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Mapping heart regeneration genes could pave the way for new treatments for heart disease

Researchers at Nanyang Technological University, Singapore have uncovered fresh insights into how stem cells develop and mature into heart muscle cells, potentially opening new avenues for treating heart disease.



Summary

- NTU researchers mapped gene activity during heart muscle cell regeneration, identifying key genes switched on after transplantation into damaged hearts.
- Genes related to metabolism, energy, and contraction were activated, while scar-forming genes were suppressed.
- The protein Midkine was found to repair damaged blood vessels and may aid recovery after heart attacks.
- The study, published in *Nature Cardiovascular Research*, could lead to new therapies for heart disease.

Researchers at Nanyang Technological University, Singapore have uncovered fresh insights into how stem cells develop and mature into heart muscle cells, potentially opening new avenues for treating heart disease. The findings, published in the journal

Nature Cardiovascular Research, are among the first to track gene activity at different stages of the heart regeneration process.

In laboratory experiments, the NTU team found that genes related to metabolism, energy generation, protein synthesis and heart muscle contraction were switched on after the cells were transplanted into damaged hearts. Conversely, the activity of genes involved in scar tissue formation was reduced. The scientists also identified a protein called Midkine that can repair damaged blood vessels and may help improve recovery after heart attacks.

The study, led by researchers from NTU's Lee Kong Chian School of Medicine, used a combination of single-cell RNA sequencing and computational analysis to map the genetic changes that occur as stem cells differentiate into heart muscle cells, known as cardiomyocytes. This detailed map could help scientists understand why the human heart has limited regenerative capacity compared to some other animals, such as zebrafish and newborn mice, which can fully regenerate damaged heart tissue.

'Our findings provide a comprehensive view of the molecular events that drive heart muscle cell formation, which is critical for developing new therapies for heart disease,' said Assistant Professor Foo Lihuan, the lead author of the study, according to an NTU news release. 'By understanding which genes are activated or suppressed during regeneration, we can potentially design strategies to enhance the heart's own repair mechanisms.'

Heart disease remains the leading cause of death globally, according to the World Health Organization, with limited treatment options available for patients who have suffered a heart attack. Current therapies focus on managing symptoms and preventing further damage, but do not regenerate lost heart muscle tissue. The NTU research suggests that reactivating certain developmental pathways could one day allow doctors to repair damaged hearts using a patient's own cells.

The study also highlighted the role of the protein Midkine, which was found to promote the growth of new blood vessels in damaged heart tissue. This could be particularly important for improving blood flow to areas of the heart that have been starved of oxygen during a heart attack. The researchers noted that Midkine's effects on blood vessel repair were observed in both cell cultures and animal models.

The NTU team plans to further investigate the therapeutic potential of Midkine and the identified gene networks in larger animal models before moving toward clinical trials. The research was supported by the National Research Foundation Singapore and the Singapore Ministry of Education.

The findings have been covered by media outlets including Life Technology (US), Medical Xpress (UK), and Lab + Life Scientist (Australia). The study adds to a growing body of research aimed at unlocking the regenerative potential of the human heart, which could transform the treatment of heart disease in the future.

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