Researchers discover potential genetic target for heart disease

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Researchers at the University of Cincinnati (UC) have found a potential genetic target for heart disease, which could lead to therapies to prevent the development of the nation's No. 1 killer in its initial stages.

These findings will be presented for the first time at the American Heart Association's (AHA) Scientific Sessions in Chicago Nov. 17.

The study, led by WenFeng Cai, PhD, a postdoctoral fellow under the direction of Litsa Kranias, PhD, AHA distinguished scientist and Hanna Chair in Cardiology in the department of pharmacology and cell biophysics, shows that a micro-RNA, known as miR765, which regulates gene expressions, can down-regulate the expression of protein phosphatase 1 inhibitor-1 (I-1) and reduce the contractility of cells that make up cardiac muscle.

"Previous studies have shown that the reduction in I-1 expression may play a role in the pathogenesis of heart disease," Cai says. "However, the underlying molecular mechanism contributing to this down-regulation is unknown.

"We wanted to see if miR765 would serve as a candidate to regulate this protein expression and affect the contractility of the cardiac muscle cells."

Using a gene transfer agent—or virus—researchers moved either miR-765 or a control agent into ventricular cells of animal models.

Data showed that the expression of I-1 messenger RNA was decreased by 20 percent in the miR765 cells of these models when compared with the control models.

"Under resting conditions, the contractile parameters were decreased in miR765-treated animal models," Cai says. "Although beta adrenergic agonist, used to speed up the pumping action of the heart, had a positive effect, the contractile function remained suppressed in the miR765 group."

Cai adds that analysis showed both phosphorylations of phospholamban and ryanodine receptor, the proteins that regulate calcium uptake and calcium release, were significantly reduced in the miR765 group both in the presence and in the absence of beta adrenergic agonist.

"These findings show that miR765 can down-regulate the expression and reduce contractility of heart cells by decreasing or deactivating a number of proteins that help the heart function at full capacity," Cai says. "This leads us to believe that miR765 may play a role in the development of heart failure.

"Hopefully, these findings will lead to future studies, helping researchers and clinicians develop a therapeutic target to stop heart disease where it first starts: in the genes."

Provided by University of Cincinnati Academic Health Center