JSPCCS-AHA Joint Session

Sat. Jul 11, 2026 9:10 AM - 10:50 AM JST | Sat. Jul 11, 2026 12:10 AM - 1:50 AM UTC | Room1（Conference Hall A）

[AHAJS] JSPCCS-AHA Joint Session（III-AHAJS）

Basic Science in Congenital Heart Disease: Morphology, Genetics & Molecular Mechanisms

Chair:Antonio Cabrera(The Ohio State University,Nationwide Children's Hospital)

Chair:Yoshihide Mitani(Prinatal Care center, Mie University Hospital)

[III-AHAJS-4] Molecular Programs Governing Fetal Differentiation and Postnatal Remodeling of the Ductus Arteriosus

Utako Yokoyama (Tokyo Medical University)

Keywords：ductus arteriosus、vascular remodeling、transcriptional regulation

The ductus arteriosus (DA) is an essential fetal vessel that maintains fetal circulation before birth, and its closure is essential for the transition to postnatal circulation. During fetal development, prostaglandin E2 (PGE_2) signaling through its receptor EP4 plays pivotal roles in establishing DA-specific vascular properties, including smooth muscle cell (SMC) differentiation, intimal thickening, and impaired elastic fiber formation. To clarify the mechanisms controlling DA-specific EP4 expression, we generated EP4 reporter mice and performed transcriptomic and epigenomic analyses, including RNA-seq, ATAC-seq, and CUT&Tag. These studies identified distal regulatory regions upstream of the Ptger4 locus that drive DA-specific EP4 expression during fetal development. Functional disruption of these regions markedly reduced EP4 expression and resulted in PDA-associated neonatal lethality. We also investigated mechanisms underlying postnatal DA remodeling. Single-cell RNA sequencing revealed that SMCs, but not other vascular cell populations, underwent marked transcriptional changes after birth. Among genes induced postnatally in DA SMCs, cyclooxygenase-2 (COX-2) showed prominent upregulation. Oxidative stress and thromboxane signaling increased COX-2 expression in DA SMCs. In vivo experiments further suggested that COX-2-derived PGE2 contributes to postnatal anatomical DA closure via the EP4-Nr4a1 axis. These findings demonstrate that distinct molecular programs regulate fetal DA differentiation and postnatal DA closure.