Developing next-generation biologic pacemakers

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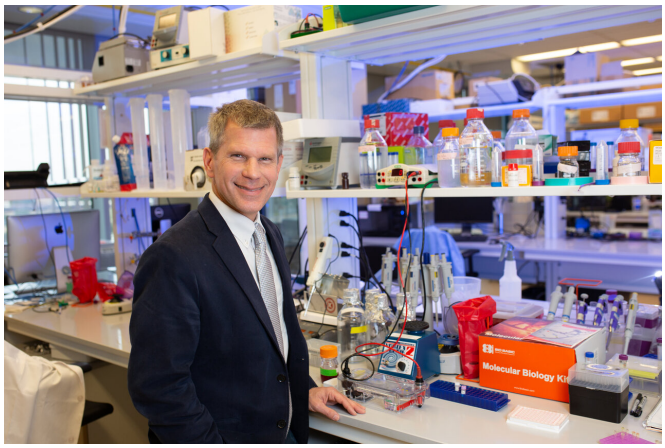

University of Houston associate professor of pharmacology Bradley McConnell is helping usher in a new age of cardiac pacemakers by using stem cells found in fat, converting them to heart cells, and reprogramming those to act as biologic pacemaker cells. Credit: University of Houston

University of Houston associate professor of pharmacology Bradley McConnell is helping usher in a new age of cardiac pacemakers by using stem cells found in fat, converting them to heart cells, and reprogramming those to act as biologic pacemaker cells. He is reporting his work in the *Journal of Molecular and Cellular Cardiology*. The new biologic pacemaker-like cell will be useful as an alternative treatment for conduction system disorders, cardiac repair after a heart attack and to bridge the limitations of the electronic pacemaker.

"We are reprogramming the cardiac progenitor cell and guiding it to become a conducting cell of the heart to conduct electrical current," said McConnell.

McConnell's collaborator, Robert J. Schwartz, Hugh Roy and Lillian Cranz Cullen Distinguished Professor of biology and biochemistry, previously reported work on turning the adipogenic mesenchymal stem cells, that reside in fat cells, into cardiac progenitor cells. Now those same cardiac progenitor cells are being programmed to keep hearts beating as a sinoatrial node (SAN), part of the electrical cardiac conduction system (CCS).

The SAN is the primary pacemaker of the heart, responsible for generating the electric impulse or beat. Native cardiac pacemaker cells are confined within the SAN, a small structure comprised of just a few thousand specialized pacemaker cells. Failure of the SAN or a block at any point in the CCS results in arrhythmias.

More than 600,000 electronic pacemakers are implanted in patients annually to help control abnormal heart rhythms. The small mechanical device is placed in the chest or abdomen and uses electrical pulses to prompt the heart to beat normally. In addition to having the device regularly examined by a physician, over time an electronic pacemaker can stop working properly.

"Batteries will die. Just look at your smartphone," said McConnell. "This biologic pacemaker is better able to adapt to the body and would not have to be maintained by a physician. It is not a foreign object. It would be able to grow with the body and become much more responsive to what the body is doing."

To convert the cardiac progenitor cells, McConnell infused the cells with a unique cocktail of three transcription factors and a plasma membrane channel protein to reprogram the heart cells in vitro.

"In our study, we observed that the SHOX2, HCN2, and TBX5 (SHT5) cocktail of transcription factors and channel protein reprogrammed the cells into pacemaker-like cells. The combination will facilitate the development of cell-based therapies for various cardiac conduction diseases," he reported.

More information: Suchi Raghunathan et al. Conversion of human cardiac progenitor cells into cardiac pacemaker-like cells, *Journal of Molecular and Cellular Cardiology* (2019). DOI: 10.1016/j.yjmcc.2019.09.015

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