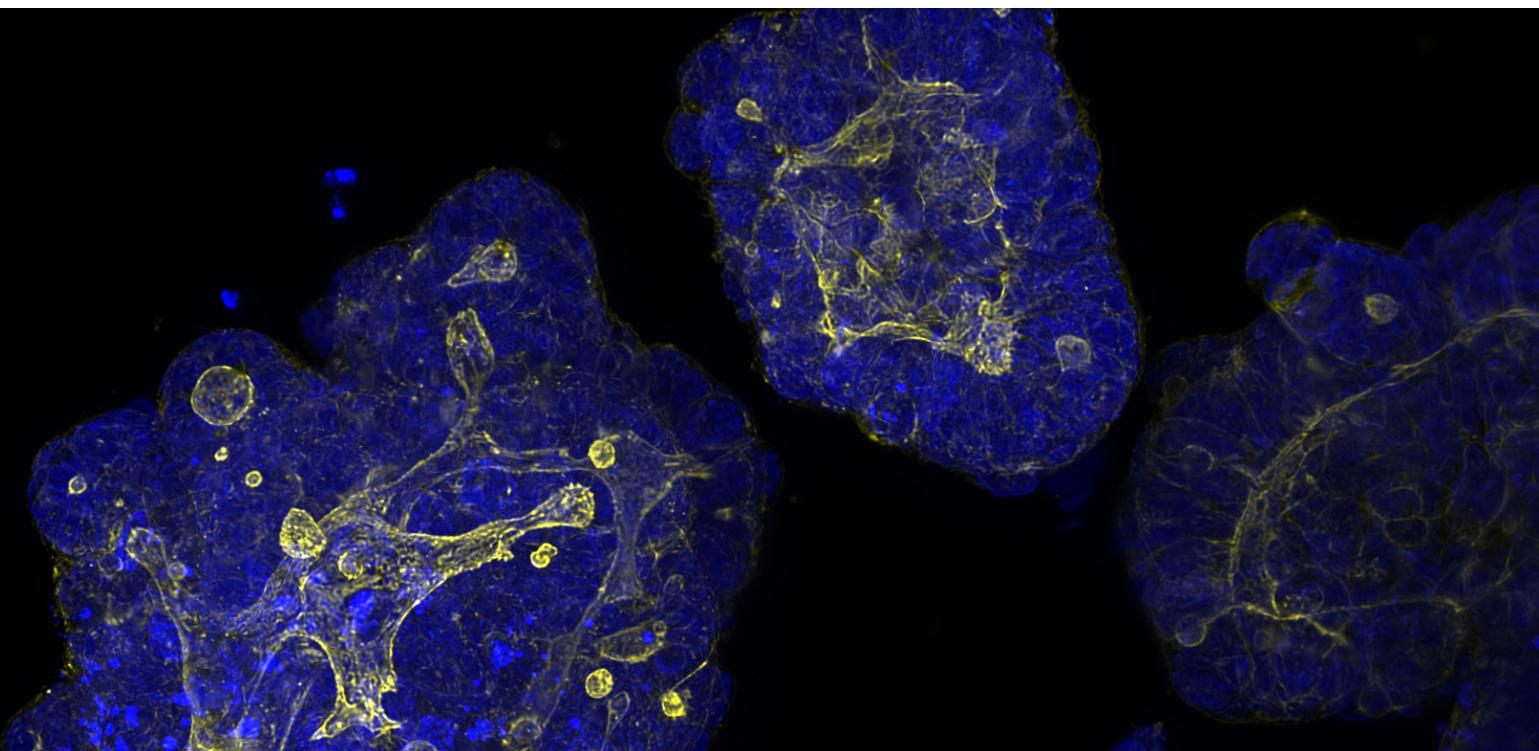
The ultimate aim is to discover and develop new cancer treatments that specifically target diseased cells, with minimal adverse side-effects.

This requires an in vitro test system that fully replicates tumour architecture and pathology to better represent patient responses to drugs than current models used in compound screening.

Organoids are three-dimensional (3D) miniature versions of the human normal or tumour tissue from which they are derived. They are in effect “mini-organs”.

Celleste specialises in expanding organoids at scale through their bioprocess to enable commercial production of reproducible patient derived organoids.

These organoids are better able to predict the efficacy of compounds in early-stage drug discovery than conventional 2D cell models.



Challenge

Cellesce believe that what takes place within and between cells in organoids reveals how potential therapeutics operate and how effective they might be after further clinical development.

3D imaging of organoids has so far been challenging due to their size and complexity, and because they are grown suspended in semi-opaque hydrogels.

It is possible, using the very latest imaging technologies and image analysis methods based on machine learning, to reveal and quantify the biological effects of treatments on three-dimensional organoid shape and function, to fully exploit the increased complexity of the organoid model.

This type of analysis has the potential to be adapted and deployed in high-throughput screening to more accurately predict potential therapeutic compounds for further development.

Solution

The A4I project set out to use Cellesce's colorectal cancer organoids and state-of-the-art imaging technology at NPL, to capture and compare many physical characteristics of organoids before and after drug treatment.

To test the effectiveness of the approach, Cellesce used clinically relevant cancer treatments and organoid lines derived from cancers with known sensitivities to these drugs.

High-resolution images of the cancer organoids were captured using NPL's expertise and M Squared Lasers' Light-Sheet Fluorescence Microscopy (LSFM) system. The images allowed visualisation of the changes to constituent cells, as well as the overall structure and shape of the organoid, following drug treatment.

The 3D image data sets were then analysed to quantify and classify the morphological responses of the organoids to the drugs and determine the optimal measurements to quantify their effects.

Impact

The project resulted in a large database of LSFM images and associated data from two colorectal cancer organoid lines exposed to four different cancer treatments.

Initial analysis of the images confirmed the relationship between organoid structure and drug treatment, establishing proof of principle that this technique can be used to assess unknown compounds in drug screens.

Further pioneering work with mass spectrometry imaging (MSI) illustrated the extent of drug penetration within the organoids, supporting the correlation between the observed effects and their application in typical drug discovery workflows.

Both Cellesce and NPL are keen to build on the promising results through further collaborative research and development. NPL is making the data available to Cardiff University and Cellesce, for further analysis in a Knowledge Transfer Partnership project. This will enable supplementary development and validation of the technique, and future commercial exploitation in drug discovery.

// The collaboration between Cellesce and the National Physical Laboratory (NPL) is seen as being very prestigious by Cellesce's Board members, investors and the academic groups we collaborate with. The experience was extremely positive and we formed good relationships with the team at NPL. We continue to explore further work and collaborations. **//**

Paul Jenkins
CEO, Cellesce



A4I

A4I is a programme that gives UK businesses, of any size, access to cutting-edge R&D expertise and facilities to help solve problems that they have been unable to tackle using standard techniques. The focus is on solving issues affecting product cost, reliability or lifetime and production problems.

