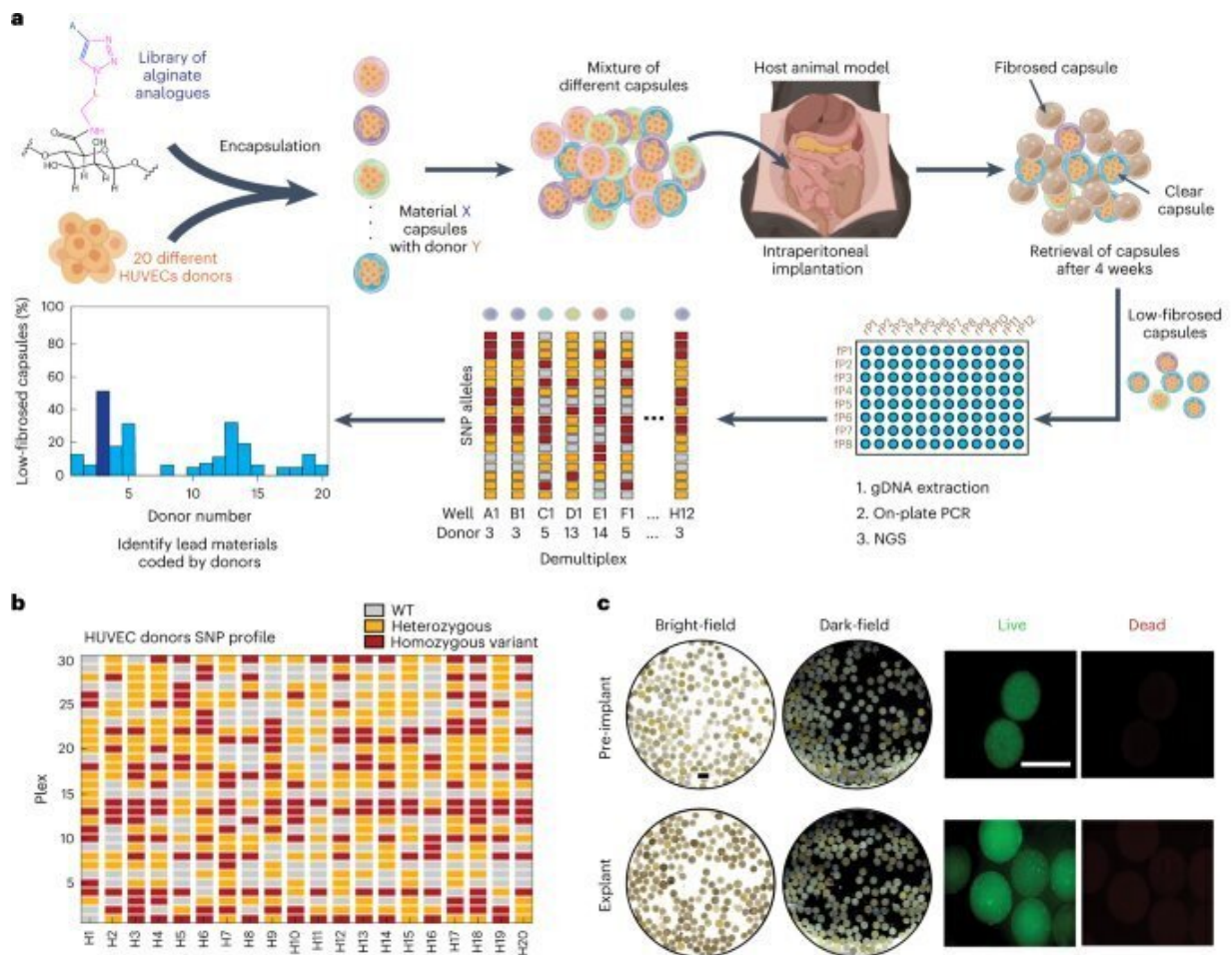


Study unlocks potential breakthrough in type 1 diabetes treatment

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Cell barcoding strategy enables high-throughput materials screening. Credit: *Nature Biomedical Engineering* (2023). DOI: 10.1038/s41551-023-01016-2

For the well over 700 million people around the globe living with type 1 diabetes, getting a host immune system to tolerate the presence of implanted insulin-secreting cells could be life-changing.

Rice University bioengineer Omid Veiseh and collaborators identified new [biomaterial](#) formulations that could help turn the page on type 1 diabetes treatment, opening the door to a more sustainable, long-term, self-regulating way to handle the disease.

To do so, they developed a new screening technique that involves tagging each biomaterial formulation in a library of hundreds with a unique "barcode" before implanting them in live subjects.

According to the study in *Nature Biomedical Engineering*, using one of the alginate formulations to encapsulate human insulin-secreting islet cells provided long-term blood sugar level control in diabetic mice. Catheters coated with two other high-performing materials did not clog up.

"This work was motivated by a major unmet need," said Veiseh, a Rice assistant professor of bioengineering and Cancer Prevention and Research Institute of Texas scholar. "In type 1 [diabetes patients](#), the body's immune system attacks the insulin-producing cells of the pancreas. As those cells are killed off, the patient loses the ability to regulate their blood glucose."

For decades, scientists labored toward what Veiseh called a "holy grail" goal of housing islet cells inside a porous matrix made out of a protective material that would allow the cells to access oxygen and nutrients without getting clobbered by the host's immune system.

However, materials with optimal biocompatibility proved very hard to find, due in part to screening constraints. On one hand, immune system

response to a given implanted biomaterial can only be assessed in a live host.

"The problem is the immune response needs to be investigated inside the body of these diabetic mice, not in a [test tube](#)," said Boram Kim, a graduate student in the Veiseh lab and co-lead author on the study. "That means that if you want to screen these hundreds of alginate molecules, then you need to have hundreds of animal test subjects. Our idea was to screen for hundreds of biomaterials at the same time, in the same test subject."

On the other hand, different biomaterial formulations look the same, making it impossible to identify high-performing ones in the absence of some telltale trait. This made testing more than one biomaterial per host unfeasible.

"They are different materials but they look the same," Veiseh said. "And once they are implanted in the body of a test subject and then taken out again, we cannot distinguish between the materials and we would be unable to identify which material formulation worked best."

To overcome these constraints, Veiseh and collaborators came up with a way to tag each alginate formulation with a unique 'barcode' that allowed them to identify the ones that performed best.

"We paired each modified biomaterial with human umbilical vein [endothelial cells](#) (HUVEC) from a different donor," Kim said.

"The HUVEC cells, because they come from unique donors, act as a barcode that allows us to tell what material was used initially," Veiseh added. "The winners are the ones that have [live cells](#) in them. Once we found them, we sequenced the genome of those cells and figured out which material was paired with it. That's how we uncovered the greatest

hits."

Trials are underway for stem cell-derived islet cell use in diabetic patients. However, current islet treatments require immunosuppression, making it a taxing way to treat type 1 diabetes.

"Currently, in order to use implanted islet cells in diabetic patients, you have to suppress the entire immune system, just as if you were trying to do an organ transplant," Veiseh said. "That comes with a lot of complications for the patient."

"They can develop cancer, they can't fight infections, so, for the vast majority of patients, it's better to actually do the insulin therapy where they inject themselves. With this biomaterial-encapsulation strategy, no immunosuppression is needed."

Placing actual HUVEC cells inside the biomaterial capsules increased the likelihood that the host immune system would detect a foreign presence. This makes the experiment more robust than simply testing for immune response to the biomaterials alone.

"We wanted to test a library of these materials, with the selection pressure of having cells inside the beads that makes it harder for the material to not get noticed by the immune system," Veiseh said. "There's a lot of interest from all the islet cell manufacturers to be able to get rid of immunosuppression and instead use these alginate hydrogel matrices to protect the implanted cells."

The new high-throughput "barcoding" approach can be deployed to screen for other medical applications using fewer live test subjects.

"That actually feeds into a lot of other projects in my lab where we're doing biologic production from cells for other disease indications,"

Veiseh said. "The same modifications can be applied to all types of materials that go into the body. This is not limited only to cell transplantation. The technology we developed can be paired with a lot of different device concepts."

"For instance, some diabetic patients use automated pump systems to self-administer insulin. The catheters on those pump systems have to be replaced every few days because they get clogged. We were able to show that coating the catheters with these new materials prevented clogging."

"With this new cell-based barcoding technology, biomaterials research just got an unprecedented boost that will accelerate the translation to clinically applicable products, and make it more affordable," said Dr. José Oberholzer, a transplant surgeon and bioengineer at the University of Virginia.

"This is a real paradigm shift. With this method, we can now screen hundreds of biomaterials at once and select those that the human body does not reject. We can protect cellular grafts from the assaults of the immune system, without the need for immunosuppressive medications," Oberholzer added.

Former Rice bioengineering professor and current NuProbe U.S. CEO David Zhang noted that "[high-throughput](#) DNA sequencing has revolutionized many biomedical fields."

"I am pleased to work with Omid to enable the development of improved biomaterials using my team's expertise in DNA sequencing," added Zhang, who was a co-investigator on the grant. "These improved biomaterials can enable durable implanted cell therapies to function as living drug factories, and can have a positively disruptive impact on patients with a variety of chronic diseases."

More information: Sudip Mukherjee et al, Screening hydrogels for antifibrotic properties by implanting cellularly barcoded alginates in mice and a non-human primate, *Nature Biomedical Engineering* (2023). DOI: [10.1038/s41551-023-01016-2](https://doi.org/10.1038/s41551-023-01016-2)

Provided by Rice University

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