The TGFβpathway is a key player for the endothelial-to-hematopoietic transition in the embryonic aorta

A. Lempereur, P.Y. Canto, C. Richard, S. Martin, J. Thalgott, K. Raymond, F. Lebrin, C. Drevon, T. Jaffredo

www.elsevier.com/locate/developmentalbiology

PII: S0012-1606(17)30720-0
DOI: https://doi.org/10.1016/j.ydbio.2017.12.006
Reference: YDBIO7644

To appear in: *Developmental Biology*

Received date: 11 October 2017
Revised date: 7 December 2017
Accepted date: 8 December 2017

Cite this article as: A. Lempereur, P.Y. Canto, C. Richard, S. Martin, J. Thalgott, K. Raymond, F. Lebrin, C. Drevon and T. Jaffredo, The TGFβpathway is a key player for the endothelial-to-hematopoietic transition in the embryonic aorta, *Developmental Biology,* https://doi.org/10.1016/j.ydbio.2017.12.006

The TGF β pathway is a key player for the endothelial-to-hematopoietic transition in the embryonic aorta.

Lempereur, A[a1] Canto[a1] P.Y., Richard, C[a], Martin, S[b], Thalgott, J[c]. Raymond, K[c], Lebrin, F[b,c], Drevon, C[a], Jaffredo, T[a*]

[a]Sorbonne Universités, UPMC Univ Paris 06, IBPS, CNRS UMR7622, Inserm U 1156, Laboratoire de Biologie du Développement; 75005 Paris

[b]CNRS UMR 7241/INSERM U1050, Center for Interdisciplinary Research in Biology, Collège de France, 11 Place Marcelin Berthelot, 75231 Paris CEDEX 05, France. [4] MEMOLIFE Laboratory of Excellence and Paris Sciences et Lettres Research University.

[c]Einthoven Laboratory for Experimental Vascular Medicine, Department of Internal Medicine (Nephrology), Leiden University Medical Center, Leiden, The Netherlands.

*Corresponding author. E mail: thierry.jaffredo@upmc.fr

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