Method and Composition for Treating Heart Failure and Cardiac Diseases

Heart failure and associated cardiac diseases is a leading cause of death in the US. Each year about 5.7 million adults suffer from heart failure in the US alone and about half of them die within 5 year of being diagnosed with a cardiac disease. In addition to being a major health concern, heart failure also leads to economic loss for the society. The combined cost of health care services, medications, and lost working hours is estimated to be over US$30 billion dollars each year. Therefore, there is an urgent need to develop better treatments for heart failure. One contributing factor to the diseases of heart failure is the overproduction of aldosterone, a hormone that enhances reabsorption of sodium and water in the kidneys. This leads to increased blood volume and blood pressure that can cause heart failure. Aldosterone production was thought to be activated by G-proteins only, and existing drugs on the market primarily target this signaling pathway. However, the NSU inventor and colleague discovered that additionally, the protein β-arrestin1 is important, and may be more critical than G-proteins, in mediating aldosterone production. To effectively suppress aldosterone production, both β-arrestin1 and G-proteins in the adrenals thus need to be inhibited. The novel method and several compositions to block β-arrestin1, at angiotensin II receptor sites are covered by the patent application.

Technology

Dr. Lymperopoulos of NSU’s College of Pharmacy and his collaborator developed a novel method that has the potential for treating cardiac diseases, including heart failure. The heart contains almost exclusively β-arrestin 1, but another isoform of this protein, called β-arrestin2, was found to directly interact with and modify SERCA2a, a crucial enzyme for stimulating the transport of Ca$^{2+}$ from the cytoplasm to the sarcoplasmic reticulum. In heart failure, this transport, and consequently, cardiac contractility, is diminished. Therefore, by increasing the amount of β-arrestin2, which, unfortunately, is very low in the human adult heart, contractility is enhanced and heart failure can be ameliorated. This technology also has the potential to be implemented as a gene therapy to induce upregulation of β-arrestin2.

Application

The technology outlined in this patent portfolio presents methods for increasing cardiac contractility in vivo for treatment of heart failure.

The intellectual property also includes a composition for increasing cardiac contractility: a β1 adrenergic receptor ligand that induces β-arrestin2 binding to the β1 adrenergic receptor.

Advantages/Benefits

As therapeutics for heart failure, compounds that promote β-arrestin2 binding and subsequently stimulating SERCA2a activity, might hold some advantages over compounds affecting only β-arrestin1 signaling. Owing to its anti-inflammatory and anti-cardiac cell death effects, β-arrestin2 gene transfer may be a safe and effective therapy for heart failure.
Status of Development

Researchers at NSU have successfully demonstrated that inhibition of adrenal GRK2 inhibition as a potential therapeutic intervention for heart failure.

Patent Status


Information on Inventors

- Dr. Anastasios Lymperopoulos—Dr. Lymperopoulos is an Associate Professor of Pharmacology at the Department of Pharmaceutical Science and Nova Southeastern University. He is a Fellow of the American Heart Association and of the European Society of Cardiology in recognition of his accomplishments and status as a cutting-edge cardiovascular researcher.

- Dr. Walter Koch—Dr. Koch is currently the William Wikoff Smith Endowed Chair in Cardiovascular Medicine at Lewis Katz School of Medicine in Temple University. He also serves as the Professor and Chair of Pharmacology. Dr. Koch contributed to the invention pertaining to therapeutic modulation of aldosterone levels in heart disease (patent application - US20130274191).

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