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Abstract

SoxF-mediated vascular network formation

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VEGF signaling is a key pathway for angiogenesis and requires highly coordinated regulation. Though the Notch pathway-mediated suppression of excessive VEGF activity via negative feedback is well known, the positive feedback control for augmenting VEGF signaling remains poorly understood. We explored how SoxF transcription factors Sox7 and Sox17 are involved in VEGF signaling during developmental angiogenesis in mice. Sox7 is expressed specifically in endothelial cells and its deletion reduced angiogenesis, substantially overlapping with Sox17 in both expression and function. Compound heterozygosity for *Sox7* and *Sox17* phenocopied vascular defects of *Sox7* or *Sox17* homozygous knockout, indicating the genetic cooperation of Sox7 and Sox17. Our data suggest that VEGF signaling up-regulates both Sox7 and Sox17 expression in angiogenesis, which then promote VEGFR2 expression, creating a positive feedback loop. Therefore, SoxF transcription factors act as positive feedback regulators reinforcing VEGF signaling and are indispensable players in developmental angiogenesis.

Sox17 is known to be critical for arterial development. Several GWAS analyses suggested *Sox17* locus as one of candidate genomic region susceptible for intracranial aneurysm, a ballooning of intracerebral arteries. We found that Sox17 is robustly expressed in arterial endothelial cells during adulthood and its deletion can induce intracranial aneurysm under hypertensive stress. We suggested Sox17 deficiency as a potential hereditary factor for intracranial aneurysm formation.

We have been exploring multifaceted function of Sox7 and Sox17 in various vascular contexts.
http://www.vbsckim.com/