



Insufficient Cell Membrane Repair Causes Heart Disease

Researchers at the University of Iowa have discovered that the heart muscle has a specific mechanism for repairing itself. This mechanism for healing and resealing heart muscle cell membranes requires the presence of a protein called dysferlin.

Heart muscle cells get damaged when we exercise rigorously. Over-exercising can actually rupture some cells. It is only due to the repair process that reseals the cell membranes that the heart stays healthy. If not, then the damaged cells would die and lead to extensive heart damage and cardiomyopathy.

Active tissues such as a beating heart or contracting muscle inevitably suffer cell membrane tears on account of physical stress and strain. Such damage requires mechanisms that can restore the tissues to full health.

In 2003, Dr. Kevin Campbell and his colleagues at UI had identified that the protein dysferlin plays a key role in the vital repair mechanism for skeletal muscle. They also found that dysferlin deficiency in humans can lead to faulty muscle membrane repair and cause three types of muscle dystrophy.

The new study, conducted at the Roy J. and Lucille A. Carver College of Medicine used laboratory mice to check the role of dysferlin in cardiomyopathy. Primary investigation by the UI research team revealed that there was no heart damage in young mice that lacked dysferlin. This was consistent with what is seen in humans with mutated dysferlin.

However, the researchers decided to check out the mice as they aged after they heard about a study on a dysferlin deficient Japanese patient which found late onset of cardiomyopathy. The researchers found that the mice started showing signs of cardiomyopathy when they were about one year old which is middle age for mice.

They also observed that when the mice were made to exercise, the stress-induced injury of their heart became exaggerated. This led researchers to the con-

clusion that cardiomyopathy can be caused by inadequate membrane repair.

To further confirm their findings, the researchers bred mice that lacked both dysferlin and the protein dystrophin. The second protein is usually found missing in patients with Duchenne muscular dystrophy. They found that mice with both these critical proteins missing had early onset of cardiomyopathy.

Additionally, the condition was much more severe in comparison to mice that were missing any one of the two proteins. The results suggested to the researchers that young Duchenne patients can get some heart protection from dysferlin in the form of delay in onset of cardiomyopathy.

The findings further expand the understanding that medical researchers have about the function of dysferlin. It shows that the protein plays a role not only in membrane repair in skeletal muscle cells but also in heart muscle cells. It also suggests that cardiomyopathy can be caused on account of insufficient repair of membranes.

If we could boost this repair mechanism, it might be possible to slow cardiac and skeletal muscle damage in muscular dystrophy patients, said Dr. Campbell, who is head of the department and a UI Professor of Neurology in addition to being investigator for Howard Hughes Medical Institute and Roy J. Carver Biomedical Research Chair in Molecular Physiology.

We hope these findings will stimulate clinicians to look at the cardiac health of muscular dystrophy patients and the overall muscle health of patients with cardiomyopathy, Dr. Campbell added in relation to their study findings which are published in the *Journal of Clinical Investigation*.