S1P-S1p2 Signaling in Cardiac Precursor Cells Migration

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Keywords
Zebra fish • Sphingosine-1-phosphate • Cardia bifida • Endoderm

During embryogenesis, zebra fish cardiac precursor cells (CPCs) originating from anterior lateral plate mesoderm migrate toward the midline between the endoderm and the yolk syncytial layer (YSL) to form cardiac tube. The endoderm functions as a foothold for CPCs as evidenced by the endodermal mutants (*cas*/*sox32*, *sox17*, *oep*, *fau*/*gata5*, and *bon*) showing two hearts (cardia bifida) [1]. Furthermore, mutant zebra fish (*toh*) lacking sphingosine-1-phosphate (S1P) transporter which is expressed in the YSL show two hearts [2], indicating the essential role for S1P-mediated signal in cardiac development. This is also supported by a S1p2 receptor mutant (*mil*) which exhibits two hearts [3]. However, it is still unclear how S1P released from YSL regulates CPC migration.

S1p2 is expressed in the endoderm. Thus, we assume that S1P released from the YSL might activate S1p2 expressed in the endoderm, thereby regulating CPC migration. One possibility is that S1p2-mediated signal controls the endoderm formation as a foothold for CPCs. Another possibility is that endodermal cells activated by S1p2 might secrete the chemokines which accelerate CPC migration or secrete the extracellular matrix proteins for guiding CPC movement.

To test these possibilities, we need to delineate the downstream signaling of S1p2. Recently, $G\alpha_{13}$ is reported to inhibit Hippo-mediator Lats1/2 kinase through a RhoGEF/Rho/Rho-kinase signaling [4, 5]. We demonstrate that the inhibition of Hippo signaling in the endoderm by activated S1p2 is essential for endodermal cell

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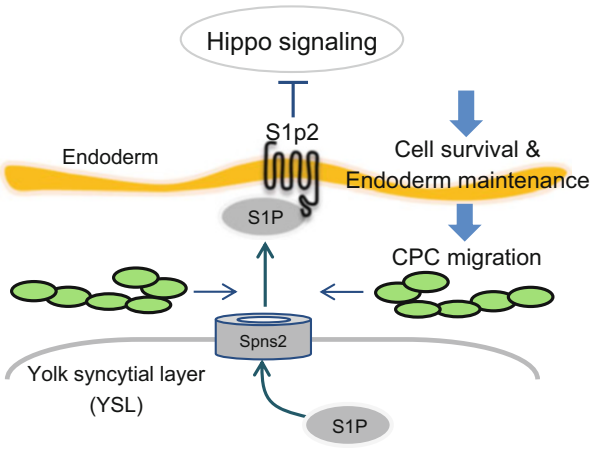

Fig. 14.1 A model of S1P-S1p2 signaling regulated CPC migration. S1P secreted from the yolk activates S1p2 in the endoderm. Hippo signaling acts downstream of S1P-S1p2 signaling and maintains the endoderm to act as scaffolds for CPC migration

survival and that the endoderm maintained by S1P signaling indeed becomes the foothold for CPC migration (Fig. 14.1).

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