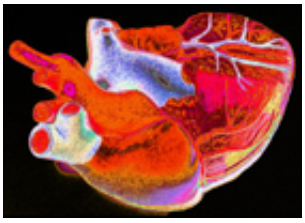
MedicalXpress

Researchers identify key proteins responsible for electrical communication in the heart

January 13 2014



Cedars-Sinai Heart Institute researchers have found that six proteins – five more than previously thought – are responsible for cell-to-cell communication that regulates the heart and plays a role in limiting the size of heart attacks and strokes.

The smallest of these proteins directs the largest in performing its role of coordinating billions of heart cells during each heartbeat. Together, the proteins synchronize the beating heart, the researchers determined.

"We now know these proteins exist," said Robin Shaw, MD, PhD, the senior author of the study published in the journal *Cell Reports*. "The findings advance our understanding of cell-to-cell communication at the root of healthy heart function. When there is less cell communication, which occurs in failing hearts, chances are greater of disturbances in heart rhythm that can result in disability or death."

Until now, scientists had recognized just one protein involved in cell-to-cell communication that occurs through conduits known as "gap junctions." The Cedars-Sinai researchers identified five additional proteins that regulate the rapid flow of electrical communication signals, coordinating heart cells to produce a stable heartbeat.

"The finding of alternative translation start sites within this important group of proteins adds startling diversity to a key biological process, namely that whereby heart cells communicate with each other electrically," said Eduardo Marbán, MD, PhD, director of the Cedars-Sinai Heart Institute. "The implications are major for arrhythmias and heart failure."

Through a phenomenon called "alternative translation," the protein-making machinery in each cell can produce shorter proteins from the same gene that encodes the largest of the proteins. Biologists had known of the existence of alternative translation but had not completely understood its physiological relevance. The Cedars-Sinai research team led by Shaw has expanded the understanding of this process and continues to study the precise role of the proteins produced by it.

The researchers also have determined that a class of drugs known as "mTOR inhibitors" – those already used for immunosuppression in organ transplants – can affect alternative translation, changing the balance of proteins in hearts cells, increasing the amount of electrical coordination in the heart. The findings suggest that mTOR inhibitors can be used to prevent erratic and sometimes fatal heart rhythms.

A properly beating heart is necessary to pump blood to the brain, lungs and other organs. When arrhythmias occur in the heart's main pumping chamber, the heart can stop, resulting in sudden cardiac arrest, the most common cause of death among heart patients. Preventing arrhythmias is a top clinical priority. The possibility of using mTOR inhibitors suggests

that drugs used to treat transplanted hearts could also be used to treat failing hearts.

Cell-to-cell communication occurs in all other organs. The same proteins that help heart cells communicate also play a role in brain function, bone development and insulin production in the pancreas. These proteins also affect the contraction of muscle cells within the uterus during childbirth and may potentially suppress cancer cells. The finding that mTOR inhibitors improve cell-to-cell communication indicates that this class of drugs could be useful to treat multiple disorders.

Provided by Cedars-Sinai Medical Center