Researcher develops new possibilities to prevent sudden cardiac death

Posted February 20, 2021

Nearly a half-million people a year die from sudden cardiac death (SCD) in the U.S. — the result of malfunctions in the heart's electrical system.

A leading cause of SCD in young athletes is arrhythmogenic cardiomyopathy (ACM), a genetic disease in which healthy heart muscle is replaced over time by scar tissue (fibrosis) and fat.

Assistant Professor of Biomedical Sciences Stephen Chelko, right, works in his laboratory with graduate student Maicon Landim-Vieira. Chelko's lab has published research providing important new insights about arrhythmogenic cardiomyopathy, a leading cause of sudden cardiac death among young athletes. Image credit: Mark Bauer/FSU College of Medicine

prevention. His findings are published in the current issue of Science Translational Medicine.

Individuals with ACM possess a mutation causing arrhythmias, which ordinarily are non-fatal if managed and treated properly. However, Chelko shows that exercise not only amplifies those arrhythmias but causes extensive cell death. Their only option is to avoid taking part in what should be a healthy and worthwhile endeavour: exercise.

“There is some awful irony in that exercise, a known health benefit for the heart leads to cell death in ACM subjects,” Chelko said. “Now, we know that endurance exercise, in particular, leads to large-scale myocyte cell death due to mitochondrial dysfunction in those who suffer from this inherited heart disease.”

Several thousand mitochondria are in nearly every cell in the body, processing oxygen and converting food into energy. Considered the powerhouse of all cells (they produce 90 percent of the energy our bodies need to function properly), they also play another important role as a protective antioxidant.

As mitochondria fail to function properly, and myocyte cells in the heart die, healthy muscles are replaced by scar tissue and fatty cells. Eventually, the heart’s normal electrical signals are reduced to an erratic and disorganized firing of impulses from the lower chambers, leading to an inability to properly pump blood during heavy exercise. Without immediate medical treatment, death occurs within minutes.

Chelko’s research gets to the heart of the process involved in mitochondrial dysfunction.

“Ultimately, mitochondria become overwhelmed and expel ‘death signals’ that are sent to the nucleus, initiating large-scale DNA fragmentation and cell death,” Chelko said. “This novel study unravels a pathogenic role for exercise-induced, mitochondrial-mediated cell death in ACM hearts.”

In addition to providing a better understanding of the process involved, Chelko discovered that cell death can be prevented by inhibiting two different mitochondrial proteins. One such approach utilizes a novel targeting peptide developed for Chelko’s research by Nunzianna Doti and Menotti Ruvo at the Institute of Biostructure and Bioimaging of the National Research Council in Naples, Italy.

That discovery opens avenues for the development of new therapeutic options to prevent myocyte cell death, cardiac dysfunction and pathological progression leading to deadly consequences for people living with ACM.