A heartbeat away? Hybrid 'patch' could replace transplants

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Because heart cells cannot multiply and cardiac muscles contain few stem cells, heart tissue is unable to repair itself after a heart attack. Now Tel Aviv University researchers are literally setting a new gold standard in cardiac tissue engineering.

Dr. Tal Dvir and his graduate student Michal Shevach of TAU's Department of Biotechnology, Department of Materials Science and Engineering, and Center for Nanoscience and Nanotechnology, have been developing sophisticated micro- and nanotechnological tools—ranging in size from one millionth to one billionth of a meter—to develop functional substitutes for damaged heart tissues. Searching for innovative methods to restore heart function, especially cardiac "patches" that could be transplanted into the body to replace damaged heart tissue, Dr. Dvir literally struck gold. He and his team discovered that gold particles are able to increase the conductivity of biomaterials.

In a study published by *Nano Letters*, Dr. Dvir's team presented their model for a superior hybrid cardiac patch, which incorporates biomaterial harvested from patients and gold nanoparticles. "Our goal was twofold," said Dr. Dvir. "To engineer tissue that would not trigger an immune response in the patient, and to fabricate a functional patch not beset by signalling or conductivity problems."

A scaffold for heart cells

Cardiac tissue is engineered by allowing cells, taken from the patient or other sources, to grow on a three-dimensional scaffold, similar to the collagen grid that naturally supports the cells in the heart. Over time, the cells come together to form a tissue that generates its own electrical impulses and expands and contracts spontaneously. The tissue can then be surgically implanted as a patch to replace damaged tissue and improve heart function in patients.

According to Dr. Dvir, recent efforts in the scientific world focus on the use of scaffolds from pig hearts to supply the collagen grid, called the extracellular matrix, with the goal of implanting them in human patients. However, due to residual remnants of antigens such as sugar or other molecules, the human patients' immune cells are likely to attack the animal matrix.

In order to address this immunogenic response, Dr. Dvir's group suggested a new approach. Fatty tissue from a patient's own stomach could be easily and quickly harvested, its cells efficiently removed, and the remaining matrix preserved. This scaffold does not provoke an immune response.

Using gold to create a cardiac network

The second dilemma, to establish functional network signals, was complicated by the use of the human extracellular matrix. "Engineered patches do not establish connections immediately," said Dr. Dvir. "Biomaterial harvested for a matrix tends to be insulating and thus disruptive to network signals."

At his Laboratory for Tissue Engineering and Regenerative Medicine, Dr. Dvir explored the integration of gold nanoparticles into cardiac tissue to optimize electrical signaling between cells. "To address our electrical signalling problem, we deposited gold nanoparticles on the surface of our patient-harvested matrix, 'decorating' the biomaterial with conductors," said Dr. Dvir. "The result was that the nonimmunogenic hybrid patch contracted nicely due to the nanoparticles, transferring electrical signals much faster and more efficiently than non-modified scaffolds."

Preliminary test results of the hybrid patch in animals have been positive. "We now have to prove that these autologous hybrid cardiac patches improve heart function after heart attacks with minimal immune response," said Dr. Dvir. "Then we plan to move it to large animals and after that, to clinical trials."

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