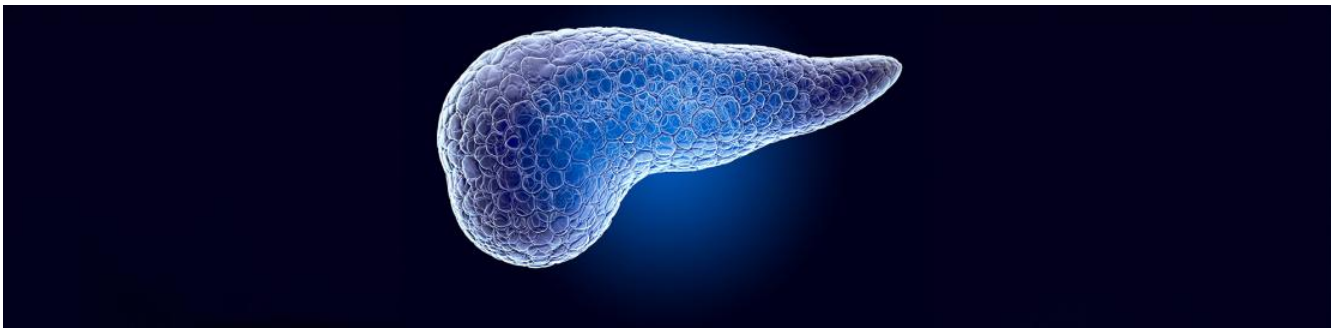
Horizon
The EU Research & Innovation Magazine

European Commission



3D-printed living cells pave way for tomorrow's medicine and cruelty-free animal products

EU-funded researchers are expanding the possibilities of 3D printing to create miniature human organs and a variety of products made from living tissue, including food.

23 August 2024 - By TEREZA PULTAROVA

3D printing has come a long way since its early days in the 1980s and is considered an essential tool in many manufacturing processes. Now, however, researchers like Italian bioengineer Dr Riccardo Levato, are taking the technique in a new and exciting direction.

What if, as well as car parts and designer furniture, we could print human organs or regenerate human tissue by bioprinting living cells?

Levato, an associate professor of biofabrication and regenerative medicine at the University Medical Center Utrecht and at Utrecht University, the Netherlands, leads a team of researchers from Belgium, Italy, the Netherlands, Sweden and Switzerland who received EU funding to do just that.

As part of a research initiative called ENLIGHT which runs from 2021 to 2025, they are developing a miniature 3D-printed pancreas made of human cells.

This, they hope, could improve the reliability and accuracy of testing of new therapies to treat diabetes and, perhaps, even one day lead to the possibility of lab-grown organs for human transplants.

Living blueprint

One of the key working materials of this research is stem cells. These are cells that have the potential to grow into many different types of human tissue – muscle cells, blood cells, brain cells – depending on the signals they receive.

Initial experiments, aimed at supporting patients with diabetes, have been carried out using insulin-producing cells grown in a lab from stem cells. Simply transplanting these cells into an ailing pancreas provides only short-term relief, however. According to Levato, this is because the cells lack proper support.

‘When you deliver these cells without structure, without vasculature, without protective material around them, they will die over time,’ he said. ‘The procedure lasts only a few years and then you have to repeat it.’

Levato and the ENLIGHT team are trying to fix this by 3D printing human tissue, living cells, to form three-dimensional implants complete with vessels. This is challenging because living cells are fragile and will not survive a normal 3D printing process.

The researchers have tackled this by using water-rich gels, called bioinks, that carry and nurture the cells during the printing process. They then need to be able to guide the process of cell differentiation so that the organ develops in line with its genetic “blueprint”. They do this using light.

Light touch

The ENLIGHT researchers have developed a novel 3D printing technique that uses light to shape the cell-containing bioink, instead of squeezing it through a nozzle like in a conventional 3D printer, which would damage the cells.

‘We essentially create a sort of light hologram of the object we want to print in the middle of this medium,’ Levato said.

‘Where you have this 3D light structure, the medium becomes solid and everywhere else it remains liquid so you can just wash it out. The cells are entrapped in the gelatine-like form, which is similar to the extra-cellular matrix in a living tissue.’

The researchers then nudge the cells to mature into insulin-producing cells by exposing them to light of specific wavelengths.

The team is currently testing their implants in the laboratory and researchers hope such 3D printed organoids can become part of standard drug development procedures before the end of the decade.

Levato cautioned, however, that it would take quite a bit longer to make the bioprinted organoids suitable for transplantation into human patients.

Cruelty-free

One of the advantages of the ENLIGHT team’s work is that it could greatly reduce the need for animal testing. Being able to print life-like human organoids would not only improve the accuracy of drug testing, but would mean that the suffering of millions of laboratory animals could be avoided.

Dr Massimo Vassalli, a professor of bioengineering at the University of Glasgow in the UK, is taking the concept of 3D printing of living tissue in a slightly different direction, but one that could also potentially relieve animal suffering.

He leads a multi-country EU-funded research initiative called PRISM-LT which aims to develop cost-effective 3D printing of a variety of living tissues. Their work, which will run until 2027, could have relevant applications in both biomedicine and food production.

‘The aim of the project is to create a platform technology to address the manufacturing of a diverse range of living tissues for application in the healthcare and food industries,’ said Vassalli. ‘In fact, beyond the more obvious medical uses, we see a big role for 3D bioprinting in sustainable and clean food production,’ he said.

The challenge, according to Vassalli, is to create complex heterogeneous tissues that truthfully mimic the texture of living materials. For example, meat contains muscle cells and fat cells, but also cells that form the

connective tissues.

To create meat that feels like the real thing, the researchers need to find ways to instruct stem cells to produce exactly the required type of tissue within a pre-defined structure – and then sustain the process over time.

Refining differentiation

The researchers are exploring an approach that mimics symbiotic processes in nature. They are mixing bacteria or yeasts – which Vassalli calls worker or helper cells – with the stem cells in a 3D printing bioink to help guide the differentiation process.

‘These cells are either bacteria or yeast that can sense the direction in which the cells are going and start producing chemicals to help them differentiate further,’ he said.

The team expect to be able to create centimetre-scale tissue cubes by the end of the project, focusing first on 3D-printed bone marrow for medical applications and a sample of marbled cultured meat.

‘Bioprinting technology offers improved flexibility in the design of the final composition of the tissue. This meets the needs of personalised healthcare applications,’ said Vassalli.

‘Food will take longer because the scale-up of the technology will take a lot of energy. A 3D printer we use in a lab wouldn’t be suitable to produce meat for a population. There is a technological gap that needs to be closed.’

Research in this article was funded by the European Innovation Council (EIC). The views of the interviewees don’t necessarily reflect those of the European Commission. If you liked this article, please consider sharing it on social media.

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