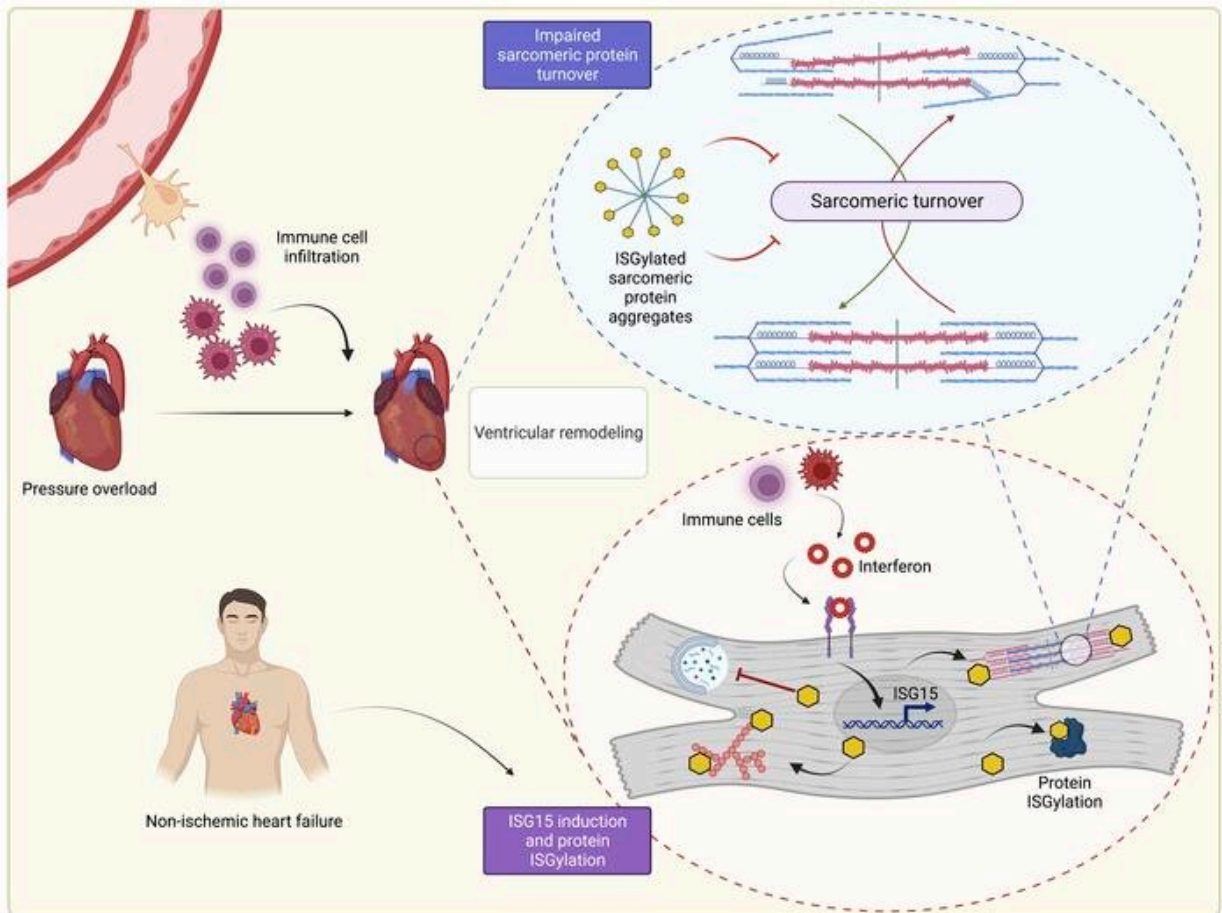


How does inflammation cause heart failure? New study reveals insights

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Graphical abstract. Credit: *Journal of Clinical Investigation* (2023). DOI: 10.1172/JCI161453

A St. Michael's-led study has uncovered a way in which inflammation of the heart can prompt the production of a protein that impairs heart function.

The study, published in the *Journal of Clinical Investigation*, describes a process by which inflammation can cause heart failure, a chronic health condition affecting hundreds of thousands of people in Canada.

"Heart failure is a major cause of illness and death. Its symptoms can include breathlessness, tiredness, palpitations or ankle swelling," said Dr. Andrew Advani, study senior author, St. Michael's endocrinologist and Keenan Chair in Medicine. "Our team wanted to understand how heart failure happens so that we can look for potential new treatments."

How inflammation impacts heart failure

Inflammation occurs when [white blood cells](#) come together in one place. Sometimes inflammation can be a good thing, for example, when white blood cells come together to fight an infection. But when inflammation happens where there is no infection it can lead to negative outcomes. Scientists have known for many years that heart failure is associated with inflammation, but it was not clear how white blood cells impair [heart function](#), says Advani.

Through a series of experiments, Advani and the team discovered that inflammation causes heart cells to produce a protein called ISG15. They found that ISG15 sticks to other proteins in heart muscle cells, causing them to stop working properly. When cell proteins stick to other proteins, this is called a post-translational modification. Post-translational modifications can affect how proteins work and they can play important roles in the development heart failure.

"This is a new idea, that this particular post-translational modification

caused by [inflammation](#) can affect the functioning of heart muscle and cause heart failure," Advani said. "The discovery opens up a whole new field of heart failure research."

He cautions that this translational research is in the early stages and it could take many years for the findings to benefit patients. Still, the results are exciting because of the potential for new treatments, including possible therapies to stop ISG15 from sticking to proteins or new ways to identify people who are at risk of developing heart failure, Advani said.

The research took place at the Keenan Research Center for Biomedical Science at St. Michael's Hospital, and was supported, in part, by the Heart and Stroke Foundation of Canada and by the Banting and Best Diabetes Center.

"This is the culmination of over five years' work by our talented team," Advani said. The work was led by Dr. Veera Ganesh Yerra, who moved from India to Toronto in 2017 to embark on [heart failure](#) research with Advani's lab. Since then, the team faced setbacks due to the COVID-19 pandemic, but still kept going, Advani said.

"We're motivated by curiosity and by the patients we look after, and we are excited by asking important questions and working together as a team to find the answers," he said.

More information: Veera Ganesh Yerra et al, Pressure overload induces ISG15 to facilitate adverse ventricular remodeling and promote heart failure, *Journal of Clinical Investigation* (2023). [DOI: 10.1172/JCI161453](#)

Provided by St. Michael's Hospital

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