

**MEDIA RELEASE
FOR IMMEDIATE RELEASE**

29 January 2018

Researchers discover molecular nets inside heart muscles which hold promise for new heart failure treatment

Singapore - Local researchers have discovered that a group of molecules, called *chondroitin sulfate*, normally found only in connective tissues such as the cartilage, accumulates and causes inflammation in the hearts of patients with heart failure.

The discovery was made jointly by the National University Health System (NUHS), A*STAR's Genome Institute of Singapore (GIS) and the National University of Singapore (NUS) Yong Loo Lin School of Medicine, and is now published in *Circulation*, a journal from the American Heart Association.

Chondroitin sulfate is a form of polysaccharide, which is a long chain of sugar molecules, usually attached to certain proteins, forming molecular 'nets' outside cells.

"In the rare disease known as Mucopolysaccharidosis (MPS) Type VI, patients have a genetic mutation that leads to systemic chondroitin sulfate accumulation. Because of this, MPS IV patients end up with multi-organ failure, including irregular heartbeats, enlarged heart muscles which may eventually result in heart failure. This evidence gives a very clear link between chondroitin sulfate accumulation and heart diseases," said Dr Zhao Rongrong from the NUHS' Cardiovascular Research Institute, who is the co-author in the study.

In this study, researchers found that diseased hearts, even from patients without MPS VI, were found to have chondroitin sulfate accumulation. Using the arylsulfatase B (ASB) enzyme, an approved treatment for MPS VI, it was demonstrated that fibrosis and disease progression was effectively treated in an animal model of heart failure.

This new treatment approach could potentially add to current treatment strategies, which include long-established medicines such as beta-blockers and ACE-inhibitors.

"There are more examples now that prove that understanding rare diseases gives us clues for how to treat common conditions. We have learnt that chondroitin sulfate molecular nets don't only accumulate inside the heart muscle of patients with MPS VI. Heart failure patients without MPS VI also have these molecular nets, which can be targeted with a medicine that is already US FDA-approved. Targeting these molecular nets may bring a fresh new treatment approach for patients with this severe debilitating disease," said Associate Professor Roger Foo, who is the lead author in this study, and

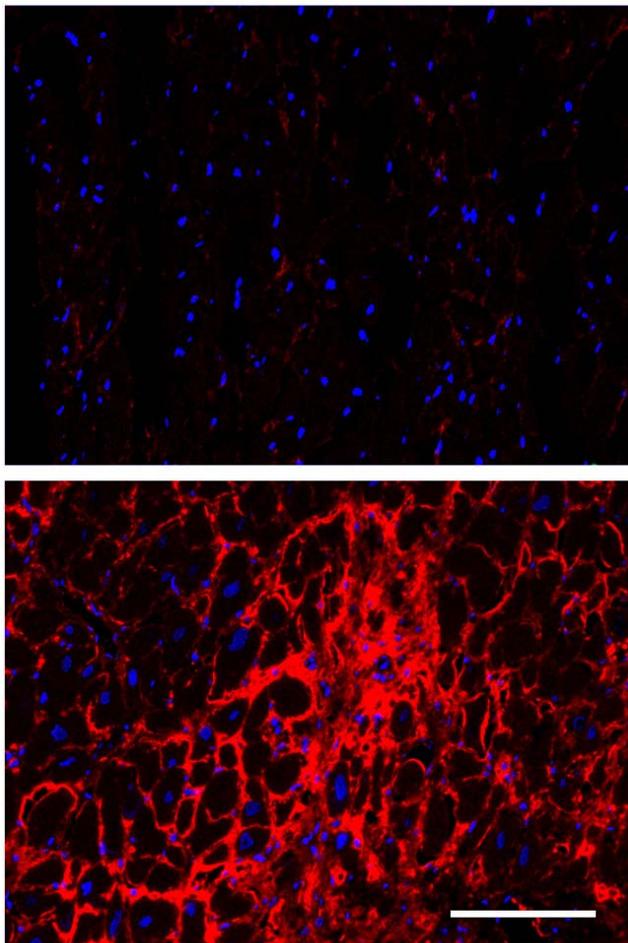
is also the Senior Consultant, Department of Cardiology at the National University Heart Centre, Singapore. Associate Professor Foo is Principal Investigator at the NUHS' Cardiovascular Research Institute and at A*STAR's GIS.

Cardiovascular disease (CVD) is a leading cause of death worldwide, with an estimated 17.7 million people dying from CVD in 2015, accounting for 31% of all global deaths. CVD also accounted for 29.6% of all deaths in Singapore in 2016. (Source: World Health Organisation and Ministry of Health, Singapore)

This research project is funded by A*STAR's Biomedical Research Council and the Singapore National Medical Research Council.

(Image)

Chondroitin sulfate (marked in red), virtually absent in healthy human heart tissue (upper panel), is found to accumulate in hearts of patients with heart failure, forming dense 'molecular nets' around the heart muscle cells (lower panel). Cell nuclei are marked in blue; scale bar represents 50 μm .



Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Circulation* under the title, "Targeting Chondroitin Sulfate Glycosaminoglycans to Treat Cardiac Fibrosis in Pathological Remodeling." *Circulation*. 2018. Zhao R, Ackers-Johnson M, Stenzig J, Chen C, Ding T, Zhou Y, Wang P, Ng S, Li PY, Teo G, Rudd PM, Fawcett JW, Foo RSY. DOI: 10.1161/CIRCULATIONAHA.117.030353

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About the Cardiovascular Research Institute of Singapore (CVRI)

The Cardiovascular Research Institute of Singapore (CVRI) based at the National University Health System has the primary objective of tackling cardiovascular disease through laboratory based research, clinical research, clinical trials, health services research, prevention and epidemiology research. CVRI collaborates with international centres for multinational, multicentre basic and clinical trials. We are also involved in outcomes-related research, setting standards for evidence-based best medical practice in Singapore.

New research initiatives, which will benefit Singaporeans, include development of a risk prediction model for heart attack using novel biochemical markers, novel hormones and genetic analysis. Other areas of research include collaborative stem cell and tissue engineering research, device innovations etc.

CVRI is also a member of the National University Health System.

For more information on CVRI, please visit <http://cvri.nus.edu.sg/>

About National University Health System (NUHS)

The National University Health System (NUHS) is an integrated Academic Health System and Regional Health System in Singapore that delivers value-driven, innovative and sustainable healthcare.

Institutions in the NUHS group include four hospitals - National University Hospital, Ng Teng Fong General Hospital, Jurong Community Hospital and Alexandra Hospital (in 2018); three National Specialty Centres - National University Cancer Institute, Singapore (NCIS), National University

Heart Centre, Singapore (NUHCS) and National University Centre for Oral Health, Singapore (NUCOHS); a polyclinic group - the National University Polyclinics (NUP); one medical centre – Jurong Medical Centre; and three academic health sciences institutions – NUS Yong Loo Lin School of Medicine (including the Alice Lee Centre for Nursing Studies), NUS Faculty of Dentistry and NUS Saw Swee Hock School of Public Health.

With member institutions under a common governance structure, NUHS creates synergies for the advancement of health by integrating patient care, health science education and biomedical research.

As a Regional Health System, NUHS works closely with health and social care partners in the public, private and people sectors to develop and implement programmes that contribute to a healthy and engaged population in the Western part of Singapore.

For more information about NUHS, please visit www.nuhs.edu.sg

About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg

About the Agency for Science, Technology and Research (A*STAR)

The Agency for Science, Technology and Research (A*STAR) is Singapore's lead public sector agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit society.

As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

For more information on A*STAR, please visit www.a-star.edu.sg