JSPCCS-Study Group for Cardiovascular Dev. Joint Session

Fri. Jul 10, 2026 2:00 PM - 3:00 PM JST | Fri. Jul 10, 2026 5:00 AM - 6:00 AM UTC | Poster Venue1（Conference Hall C）

[JSCDJS-P1] 日本小児循環器学会・第25回日本心臓血管発生研究会 合同セッション（II-JSCDJS-P1）
ミニオーラル（eポスター）1

座長:白井 学(国立循環器病研究センター)
座長:岩瀬 晃康(東京大学アイソトープ総合センター)

[II-JSCDJS-P1-5] レポーターゼブラフィッシュを用いた、EP4発現調節機序の解明

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Keywords：EP4、reporter zebrafish、drug screening

Background: Prostaglandin E_2 receptor, EP4, expression increases in the ductus arteriosus (DA) at birth and greatly contributes to its closure. However, the molecular mechanisms regulating EP4 expression remain unclear. Zebrafish lay large number of eggs, and transparent larvae allow high-throughput screening and direct observation of the developmental process with fluorescent reporters.
Objective: The aim of this study was to establish a reporter zebrafish line to identify factors regulating EP4 expression.
Methods: We injected the upstream region of *ptger4b* and GFP cDNA into fertilized eggs with the Tol2 transposon system. We examined fluorescent signals of the zebrafish lines in comparison with the endogenous *ptger4b* expression pattern which was confirmed by *in situ* hybridization, and conducted drug screening using the line.
Results: Focusing on the potential promoter regions of the zebrafish *ptger4b*, highly homologous to the human PTGER4 gene encoding EP4, we established two transgenic lines, Lines 1246 and 315. We detected endogenous *ptger4b* expression in the neural crest. It was consistent with the EGFP signal in Line 1246. The drug screening using pooled compounds identified 76 candidates enhancing fluorescence intensity out of 3090 compounds in the FDA-approved drug library. Most of the drugs had purposes other than cardiovascular disease, such as infectious diseases.
Conclusion: We identified *ptger4b* gene expression in the neural crest, the origin of the DA, in Line 1246. We will further narrow down the candidates to identify compounds that regulate EP4 expression.