Seeking immunity:

Researchers aim to characterize immune diversity

Prize Response:

A summary of the headlines in biomedicine

Shots with teeth:

Scientists keep up efforts to improve the rabies vaccine

Startups tout commercially 3D-printed tissue for drug screening

The promise of using specially designed printers to create biomaterials for medical purposes continues to make headlines. Two years ago, for example, researchers at the University of Michigan announced they had helped save the life of an infant suffering from a failing trachea by creating part of a windpipe replacement using a printing device that created a specially modeled biocompatible plastic called polycaprolactone. But whereas this and other medical applications of 3D printing have largely focused on custom-designed implants made to treat a specific condition, industry and academia are increasingly considering the potential of 3D-printed cells and tissues for screening experimental therapeutic compounds, in hopes of reducing costs, shortening timelines and reducing the need for animal research in drug development.

Several academic and commercial labs have already printed tiny, 3D organ-like structures called organoids; each of these tiny models might consist, for example, of kidney, cardiac or skin cells. But producing these from scratch can be labor intensive. Organovo hopes to offer a customizable alternative. In November, the San Diego-based company began offering its 3D-printed 'exVive3D' liver tissue models to screen pharmaceutical drugs in an effort to provide better predictors of liver toxicity early in the research pipeline. Organovo worked with the Swiss pharmaceutical company Roche in the earlier stages of developing the model tissue as a screening product, and plans to offer it as a part of their contract research services to drug companies.

"Three-dimensional printing has really advanced in the last few years, especially for printing tissues," explains Anthony Atala, director of the Wake Forest Institute for Regenerative Medicine, a leading center for bioprinted tissues. "To create miniature organ structures that can be used for drug testing is a major area of interest right now and one of the advantages is [that] instead of

Model organ: Cells taken from the liver (pictured) are used to print structures that model the tissue.

using animal models, you can use organoids that can replicate some of the functionality of the organ."

Currently, live tissue can be 3D printed either by using a biodegradable scaffold (printed by a machine in thin layers) that can direct the pattern in which the cells are arranged, or by orchestrating the printing process without a scaffold at all and simply printing cells atop one another in specific arrangements. The scaffold-free exVive3D liver tissue consists of human liver cells, including primary hepatocytes, stellate cells and endothelial cells. Donor human liver cells are used to prepare a 'bioink', that is fed into a specialized 3D printer which patterns the cells, layer by layer, to build a 3D structure that is about 500 mm in thickness. According to Sharon Presnell, Organovo's chief technology officer, after an incubation time of 60 hours these cells form vascular structures, produce liver proteins such as albumin and fibrinogen, display enzyme markers and stay viable for at least 42 days.

Model behavior

Organovo is far from alone in aiming to provide 3D-printed tissues for drug

research. In Vancouver, Canada, the startup Aspect Biosystems is developing technology for the same purpose. Likewise, Texas-based Nano3D Biosciences offers technology for scientists to print 3D spheroids that mimic native tissue environments. In October, researchers from Nano3D Biosciences and the Houston Methodist Research Institute published a study showing that they could construct 3D tissue models of breast tumors; preliminary tests using chemotherapy drugs such as doxorubicin suggested that these 3D models might better model actual tumor response to therapeutics than 2D cell cultures (*Sci. Rep.* doi:10.1038/srep06468, 2014).

According to its proponents, 3D printing offers greater reproducibility in experiments compared with other tissue models because it allows the user to control the structure of the tissue. "Because of the printing we are able to create the architecture in those tissues, such that we can print the cell types in specific patterns," says Presnell. This can allow different cell types to share spatial relationships that mimic human livers better than other existing models.

Still, some scientists say that more research is needed to understand whether the purported advantages of 3D-printed tissues over 2D cultures bear out. Brian Derby, a material scientist at the University of Manchester in the UK, says that people from the pharmaceutical industry are very interested in the concept of such drug development models but he is "not convinced" until more scientific literature demonstrates that those currently being offered work well.

Atala, for his part, remains optimistic about the efforts of Organovo and others to make 3D-printed models available for drug development. "It's hard to say which one will work best," he says "But it's good that they're coming out with this technology, because they can show that these things actually work"

Manasi Vaidya