Medizinische Universität Graz

Rector's Office
Auenbruggerplatz 2, A-8036 Graz

Thomas Edlinger, BA
Public relations and event management

thomas.edlinger@medunigraz.at
Tel. +43 / 316 / 385-72055
Fax +43 / 316 / 385-72030

Press release
For immediate publication

Heart failure: Research at Med Uni Graz examines its origin
Focus on age-related heart disease

Graz, 1 June 2022: Cardiovascular disease is still the most common cause of death worldwide. If the heart is too weak to supply the body with enough blood and therefore essential nutrients and oxygen, there is heart failure (or cardiac insufficiency). In Austria alone there are 250,000 people with cardiac insufficiency—and its prevalence is constantly increasing due to longer life expectancy. Med Uni Graz researchers and an international team directed and coordinated by Simon Sedej and Mahmoud Abdellatif have targeted a specific mechanism in the body that may be responsible for an increase in heart failure in later life.

The mystery behind IGF-1

Research focuses on the insulin-like growth factor 1 (IGF-1) signaling pathway. Clinical and experimental investigations verify that IGF-1 in the heart plays an important role in regulating growth, myocardial contractility and metabolism. IGF-1 also appears to be responsible for age-related impairment in cardiac function. With heart failure, there is often evidence of increased IGF-1 receptor activity, which is why researchers have now investigated on mice what consequences this increased IGF-1 activity can have over the course of a lifetime. "Previous experimental studies of mice have shown that increased IGF-1 receptor activation in the heart can have both negative and positive effects on cardiac function. Despite the great relevance of the cardiac IGF-1 signaling pathway on cardiac function, these controversial results remained unexplained for a long time," explains Simon Sedej.

To analyze the effects of higher or lower IGF-1 receptor activation over the course of a lifetime, two mouse models were investigated that exhibited higher or lower IGF-1 signaling activity in the heart. Researchers were able to directly compare how changes in normal IGF-1 signaling activity have an impact on cardiac function over the course of a lifetime.

Playing both sides of the fence

Researchers have discovered that young mice with increased IGF-1 signaling activity have better cardiac function than normal mice, yet it deteriorates more quickly over the course of their lives. Heart failure develops earlier and ultimately leads to a shorter life expectancy. The young mice with reduced IGF-1 signaling activity initially exhibited poorer cardiac function that improved later in life and contributed to a longer life expectancy.

Briefly summarized: In the mouse model, high IGF-1 signaling activity in the heart has a positive effect on cardiac muscle growth, contractility and metabolism in youth, yet in

later life, lower IGF-1 signaling activity in the heart is more advantageous for cardiac function and increased life expectancy.

Conclusions for the future

This research explains the previous controversial results and provides important indications of potential reasons for the development of heart failure in advanced age that should be the subject of further investigations. "Our study delivers important findings on the decisive role of fine tuning of the cardiac IGF-1 signaling pathway: what its advantages are during the early stages of life and how to avoid harmful effects on aging cardiac muscle. Thus it opens up perspectives for therapy for age-related heart disease and lays the cornerstone for future studies. These studies will show whether pharmacological inhibitors of the IGF-1 signaling pathway that are currently being used in cancer therapy might be able to prevent age-related heart disease," explains Simon Sedej.

Further information and contact:
Simon Sedej
Medical University of Graz
Department of Internal Medicine
Division of Cardiology
Tel.: +43 316 385 72742
Email: simon.sedej@medunigraz.at

Mahmoud Abdellatif
Medical University of Graz
Department of Internal Medicine
Division of Cardiology
Email: mahmoud.abdellatif@medunigraz.at

Profile: Simon Sedej
Simon Sedej studied biology in Ljubljana (Slovenia) and completed his doctoral studies in the field of biomedicine. He finished his habilitation in 2011 and has been an associate professor of cardiac physiology at the Division of Cardiology since 2015. He conducts research on mechanisms of aging in the heart and new therapeutic approaches to treating age-related heart failure, which is often closely connected to metabolic disease.

Profile: Mahmoud Abdellatif
Mahmoud Abdellatif studied medicine in Egypt and Spain and completed the PhD program in molecular medicine in Graz. Since 2022 he has been a Marie Curie Postdoctoral Fellow at Sorbonne University in Paris. In recent years he has regularly received prestigious awards for his research in the field of heart failure.

The publication is available online:
https://www.ahajournals.org/doi/abs/10.1161/CIRCULATIONAHA.122.059863