Yang Lei, Pediat Therapeut 2015, 5:3
http://dx.doi.org/10.4172/2161-0665.S1.008

OMICS International
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International Conference and Exhibition on
Pediatric Cardiology
August 25-27, 2015 Valencia, Spain

Succinate receptor GPR91 is involved in pressure overload-induced right ventricular hypertrophy

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Background: Pulmonary arterial hypertension is characterized by increased pressure overload leading to Right Ventricular Hypertrophy (RVH). GPR91 is an orphan G-Protein-Coupled Receptor (GPCR) that has been characterized as a receptor for succinate; however, its role in RVH remains unknown.

Methods & Results: We have investigated the role of succinate-GPR91 signaling in a Pulmonary Arterial Banding (PAB) model of RVH in SD rats due to pressure overload. We found that GPR91 was located in cardiomyocytes. In both sham and PAB rats, treated with succinate further aggravated RVH, up-regulated RVH genes and increased the p-Akt/t-Akt level *in-vivo*. *In-vitro*, succinate up-regulate the levels of the hyper trophic gene marker and also the p-Akt/tAkt levels in cardiomyocytes. All these effects were inhibited by an antagonist of PI3K, wortmannin, both *in vivo* and *in vitro*. Finally, we noted that the GPR91-PI3K/Akt axis was also up-regulated compared with that in human RVH.

Conclusions: Our findings indicate that succinate-GPR91 may be involved in RVH via PI3K/Akt signaling *in vivo* and *in vitro*. GPR91 may be a novel therapeutic target for pressure overload-induced RVH.

Biography

Yang Lei got his Doctorate degree of Pediatrics from Nanjing Medical University. After his graduation, he was engaged in clinical and research work of Congenital Heart Disease in Nanjing Children's Hospital affiliated to Nanjing Medical University. So far, he has chaired and completed development of science and technology of Nanjing Medical University foundation project. His study has been based on the development mechanism of the occurrence, clinical diagnosis and treatment in children with congenital heart disease. He has published 7 SCI papers. As the first inventor, he obtained 2 national patents (authorized), as the second inventor; he obtained 1 national patent (authorized).

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