'Rambo' protein may not be so violent after all

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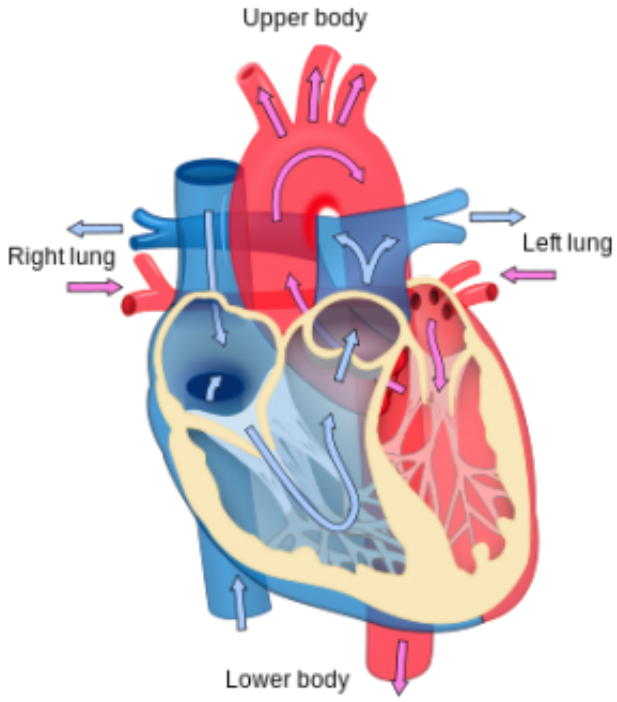

Heart diagram. Credit: Wikipedia

A protein dubbed 'Bcl-Rambo' can protect against heart failure, suggests new research from King's College London and funded by the British Heart Foundation (BHF).

The Bcl-Rambo protein (also known as Bcl2-L-13) was named by a Japanese scientist because it was thought to be involved in activating cell

death - 'Rambo' also means violence in Japanese. However, it seems that the Rambo movie character's protein counterpart has actually been misjudged. New research shows for the first time that the Bcl-Rambo protein may not be so violent after all and is actually involved in an essential and protective process which is implicated in heart failure.

Controlled regulation of this protein may help to limit the development of heart failure. The research, published in the *Nature Communications* journal today, will open doors for scientists to develop new therapies to improve the outlook for people suffering with heart failure, a condition for which there is currently no cure.

There are around 175,000 heart attacks in the UK each year - one every three minutes. For those who survive a heart attack there is a risk that the heart will have been damaged and this can lead to heart failure. Over half a million people in the UK are living with heart failure. It can have a huge impact on a person's life, leaving them tired, short of breath and unable to do everyday activities like walking up stairs or washing by themselves.

The BHF-funded researchers, working with colleagues in Japan on cells derived from humans and mice, discovered the Rambo protein is involved in safely clearing damaged mitochondria from cells. Mitochondria are small structures within cells which are often referred to as their powerhouses. They produce vital energy needed for cells to work properly. Damaged mitochondria are removed by a process called mitophagy - killer vesicles are activated to engulf and degrade the damaged mitochondria. The process of mitophagy is essential, and mistakes in this process have been linked to the development of heart failure.

We now know for the first time that the Bcl-Rambo protein is involved in the process of mitophagy in mammalian cells. If researchers can find

ways of regulating this protein, we may be able to control the process of mitophagy and develop new treatments to limit the development of heart failure.

BHF Professor Kinya Otsu from King's College London, who led the research, said: "Knowing that the process of mitophagy is implicated in heart failure is one thing, but we need to know more about the molecules and pathways involved in the process so that we can work towards finding a treatment for heart failure. The discovery of the Rambo protein's importance in protecting cells represents a significant step forward in the understanding of disease processes at the cellular level.

"Mitophagy is linked to a number of diseases and is of growing interest to scientists. As well as heart failure, neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease have all been linked to problems related to mitophagy."

Professor Jeremy Pearson, Associate Medical Director at the British Heart Foundation, which helped fund the research, said: "More than half a million people in the UK are living with the devastating effects of heart failure - a disabling condition that in its severest form has a life expectancy worse than many cancers. There is currently no cure and limited options to reduce the development of the condition.

"This elegant piece of discovery science research has shed light on the misunderstood Rambo protein which may in fact protect heart cells from death in heart failure, revealing a possible target for therapy. Further research is now needed to develop methods to control the activity of the protein in heart cells."

Provided by King's College London