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NTU Maps Heart Regeneration "Gene Map": Providing Clues for New Treatments for Heart Disease

Why is myocardial damage so difficult to repair itself? A new study published in **Nature Cardiovascular Research** by the LKCMedicine team at Nanyang Technological University uses spatial transcriptomics to map the genome, revealing the growth mechanism of cardiovascular progenitor cells (CVPs) in damaged hearts and identifying midkine, a key factor promoting angiogenesis. Learn how stem cell therapy can bring new hope to heart disease treatment and explore cutting-edge breakthroughs in myocardial regeneration!

Why is it so difficult for the heart muscle to repair itself once it is damaged by a heart attack? And how do stem cells grow, mature, and participate in tissue repair within a damaged heart?

A new study by a team at Nanyang Technological University's Lee Kong Chian School of Medicine (LKC Medicine) has created a clearer "genetic map" for these issues. This finding is expected to help scientists further develop new therapies that promote heart repair.

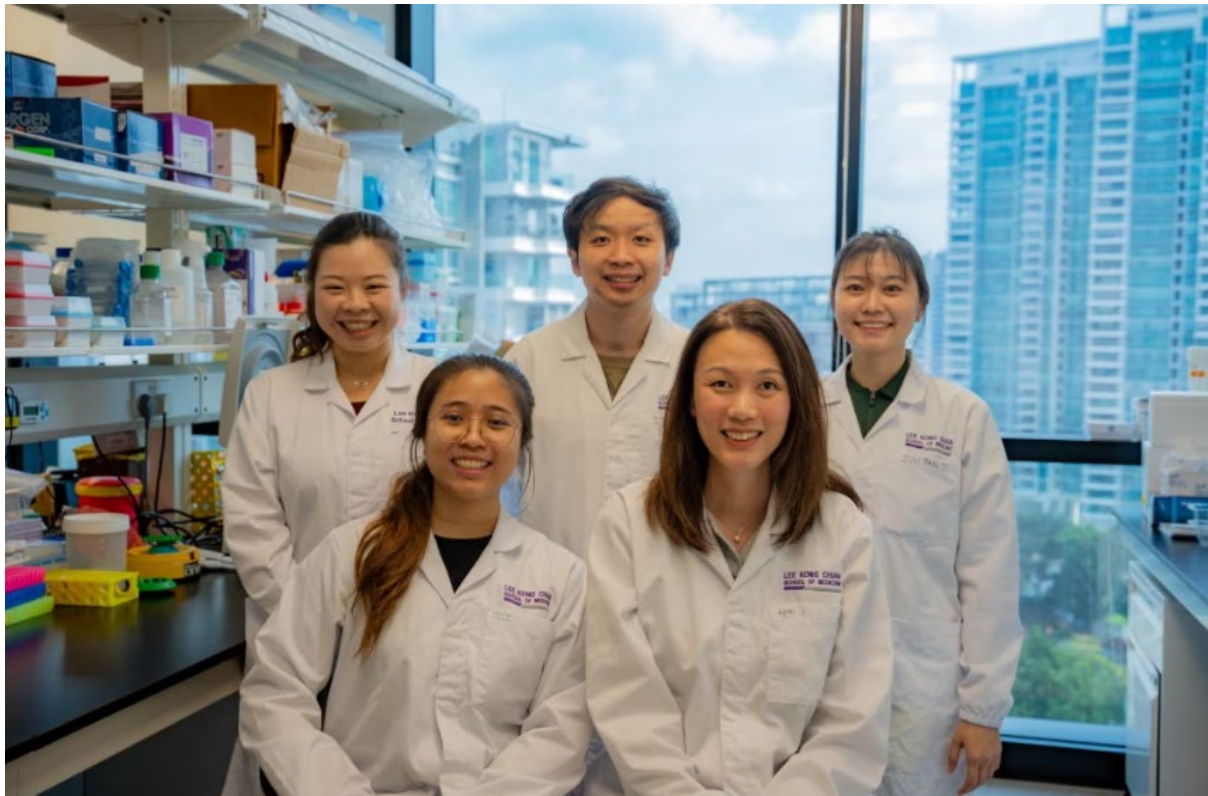
The study, led by Lynn Yap, Assistant Professor at LKC Medicine, has been published in the academic journal *Nature Cardiovascular Research*.

Why is it difficult for a damaged heart to repair itself?

When the coronary arteries are blocked, oxygen and nutrients cannot reach the heart muscle normally, and heart muscle cells may die. Unlike tissues such as skin, the regenerative capacity of adult heart muscle is very limited.

The body typically "fills in" damaged areas with scar tissue, but these tissues have limited contractile ability. Over time, the heart's pumping function may gradually decline, increasing the risk of heart failure.

Therefore, scientists hope to use stem cells to repair damaged tissue. The research team focused on cardiovascular progenitor cells (CVPs) derived from human pluripotent stem cells. These cells can further develop into different cells that make up the heart, providing a potential pathway for myocardial regeneration.



Mapping the "space-time" of gene activity

Researchers transplanted CVPs into a pig model of heart injury and observed how these cells matured into cardiomyocytes at different time points.

The team used spatial transcriptomics technology. This technology can not only record the activity of thousands of genes simultaneously, but also preserve information about the specific locations of these genes within the tissue. It can be understood as taking "heat maps of gene activity" of the heart tissue at a microscopic scale.

Increased activity after transplantation:

Genes related to metabolism, energy production, protein synthesis, and myocardial contraction

Decreased activity:

Genes related to scar tissue formation

These changes suggest that transplanted cells can integrate into a damaged heart and may help improve tissue repair and reduce scar formation.

Key Clue: Midkine, which promotes angiogenesis

Heart repair requires not only new cardiomyocytes but also a continuous supply of oxygen and nutrients from blood vessels. The research team further discovered that transplanted stem cells produce a growth factor called Midkine.

Experiments show that increasing the production of midkine can enhance the ability of vascular endothelial cells to migrate and form new blood vessels; modified stem cells that can produce more midkine have also promoted angiogenesis in mouse experiments.

Midkine may be an important target for helping the heart rebuild its blood supply and improving recovery after a heart attack.

This discovery also provides new experimental evidence for the long-standing debate about the role of midkine in cardiac repair.

How far are we from actually using it for patients?

It is important to emphasize that this study is still in the preclinical stage . The current results are from pig heart models, cell experiments, and mouse experiments, and do not mean that the relevant therapies can be used for patients.

Next, the team will further investigate the specific mechanisms by which Midkine exerts its effects, hoping to eventually apply it to the treatment of heart disease. The researchers have also established a publicly searchable web application to share the gene expression data obtained in this study, allowing researchers worldwide to continue their exploration.

From observing every step of changes in stem cells to identifying key proteins that may promote angiogenesis, this research brings scientists closer to understanding the complete process of heart repair and opens up new possibilities for future stem cell therapies and treatments for heart disease.

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