NOVA SOUTHEASTERN UNIVERSITY
Office of Research and Technology Transfer

Method and Compositions for Treating Heart Failure and Disease

Technology:

A contributing factor to the disease of heart failure is the overproduction of aldosterone, a hormone that increases reabsorption of sodium and water into the kidneys. This causes high blood volume and blood pressure that can result in heart failure. Aldosterone production was solely thought to be activated by G-proteins, and existing drugs on the market primarily target this signaling pathway. However, the NSU inventor and colleague discovered that additionally, the protein β-arrestin 1 is important, and may be more critical than G-proteins, in mediating aldosterone production. To effectively suppress aldosterone production, both β-arrestin 1 and G-proteins thus need to be inhibited. The novel method and several compositions to block β-arrestin 1 at angiotensin II receptor sites are covered by the patent application.

The patent portfolio also includes methods for increasing cardiac contractility *in vivo* for treatment of heart failure. The heart contains almost exclusively β-arrestin 1, but a second β-arrestin protein that occurs in minimal amounts, β-arrestin 2, 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; by increasing the amount of β-arrestin 2, contractility is enhanced and heart failure can be reversed. The intellectual property also includes a composition for increasing cardiac contractility: a β1 adrenergic receptor ligand that induces β-arrestin 2 binding to the β1 adrenergic receptor.

Opportunity:

Heart failure and disease is a leading cause of death in the US. Decisions regarding treatment would be dependent on the efficacy of medication on both β-arrestin 1 and G-protein signaling pathways. Compounds inhibiting β-arrestin 1 signaling show promise as a therapeutic; in contrast, drugs tested recently in clinical trials to promote this signaling from the angiotensin receptor in the heart did not provide benefits over the placebo.

In addition, compounds that promote β-arrestin 2 binding and subsequently stimulating SERCA2a activity could be used as therapeutics for heart failure. Further experiments also indicate that due to its anti-inflammatory and anti-cardiac cell death effects, β-arrestin 2 gene transfer may be a safe and effective therapy for heart failure. Since β-arrestin 2 is required for the proper processing of SERCA in the heart, β-arrestin 2 gene transfer may also be complementary to and necessary for SERCA gene therapy to be effective.

Nova Southeastern University is seeking to develop collaborative partnerships and licensing opportunities for these technologies.

Inventors: Drs. Anastasios Lymperopoulos and Walter Koch. Dr. Lymperopoulos is a Fellow of the American Heart Association and was recently elected Fellow of European Society of Cardiology in recognition of his accomplishments and status as a cutting-edge cardiovascular researcher.

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