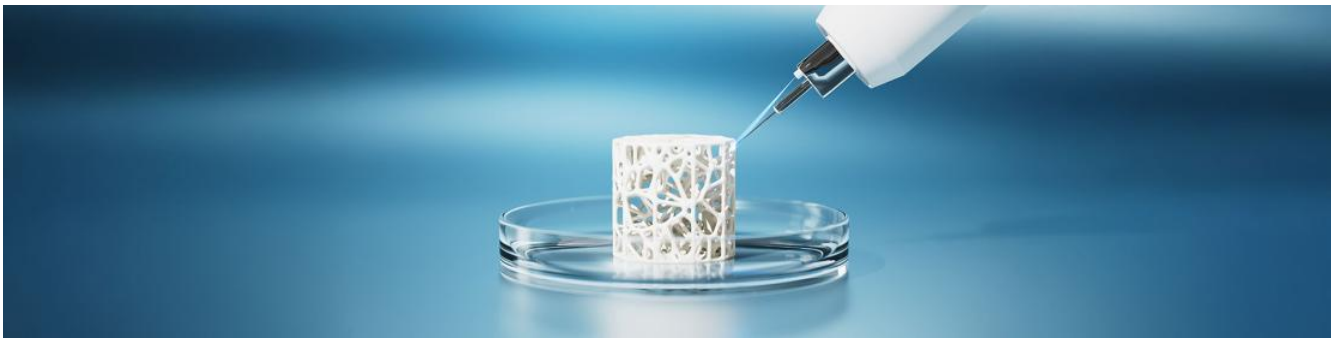
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3D printing gets a living upgrade

EU-funded researchers have developed a 3D bioprinting technique to grow living bone, fat and muscle tissue in the lab, opening doors to applications ranging from leukaemia research to cultivated meat.

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Nature has spent billions of years perfecting the art of building with living cells. A team of researchers is now learning from that process – and finding ways to speed it up.

For Massimo Vassalli, professor of bioengineering at the University of Glasgow, the goal is to understand not only how living tissues form, but how they can be recreated in the laboratory.

Vassalli is the scientific coordinator of PRISM-LT, a five-year EU-funded project which runs until 2027. The team is developing a 3D bioprinting platform to create complex living tissues, with applications ranging from biomedical research to cultivated meat.

At the heart of the project is a concept that sounds almost futuristic: engineered living materials, or ELMs.

These are materials made partly or entirely from living cells – including microorganisms such as bacteria or fungi – that can grow, respond and adapt to their environment. ELMs can self-organise and self-repair in ways conventional static materials cannot.

“Engineered living materials can have additional and dynamic features that we simply can’t replicate in traditional static materials,” said Vassalli.

Building with living cells

ELMs could transform industries from healthcare to food production, but turning that potential into reality means solving a hard biological problem: how to print living cells into complex structures without killing them or losing control of how they develop.

The PRISM-LT team is tackling this by building living tissues from tiny capsules containing living cells and a gel-like scaffold material known as bioink.

“Rather than printing a continuous stream of bioink, we work with encapsulated living building blocks,” explained Laura Martinelli, project coordinator of PRISM-LT and CEO of In Society, a research organisation based in Udine, Italy.

“These capsules can either be precisely positioned by a robotic arm or bioprinted layer by layer to create complex tissue architectures.”

Conventional methods print cells in a continuous flow of material, without the biological guidance that living microorganisms can provide. Here, each capsule is a biological unit carrying both the scaffold and engineered microbes that help steer the cells as they develop.

Those microbes have been genetically engineered to act as biological guides. They sense when stem cells – cells that can develop into many different tissue types – begin to transform, and respond by releasing chemical signals known as growth factors that direct them toward the desired tissue type.

The manufacturing process is fast, taking anywhere from minutes to an hour. What follows is slower: a maturation period of around three weeks, during which stem cells develop into bone, fat or muscle tissue. The team can currently produce roughly one square centimetre of thin tissue and is working toward a one cubic centimetre block.

What makes this especially tricky is that the process requires placing living components that do not naturally belong together in the same environment.

“We need to create a symbiotic relationship between two systems that were not made to live together, such as yeast and stem cells,” said Vassalli. “The main challenge is to create conditions that are good enough for yeast or bacteria, as well as the stem cells while they differentiate.”

This curiosity about biological interaction was at the origin of the project. “We started this research because we were curious about this interaction,” Vassalli said. “In essence, this is also how evolution occurred. Single-cell organisms interacted and evolved into nature as we know it.”

From bone marrow to the dinner plate

The researchers are working to recreate two specific tissue types. One is the interface between bone and fatty tissue found in bone marrow for biomedical research.

The other is muscle-fat structures which replicate the fat streaks that give real meat its texture and flavour, a quality that has long eluded cultivated, or lab-grown, meat.

The platform will also be used to create miniature tissue models that mimic the structure of human organs, which could be used in drug testing and to support personalised medicine.

“The project aims to deliver a platform that can engineer different tissues serving very different purposes, but using the same principles,” said Martinelli.

In the health domain, the focus is on building 3D bone marrow models to study drugs for conditions that affect it, such as leukaemia.

On the food side, achieving the right fat distribution matters greatly for consumer acceptance. “Thanks to our bioprinting technology, we can achieve the right texture in alternative meats, which creates an opportunity to bring it to the market,” said Martinelli.

Bringing the technology to the public will require time. “We are still far from real-world applications,” she said. “We focus on principles and mechanisms to see what is feasible. However, we are already taking the future

challenges into account."

Consumer perception is one of those challenges. When developing cultivated meat, the researchers chose to work with yeast rather than bacteria. "It would be difficult to explain to consumers that the meat was created using bacteria," Martinelli said.

Beyond the lab: the regulatory frontier

Scientific progress is only part of the challenge. Getting engineered living materials into medicine or food production will also require new regulatory thinking.

Because ELMs combine living cells and, in some cases, genetically modified microorganisms, they do not fit neatly into existing regulatory frameworks – designed for conventional medicines or standard food products, not materials that are, in a sense, alive.

In collaboration with the European Innovation Council, the team is already engaging with regulators, including the European Medicines Agency, to explore what rules and approvals these materials might eventually need.

"We need to reach a new attitude toward this technology," said Martinelli. "The collaboration helps us create a pathway towards the use of ELMs."

Vassalli added that ELMs could be "extremely powerful" if widely applied. "When we started the project, we had two main questions: is this feasible, and is it scalable? We can now say that it is feasible."

Scalability is the next challenge. If the team succeeds, it could be a step closer to a future where living materials take their place alongside the conventional ones we already take for granted.

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More info

- PRISM-LT (CORDIS)
- PRISM-LT project website