Transplanting gene into injured hearts creates biological pacemakers

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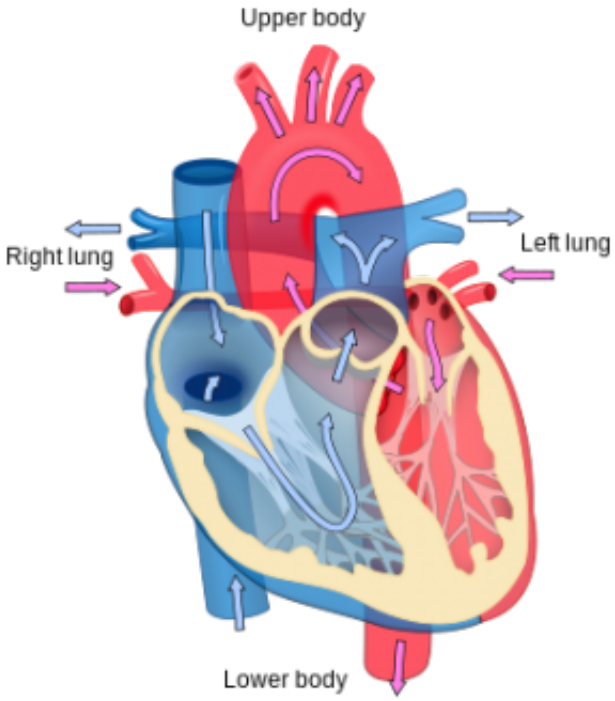

Heart diagram. Credit: Wikipedia

Cardiologists at the Cedars-Sinai Heart Institute have developed a minimally invasive gene transplant procedure that changes unspecialized heart cells into "biological pacemaker" cells that keep the heart steadily beating.

The laboratory animal research, published online and in today's print edition of the peer-reviewed journal *Science Translational Medicine*, is the result of a dozen years of research with the goal of developing biological treatments for patients with heart rhythm disorders who currently are treated with surgically implanted pacemakers. In the United States, an estimated 300,000 patients receive pacemakers every year.

"We have been able, for the first time, to create a biological pacemaker using minimally invasive methods and to show that the biological pacemaker supports the demands of daily life," said Eduardo Marbán, MD, PhD, director of the Cedars-Sinai Heart Institute, who led the research team. "We also are the first to reprogram a heart cell in a living animal in order to effectively cure a disease."

These laboratory findings could lead to clinical trials for humans who have heart rhythm disorders but who suffer side effects, such as infection of the leads that connect the device to the heart, from implanted mechanical pacemakers.

Eugenio Cingolani, MD, the director of the Heart Institute's Cardiogenetics-Familial Arrhythmia Clinic who worked with Marbán on biological pacemaker research team, said that in the future, pacemaker cells also could help infants born with congenital heart block.

"Babies still in the womb cannot have a pacemaker, but we hope to work with fetal medicine specialists to create a life-saving catheter-based treatment for infants diagnosed with congenital heart block," Cingolani said. "It is possible that one day, we might be able to save lives by replacing hardware with an injection of genes."

"This work by Dr. Marbán and his team heralds a new era of gene therapy, in which genes are used not only to correct a deficiency disorder, but to actually turn one kind of cell into another type," said Shlomo Melmed, dean of the Cedars-Sinai faculty and the Helene A. and Philip E. Hixson Distinguished Chair in Investigative Medicine.

In the study, laboratory pigs with complete heart block were injected with the gene called TBX18 during a minimally invasive catheter procedure. On the second day after the gene was delivered to the animals' hearts, pigs who received the gene had significantly faster heartbeats than pigs who did not receive the gene. The stronger heartbeat persisted for the duration of the 14-day study.

"Originally, we thought that biological pacemaker cells could be a temporary bridge therapy for patients who had an infection in the implanted pacemaker area," Marbán said. "These results show us that with more research, we might be able to develop a long-lasting biological treatment for patients."

If future research is successful, Marbán said, the procedure could be ready for human clinical studies in about three years.

More information: "Biological pacemaker created by minimally invasive somatic reprogramming in pigs with complete heart block," by Y.-F. Hu et al. *Science Translational Medicine*, stm.sciencemag.org/lookup/doi/ … scitranslmed.3008681

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