

Enzyme prevents fatal heart condition associated with athletes

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Scientists have discovered an important enzyme molecule that may prevent fatal cardiac disorders associated with cardiac hypertrophy – the leading cause of sudden cardiac death in young athletes.

Cardiac hypertrophy is a disease of the [heart](#) muscle where a portion of the tissue is thickened without any obvious cause. It is commonly linked to high blood pressure (hypertension) and excessive exercises and results in a shrinking of the heart chamber and a reduction of its blood-pumping volume.

The condition is also associated with fatal cardiac disorders related to irregular heart beats (arrhythmias), leading to millions of deaths worldwide each year, and is perhaps the most well-known cause of sudden cardiac arrest in young sports people.

The researchers used laboratory experiments and computer simulations to show that the [enzyme](#) MKK4 is involved in preventing arrhythmias. They believe it does this by modifying another protein, connexin, which forms an electrical bridge between adjacent heart cells to ensure the conduction of electrical activity across the heart as an excitation wave, triggering synchronised mechanical contraction of the heart with a regular heartbeat rhythm.

The multidisciplinary team, writing in *The Journal of Biological Chemistry*, found that loss of the MKK4 protein disrupts the spatial distribution of connexin, resulting in reduced and non-uniform electrical

coupling between heart cells.

This causes a fragmented excitation wave in the heart, leading to uncoordinated heart muscle contraction and irregular heart rhythm. As a result, the heart loses its power to pump blood efficiently, causing disability or sudden cardiac death.

"Using experimental measurements together with detailed computer models, we were able to simulate the electrical activity in cardiac tissue with disrupted electrical coupling between adjacent cardiac cells," said Dr Xin Wang, in Manchester's Faculty of Life Science.

"The information generated from this study will help us to identify whether the MKK4 enzyme could become a therapeutic target for the treatment of cardiac arrhythmias in association with cardiac hypertrophy."

Co-author Professor Henggui Zhang, a biophysicist in Manchester's School of Physics and Astronomy, added: "This research means it would be possible to identify the most important factor behind the sudden cardiac death associated with [cardiac hypertrophy](#), which can affect people of any age with hypertension and also healthy well-trained athletes."

Provided by University of Manchester

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