IMPACT PROFILE

Investigating Blood Vessel Dysfunction to Improve Outcomes for Patients with Atrial Fibrillation

Translational Science Benefits Model

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A career development award supporting discovery of the molecular mechanisms of atrial fibrillation (AFib) to enable targeted therapies and reduce disease burden.

The Challenge

Current therapies for AFib are suboptimal because we have an incomplete understanding of the causal mechanisms by which endothelial dysfunction (improper function of the inner lining of blood vessels) promotes AFib.

The Approach

Cardiovascular patients with and without AFib were recruited for ultrasound imaging of their coronary artery vessel function. Images were assessed to determine the burden of endothelial dysfunction.

A large animal model of AFib was used to test if targeted injection of plasmids to inhibit atrial ET-1-Gα_q signaling would attenuate of the development AFib.

The Impact

AF is an emerging epidemic, with an estimated **12.1 million U.S. patients with AFib by 2030**. Optimization of gene therapy targeting ET-1 signaling may lead to novel, mechanism-guided treatments for AFib. This could **transform treatment for AFib**, reducing complications and patient morbidity, including stroke.

In addition, ET-1 signaling is also known to play a role in other forms of heart disease, such as heart failure and pulmonary hypertension. Therefore, the results of this study **may lead to the identification of novel treatment options for a broader patient population**.

RESEARCH HIGHLIGHTS

The molecular mechanisms of AFib study found:

- Coronary microvascular dysfunction was more pronounced in patients with AFib.
- Animals treated with plasmids expressing Gα_q inhibitory peptides were less susceptible to induction of AFib and had less scarring (fibrosis) in their left atrium when compared to control animals.
- ET-1-Gα_q signaling plays an important role in heart failure-related atrial remodeling.

Key Benefits

The molecular mechanisms of AFib study has potential clinical benefits.

Biological Factors & Products: Potential for novel and patient-specific gene therapy tools through advanced understanding of molecular mechanisms.

Guidelines: Potential for defining phenotypes of AFib patients & tailored guidelines for patient care.

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