A novel tool to study life-threatening arrhythmias: A genetically engineered pig

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Researchers at NYU Langone Medical Center have developed the first large animal model of an inherited arrhythmic syndrome - an advance that will lead to a better understanding of the biologic mechanisms important in normal heart conduction and rhythm. The novel pig model points the way toward development of better treatments for inherited forms of life-threatening arrhythmias, which are a significant cause of sudden cardiac death.

The findings, published online today in the *Journal of Clinical Investigation*, shed light on what causes lethal arrhythmias in the face of abnormal cardiac sodium channels. The proper functioning of these channels is essential for maintaining normal conduction in the heart. Disease-causing mutations in cardiac ion channels, technically referred to as "channelopathies," can lead to progressive cardiac conduction disorders, atrial and ventricular arrhythmias, and sudden cardiac death.

"By developing a genetically engineered pig sodium channelopathy model, we are now able to examine the mechanisms responsible for lethal arrhythmias in a human-like heart and investigate new therapies aimed at reducing sudden cardiac death," said lead author David S. Park, MD, PhD, assistant professor, Leon H. Charney Division of Cardiology, Department of Medicine at NYU Langone.

Until now, researchers have primarily used cultured heart cells and mouse models to study cardiac arrhythmias. "But because of similarities of the pig heart to human hearts, research with the pig model will prove invaluable in gaining further insights into the mechanisms that underlie life-threatening arrhythmias," said Glenn I. Fishman, MD, the study's senior author, and Director of the Leon H. Charney Division of Cardiology at NYU Langone.

Both Drs. Fishman and Park envision a future where novel therapies, such as drugs that can enhance cardiac sodium channel expression or radiofrequency ablation procedures, can first be tested in the pig model before application to patients. "A better understanding of arrhythmia mechanisms should yield better therapies in the future," said Dr. Park.

Provided by New York University School of Medicine

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