Scientists identify genetic link for a 'heavy heart'

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(Medical Xpress) -- An international research team led by Imperial College London has for the first time pinpointed a single gene associated with one of the leading causes of heart thickening and failure.

Scientists have found that the Endog gene in rats and mice influences the thickness of the muscular heart wall, how well the heart pumps and how much fat accumulates inside the organ.

The researchers say the findings, published today in the journal Nature, bring them one step closer to developing new treatments that target the underlying causes of heart conditions, rather than just treating the symptoms.

Professor Stuart Cook from the Medical Research Council (MRC) Clinical Sciences Centre at Imperial College London, who led the study, said: “Our study shows that the Endog gene, which was previously thought to be involved in cell death, actually plays an important role in the enlargement of the heart, which can lead to heart failure and eventually death in the worst cases. We found that a faulty copy of this gene causes the heart to become thick and fatty, making it ‘heavy’ with poor function.

“It does this by interfering with the heart cells’ energy source – the mitochondria. Like any other muscle in our body, the heart needs energy to keep it pumping. If the mitochondria don’t work properly, the heart struggles to make enough energy and the cells produce toxic by-products, called reactive oxidative species, which increase thickening of the heart wall.”

Enlargement of the heart is one of the many causes of heart failure, where the heart can’t pump blood around the body properly because the muscle is weak, stiff or has been damaged.

While some cases of enlarged heart are caused by other medical conditions, such as diabetes or high blood pressure, a person’s genetic makeup can also play an important role.

Previous studies have shown a link between heart wall thickening (cardiac hypertrophy) and several sections of the genetic code, but this is the first time researchers have isolated a single gene, using sophisticated DNA sequencing approaches.

“Our findings give us a new insight into how the mitochondria exert control over the thickness of main chamber of the heart,” added Professor Cook. “We can now start to investigate new ways to develop treatments which target the mitochondria and toxic oxidative molecules.”

Professor Amanda Fisher, Director of the MRC Clinical Sciences Centre at Imperial, said: “What’s fascinating about this study is that it identifies the function of a gene which was totally unpredicted to be involved in enlargement of the heart. This discovery emphasises the importance of deciphering the genetic code of a broad range of mammals alongside that of humans eventually to allow us explore new avenues for better targeted drugs.”

Professor Peter Weissberg, Medical Director of the British Heart Foundation, said: “This study has discovered a gene which seems to hold the key to causing a ‘heavy heart’. An enlarged or heavy heart is a significant cause of multiple heart problems – including heart failure – that can have a profound impact on people’s quality of life. “The finding could pave the way for new treatments to prevent the development of a heavy heart. Hopefully, in the future, we’ll be able to target the root cause of some patients’ heart conditions rather than treating the resulting symptoms.”

The research was a collaboration between scientists in Europe, the US and Japan, and was co-funded by the MRC, the Fondation Leducq, the UK National Institute for Health Research and the British Heart Foundation amongst others.

More information: C. McDermott-Roe et al. ‘Endonuclease G is a novel determinant of cardiac hypertrophy and mitochondrial function.’ *Nature*, 6 October 2011.

Provided by Imperial College London