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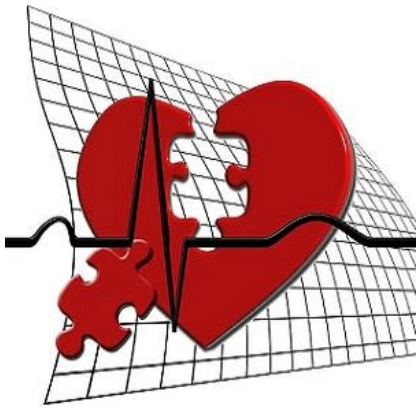
Link between short telomeres and cardiomyopathy



Stanford-led research has found that people with cardiomyopathy have abnormally short telomeres in the muscles that contract the heart. The finding, published in the Proceedings of the National Academy of Sciences, could lead to new pathways for drug discovery.

A telomere is a DNA sequence that serves as a protective cap on the ends of chromosomes. It remains unclear whether the stunted telomeres directly affect the function of the cardiomyocytes or arise as a result of heart failure. Still, the new finding opens the door to an intriguing line of research and drug discovery, researchers say.

It also may one day allow researchers and clinicians to identify people at risk for heart failure due to cardiomyopathy. A cardiomyopathy is a condition in which the heart is unusually large, thickened, or stiff, affecting its ability to pump blood effectively.

“The shortening of telomeres in cardiomyocytes appears to be a reliable hallmark of cardiac failures that arise due to genetic defects, and it’s very specific to cells that require the missing contractile proteins such as dystrophin, troponin T, or myosin heavy chain, among others,” says Helen Blau, professor of microbiology and immunology at Stanford University and a member of the Stanford Cardiovascular Institute.

In most cells, telomeres naturally shorten each time the cell divides. But cardiomyocytes divide infrequently, and their telomere lengths remain relatively stable throughout one’s life.

In earlier work, Blau and colleagues found that, in mice, telomere shortening triggered a DNA-damage response that compromised the function of the cells’ energy generators, or mitochondria. As a result, cardiomyocytes were unable to efficiently pump blood throughout the body.

Blau, lead author Alex Chang, an instructor of cardiovascular medicine and of microbiology and immunology, and colleagues at Stanford’s Cardiovascular Institute collaborated in this new study to test the hypothesis that telomere shortening is a general hallmark of genetic hypertrophic cardiomyopathy (HCM) or dilated cardiomyopathy (DCM) as a result of mutations in contractile proteins essential to cardiac function.

The study compared the telomere length in cardiomyocytes from 11 patients with dilated or hypertrophic cardiomyopathy due to genetic mutations with nine people who had died from causes unrelated to heart disease.

Chang and co-researchers found that telomeres from the cardiomyopathy patients were about 25-40 percent shorter than those of the control subjects. In contrast, the telomere length in nonbeating heart cells of the blood vessels did not vary significantly between the two groups.

Chang saw similar results in cardiomyocytes generated from induced pluripotent stem cells: Those generated from people with cardiomyopathies had significantly shorter telomeres than those generated from unaffected relatives.

“Within 20 days we could see the telomere shortening happening in the laboratory-grown cardiomyocytes from diseased patients, suggesting this is a cell-intrinsic property,” Blau says.

The ability to use iPS cell technology to generate affected cardiomyocytes also means that it should be possible to quickly and easily test for compounds or drugs that interfere with the telomere shortening with a view to finding drugs to abrogate the disease in humans, the researchers believe.

Source: Stanford University
Image Credit: Pixabay

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