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# Singapore identifies gene that controls scarring in damaged hearts

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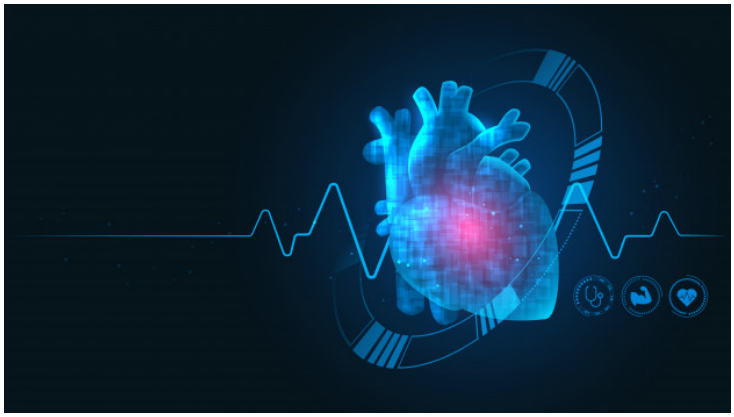
**Developed a method to "Silence the gene", called WWP2 at the early stages of cardiomyopathy to delayprogression to heart failure**



Scientists at Duke-NUS Medical School in Singapore have identified a gene that controls the behaviour of a specific type of cardiac macrophage responsible for excessive scarring during the early phases of common heart diseases or cardiomyopathies. When the gene, called WWP2, is blocked, heart function is improved and scar tissue formation is slowed, delaying the progression to heart failure.

“Scarring or fibrosis of the heart, as in non-ischaemic cardiomyopathies, is a progressive condition and global health concern,” explained Associate Professor Enrico Petretto, Director of Duke-NUS’ Centre for Computational Biology and a systems geneticist with the School’s Cardiovascular & Metabolic Disorders (CVMD) Programme. “In its earliest stages, it is characterised by an inflammatory phase, so intervening at that point could significantly delay disease progression.”

Using single cell RNA sequencing, the team found when fibrosis is triggered, a wide range of different macrophages, immune cells that clear foreign material in the body, are activated in a preclinical model of heart disease.

While macrophages are mostly known for their role in removing cancer cells, microbes and cellular debris, they also help with the regeneration of healthy muscle cells. However, a subset of these cardiac macrophages are controlled by WWP2. These WWP2-expressing macrophages actively promote scarring by triggering local cardiac cells (fibroblasts) to produce collagen in an uncontrolled manner, fuelling scar tissue formation.

“We are now developing small molecule inhibitors that target a specific form of the WWP2 protein, which have already shown promising anti-fibrotic results in cells. We believe these could hold therapeutic potential for treating fibrotic conditions like non-ischaemic cardiomyopathies, and may prove effective in other fibrotic diseases where WWP2 is involved”, said Associate Professor Enrico Petretto.