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The $TGF\beta$ pathway is a key player for the endothelial-to-hematopoietic transition in the embryonic aorta

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ACCEPTED MANUSCRIPT

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SUMMARY

The embryonic aorta produces hematopoietic stem and progenitor cells from a hemogenic endothelium localized in the aortic floor through an endothelial to hematopoietic transition. It has been long proposed that the Bone Morphogenetic Protein (BMP)/Transforming Growth Factor ß (TGFß) signaling pathway was implicated in aortic hematopoiesis but the very nature of the signal was unknown. Here, using thorough expression analysis of the BMP/TGFß signaling pathway members in the endothelial and hematopoietic compartments of the aorta at pre-hematopoietic and hematopoietic stages, we show that the TGFß pathway is preferentially balanced with a prominent role of Alk1/TgfßR2/Smad1 and 5 on both chicken and mouse species. Functional analysis using embryonic stem cells mutated for *Acvrl1* revealed an enhanced propensity to produce hematopoietic cells. Collectively, we reveal that TGFß through the Alk1/TgfßR2 receptor axis is acting on endothelial cells to produce hematopoiesis.

Keywords: hematopoieisis, endothelium, aorta, embryo, endothelial-to-hematopoietic transition, TGFß, Alk1, ES cells.

¹ Equal contribution

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