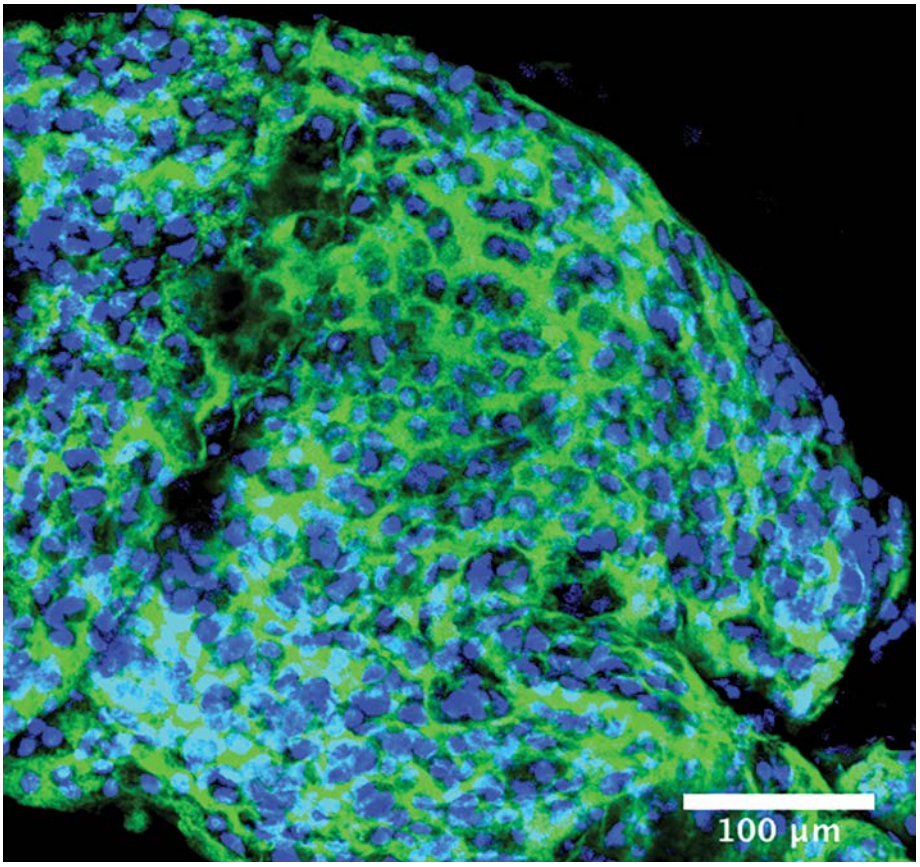
A 3D revolution

A novel 3D cell culture platform is enabling scientists to generate microtissues that closely mimic the behavior of human tissues from virtually any cell type. This proprietary technology is easily automated, offering speed and versatility, combined with consistency and reproducibility, for high throughput applications.

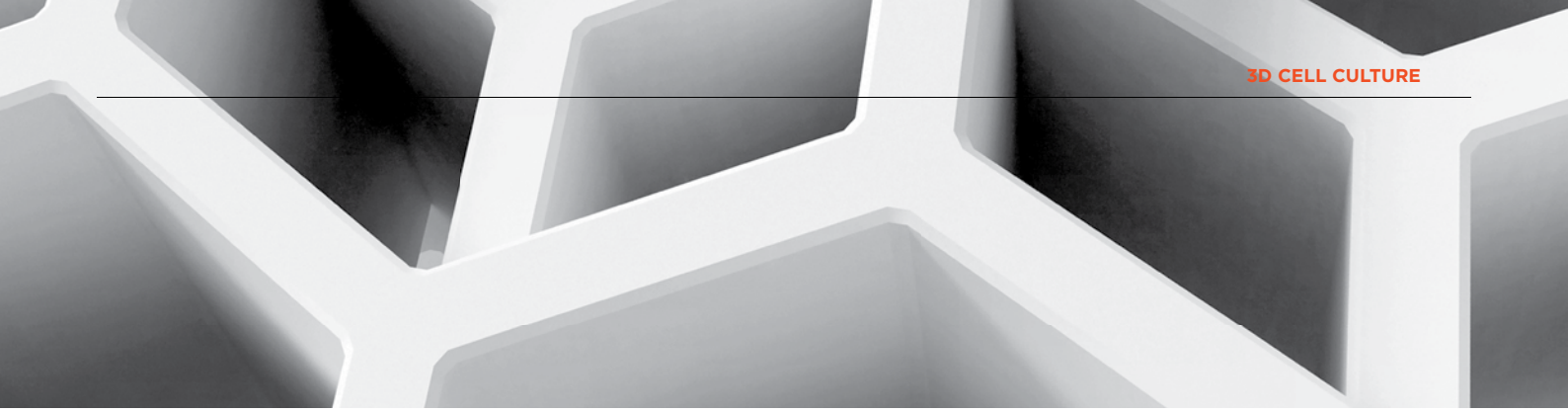
Classical 2D cell culture is a well-proven technique widely used in biological assays, drug screening and many other research areas. However, cells grown in a monolayer behave very differently to cells in a real tissue, and so the response of 2D cultured cells to drugs under development is not an ideal indicator of the likely *in vivo* response. The 3D Bloom® Biopolymer Platform from CellSpring, an ETH Zurich spin-out, is showing promise for improving the predictive capabilities of *in vitro* preclinical testing for drug safety and efficacy. This proprietary technology can generate 3D microtissues in just 30 minutes – far less than the hours or days required by other methods – and is easily automated on a liquid handling workstation. Chris Millan, Chief Technical Officer at CellSpring, explained: "3D Bloom offers several advantages compared to other methods of creating 3D microtissues. Scaffold-free approaches – spheroids and hanging-drops – for example, take three to five days to generate a 3D structure. With 3D Bloom, two naturally-derived biopolymers are sequentially pipetted into a standard multiwell plate, where a spontaneous, cell-friendly cross-linking reaction assembles the cells into a 3D structure in as little as 30 minutes."



3D Bloom allows rapid, automated generation of 3D cell cultures

Chris continued: "Scaffold-free methods are also extremely dependent on cell type and donor, and may not always be able to form 3D structures, whereas 3D Bloom can incorporate virtually any cell type into the system. A further restriction of the spheroid technique is that it is not generally possible to have more than 10,000 cells per microtissue. This limits the downstream readout, as it is difficult to generate enough DNA or protein to establish what is happening with those cells. In contrast, 3D Bloom is viable over a very wide range – from 5,000 to 2 million cells per microtissue – removing this limitation. Variability is another potential issue; scaffold-based processes use materials isolated from animals and consequently may vary between batches by as much as 50 %. Our technology, being very chemically defined, offers almost 100 % reproducibility."

"At the moment, our focus is on high throughput testing of new cancer drugs, looking specifically at the expression of targets of interest to pharmaceutical companies, which are generally over expressed by cells cultured in our system. As a result, the sensitivity of the system to candidate drugs is higher than with conventional methods, which is an advantage when you're trying to compare numerous different formulations to determine the best candidates," said Chris. "Performing this work manually is both time consuming and operator dependent, and so automation is clearly the way forward. Through the ETH Innovation and Entrepreneurship Lab (ieLab), we made contact with Tecan, and have worked closely with the company since then to automate our technology on a Freedom EVO® platform."



"Initially, Tecan's specialists worked side by side with us, showing us how to program the system and automate our 3D cell culture method. The Freedom EVO proved extremely straightforward to operate, and we can easily adjust the scripts ourselves if necessary. It's been incredible; speed and reproducibility have improved tremendously. We can now reliably process 10 plates in the time it takes to run a single 96-well plate manually, and staff are free to carry out other tasks. In the next phase of the collaboration, we plan to investigate co-culture models, incorporating different cell types into a single microtissue. This cannot be performed manually – you do not have enough control when positioning small droplets by eye – but the liquid handling platform should be able to accomplish it quite easily. It's very apparent to us that we will be selling our products exclusively for automated platforms, and particularly the Freedom EVO, which will also form the basis of our in-house service offering. There is no doubt that automation has helped us get to market much faster than would otherwise have been possible, and the collaboration has gone so well that we are now entering into a co-marketing agreement with Tecan," Chris concluded.

To find out more about Tecan's 3D cell culture solutions, visit www.tecan.com/3dcellculture

To learn more about CellSpring, go to www.cellspring.co

CellSpring's Kramer Schmit (CEO, left) and Chris Millan (CTO, right) are hoping the partnership with Tecan will expand the potential of the 3D Bloom platform for screening applications

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