The roles of Meis1 oncogene products on the development of endothelial cells in zebrafish

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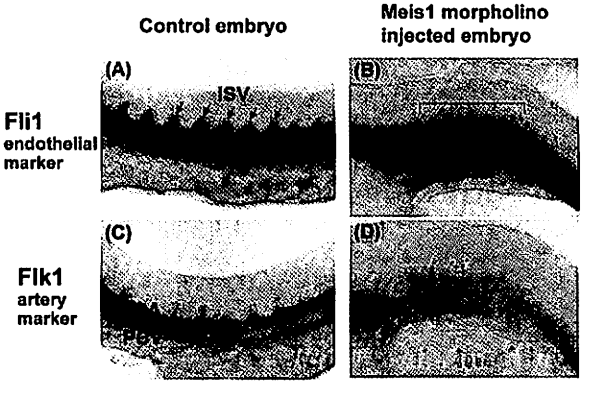
Meis1 (myeloid ectopic viral insertion site1) encodes a homeobox domain transcription factor, and was originally identified as one of the common viral integration sites in acute myeloid leukemia of retrovirus-infected mice. Meis1 is also frequently found up-regulated along with Hox genes in human leukemias and cooperates with Hox genes to accelerate the onset of leukemia. In addition to the roles of Meis1 on leukemogenesis, its function on normal hematopoietic development has been also investigated. Previous reports showed that Meis1-deficient mice died by embryonic day 14.5 with the reduction of megakaryocytes and definitive hematopoietic stem cells (HSCs) suggesting that Meis1 is involved in the generation of definitive HSCs.

Zebrafish is a useful model organism for studies of hematopoietic and vascular development, and the developmental processes are definitively conserved between zebrafish and mammals. Thus we use zebrafish in order to investigate the function of Meis1 during normal development. Knockdown of *meis1* by antisense *meis1*morpholino led to the impairment of intersegmental vessel formation in the zebrafish embryo. In *meis1* morphants, the expression of an artery marker (*ephrinB2*) was reduced in dorsal aorta, and the expression of vein markers (*flt4, ephB4*) was expanded in dorsal aorta and posterior cardinal vein, suggesting the severe defects on artery development. Furthermore, the expression of *vascular endothelial growth factor* (*vegf*) receptor, *flk1*, was significantly decreased in these embryos. Interestingly, *flk1* morpholino-injected embryos exhibited similar defects as *meis1* morphants. Thus, these results implicate that *meis1* is a novel regulator involved in vascular development and endothelial cell differentiation, presumably affecting the *vegf* signaling pathway.



Meis1 oncogene product is involved in vascular(ISV) development and artery(DA) differentiation in zebrafish