

How the heart maintains its shape and function – and what can go wrong

A team from the DZHK sites in Heidelberg/Mannheim and Berlin has discovered that a single enzyme in the heart plays a key role in determining whether the organ develops in a healthy manner. If this molecular protective factor is missing, serious congenital heart defects can develop.

For the heart of an unborn child to develop properly, many different cell types must work together in a highly coordinated way. Particularly important are the cells that line the inner walls of the heart's blood vessels — the so-called endothelial cells. They are in constant communication with the heart muscle cells, regulating when these cells grow, divide, or enter a resting state.

A team involving the DZHK sites in Heidelberg/Mannheim and Berlin has now discovered that a specific protein plays a key role in these endothelial cells: RNF20. It ensures that genes are active to the right extent and that the endothelial cells retain their identity.

Without RNF20, the cells lose their original function and transform into other cell types. This disrupts the signals to the heart muscle cells. The heart then grows unevenly, beats irregularly or does not develop fully.

Less RNF20 in congenital heart defects

In animal experiments, the loss of RNF20 led to severe malformations in the embryonic phase and even embryo death. The researchers also found significantly less RNF20 in the endothelial cells of the hearts of children with congenital heart defects compared to healthy controls.

In the long term, the results could help to better understand the causes of congenital heart defects and develop new diagnostic or therapeutic approaches. In the future, changes in the RNF20 signalling pathway could potentially be used as biological markers to identify high-risk pregnancies at an early stage. Targeted interventions in disrupted signalling pathways – such as slowing down overactive growth factors – could also open up new avenues for treatment.

RNF20 therefore acts as a protective mechanism that maintains the delicate balance in the heart. If this mechanism fails, key growth and communication processes become disrupted, which can result in congenital heart defects.

Publication:

Dou Y, Tetik-Elsherbiny N, Gao R, et al. Endothelial RNF20 suppresses endothelial-to-mesenchymal transition and safeguards physiological angiocrine signaling to prevent congenital heart disease. *Nat Commun.* 2025;16(1):9480. Published 2025 Oct 27. doi:10.1038/s41467-025-65291-0

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Further information

- German Center for Cardiovascular Research (DZHK)