Identification of novel angiogenic pathways independent of Vegf signaling

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Vascular endothelial growth factors (Vegf) are proteins that stimulates the formation of blood vessels. Among these, Vegf A is the most characterized Vegf molecule and is a key player for the formation of a functional vascular system. Zebrafish (*Danio rerio*) embryos deficient for *vegfaa* display a severe vascular phenotype and lack most of their blood vessels. Furthermore, *vegfaa* mutant embryos exhibit defects during the process that drives the arterial venous differentiation and are embryonic lethal.

Here, we aim to identify novel angiogenic pathways that promote vascular growth independent of the main vascular growth factor Vegf A in zebrafish. For this purpose, we performed a high-throughput screening of small bioactive molecules on homozygous *vegfa* zebrafish embryos. As a read-out we analyzed the arterial venous differentiation of the DA and PCV and the blood flow. From about 3000 tested small molecules from our primary screen, 43 compounds were able to rescue arterial venous differentiation and blood flow in the *vegfa* mutants. Furthermore, we will now start the validation of the putative hits from the screen and investigate the molecular pathways and key modulators. The final hits from our screen have the potential to promote vascular growth independent of Vegf A. Our results will improve the knowledge of Vegf A-independent vascular growth, which have the potential to be used as therapeutic targets.

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