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A new molecular therapeutic target in heart failure: Regulation of aldosterone levels by adrenal Beta arrestin-1

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Heart failure (HF) is the number one killer disease in the western world and new and innovative treatments are urgently needed. Aldosterone is a cardio toxic hormone, whose levels are elevated in HF, contributing significantly to HF progression after myocardial infarction (MI). Consequently, it represents a major drug target in HF. It is produced by the adrenal cortex after angiotensin II (AngII) activation of AngII type 1 receptors (AT1Rs), G protein-coupled receptors (GPCRs) that also signal independently of G proteins. The ı-arresting (ıarrs) are two ubiquitously expressed proteins (two isoforms: ıarr1 and -2) that terminate G protein signalling by these GPCRs (including the AT1Rs) via binding the receptor and physically uncoupling it from G proteins. However, over the past decade, it has become clear that ıarrs also serve assignal transducers in their own right, independently of G proteins. This presentation will discuss one of the exciting latest developments in the field of ıarr-mediated signalling physiology, coming from our lab: promotion of AngII-dependent aldosterone synthesis and secretion by adrenal ıarrs, which underlies the hyper aldosteronism that accompanies and aggravates HF.Ways of genetically inhibiting adrenal ıarr actions in vivo, which proves to be beneficial in HFexperimental animals, will also be described. Finally, data from a screening of the currently available AT1R antagonist drugs (sartans) for their ability to inhibit adrenal ıarr activity will be presented, in an effort to identify the most efficacious agents within this very important cardiovascular drug class at inhibiting adrenal ıarrs, and hence suppressing aldosterone, in HF.

Biography

Anastasios Lymperopoulos received his Ph.D. in Pharmacology from the University of Patras, Greece The major turning point in his career came when he joined the lab of Dr. Walter Koch, a former postdoctoral fellow of world-renowned Professor Robert Lefkowitz`s lab at Duke. His research has culminated in several successes, awards and honours, the most prominent being his leadauthor publication in the prestigious journal “Nature Medicine”, and a Scientist Development Grant from the American Heart Association. He has also been a finalist for the AHA-sponsored Melvin L. Marcus Young Investigator, and the European Society of Cardiology`s Cardiovascular Awards in the past.