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DNA from heart's own cells plays role in heart failure by mistakenly activating immune system

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DNA from the heart's own cells plays a role in heart failure by mistakenly activating the body's immune system, according to a study by British and Japanese researchers, co-funded by the British Heart Foundation (BHF). Scientists from King's College London and Osaka University Medical School in Japan showed that during heart failure – a debilitating condition affecting 750,000 people in the UK – this 'rogue DNA' can kick start the body's natural response to infection, contributing to the process of heart failure.

During heart failure immune cells invade the heart, a process called inflammation. The process makes heart muscle less efficient, reducing its ability to pump blood around the body. Inflammation is usually only activated when the body is facing a threat, such as an infection by a bacteria or virus.

The study, to be published today in the journal *Nature*, shows in mice that inflammation in the heart can be caused by the body's own DNA. The DNA escapes when a natural process to break down damaged cell components, called autophagy, becomes less efficient. Autophagy can stop working correctly when cells are under stress, such as during heart failure.

The problem DNA comes from energy-generating structures in heart cells, called mitochondria. Mitochondrial DNA triggers inflammation

because it resembles DNA from bacteria, triggering a receptor in immune cells called Toll-like Receptor 9 (TLR9).

Mitochondria fascinate scientists because they seem to have evolved from bacteria more than 1.5 billion years ago, when primitive forms of life recruited bacteria to help them produce their energy. Although this pact with bacteria is one of evolution's success stories, this study shows that the human immune system still recognises the bacterial fingerprint in mitochondrial DNA, triggering a response from the immune system.

Professor Kinya Otsu, recently announced as BHF Professor of Cardiology at King's College London, who led the study, said: 'When mitochondria are damaged by stress, such as during heart failure, they become a problem because their DNA still retains an ancient bacterial fingerprint that mobilises the body's defences.

'We previously showed that damaged mitochondria build-up during heart failure, when the natural processes of cell breakdown become less effective. Now we've shown that the DNA fingerprint that we retain in our mitochondria causes our own immune system to turn against us.'

Dr Shannon Amoils, Research Advisor at the BHF, said: 'This intriguing discovery is an important breakthrough in our understanding of why, during heart failure, the immune system becomes activated without the presence of any obvious external threat. This inflammation in the heart plays an important role in the disease process.

'Heart cells are packed with mitochondria, which provide the power the heart needs to pump blood around the body, and this study shows that, during heart failure, DNA from these mitochondria at least partly causes the problem. This research points towards new avenues of exploration that could hopefully lead to treatments for heart failure in the future.'

Professor Kinya Otsu was recently awarded more than £3 million by the BHF to carry out his pioneering work.

More information: Takafumi Oka et al (2012). *Nature*. Mitochondrial DNA That Escapes from Autophagy Causes Inflammation and Heart Failure. doi:10.1038/nature10992

Provided by King's College London