

Inflammatory link discovered between arthritis and heart valve disease

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The research could lead to improved treatments for rheumatoid arthritis, and suggests investigating existing medicines that dampen inflammation to treat heart valve diseases, such as rheumatic heart disease. Credit: Walter and Eliza Hall Institute of Medical Research

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The team, led by Walter and Eliza Hall Institute researcher Dr Philippe Bouillet, Dr Derek Lacey and colleagues, identified critical regions of the DNA that control production of the inflammatory protein, called TNF (tumour necrosis factor).

Rheumatoid arthritis is a chronic inflammatory disease that affects two per cent of the Australian population, causing debilitating joint pain and damage. Many people with rheumatoid arthritis make too much TNF, which recruits immune cells that damage the joints and keeps the body in a perpetual state of inflammation.

The link between TNF overproduction and the development of rheumatoid arthritis has been known for many years. However Dr Bouillet's team has identified new regions of the DNA critical for destabilising the molecule.

"People with rheumatoid arthritis have too much TNF in their joints and in their blood," Dr Bouillet said. "We have identified a previously unknown way that the body destabilises the molecules during the process of TNF production to stop too much of the protein being made. We could essentially develop agents that put a spanner in the works, stopping the factory production of TNF."

Treating rheumatoid arthritis patients with drugs that 'mop up' excess TNF has been very effective in managing the disease, Dr Bouillet said. However they do have a downside.

"Up to 50 per cent of patients become unresponsive to anti-TNF drugs because they develop immunity to this foreign protein," he said. "We think targeting the

regions of the DNA that destabilise the molecule could be an innovative way to interfere with protein production to dampen the amount of TNF being made."

The study identified that existing drugs that mop-up excess TNF could help in treating inflammatory diseases affecting heart valves.

"This is the first time that we have linked the overproduction of TNF to heart valve disease," Dr Bouillet said. "While it seems that genetics makes a substantial difference to the severity of the heart disease in our models, it does suggest that in humans we may be able to better diagnose heart valve [disease](#) in people with [rheumatoid arthritis](#) in the future."

Dr Bouillet also said that existing drugs that block and remove TNF could be investigated for treating heart valve diseases.

"Clinicians have trialled drugs that target TNF in the past, but for diseases of the heart muscle and with poor effect," Dr Bouillet said. "Our studies suggest that excessive TNF drives heart valve - rather than heart muscle - diseases, and may be worth investigating for inflammatory diseases affecting the [heart valves](#), such as [rheumatic heart disease](#)."

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Provided by Walter and Eliza Hall Institute

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