Title: Prostaglandin E_2 promotes vascular remodeling of the ductus arteriosus

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Abstract (upto 300 words)

Prostaglandin E_2 (PGE_2), a family of prostanoids, is the most potent vasodilator of ductus arteriosus (DA) and regulates inflammatory processes in various tissues. The DA, a fetal arterial connection between the main pulmonary artery and the descending aorta, closes immediately after birth. In addition to the well-known vasodilatory role of PGE_2, we found novel roles of PGE_2 in vascular remodeling of the DA. PGE_2-EP4-adenylyl cyclase-cyclic AMP (cAMP)-protein kinase A (PKA) signaling during gestation promotes hyaluronic acid-mediated neointimal cushion formation that helped structural closure of the vascular lumen. Among the isoforms of adenylyl cyclase, adenylyl cyclase type 6 plays an important role in hyaluronic acid-mediated neointimal cushion formation. Another target of cAMP, Epac, has an acute effect on promoting smooth muscle cell migration without hyaluronic acid production and thus intimal thickening in the DA. Both EP4-cAMP downstream targets, Epac and PKA, regulate vascular remodeling in the DA. In addition, we found that PGE_2 receptor EP4- PLC signaling promotes degradation of the mature lysyl oxidase protein, a cross-linking enzyme for elastic fibers, in the DA, leading to decreased elastogenesis. Therefore, signalling through PGE_2-EP4 plays two essential roles in DA remodeling, namely, intimal thickening and poor elastogenesis. Our data strongly suggest that PGE_2-EP4-mediated treatment for the DA should be carefully considered in terms of vascular remodeling. We will review the role of PGE_2 in DA closure in this session.

Biography (upto 150 words)

I am a Professor of Cell Physiology at The Jikei University since 2012. I graduate from Hirosaki University in 1984 and had worked as Pediatrician for 9 years at Yokohama City University. I was a postdoctoral researcher for 4.5 years at department of Medicine, University of California, San Diego. My research interest is to study the mechanisms of development of the cardiovascular system and the regulation of calcium signaling in the heart, especially the molecular mechanisms of ductus arteriosus closure. I have over 100 publications including Cell, Nature, Circulation that have been cited over 300 times, and my publication H-index is over 20. I have several awards such as Yokohama Medical Award (2003), Umehara Award (Yokohama Foundation of Advanced Medical Science)（2010）, The Japan Pediatric Society Scientific Research Award（2011）, Takao Award (Japanese Society of Pediatric Cardiology and Cardiac Surgery) (2014).

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