Neuropilin 1 (NRP1) mainly acts as a mediator of chemorepulsive cues during zebrafish trunk vascularisation

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Sprouting blood vessels are led by filopodia-studded endothelial tip cells that respond to both angiogenic and chemorepulsive signals. Neuropilin 1 (NRP1) is known to localise to tip cell filopodia and functions as a transmembrane receptor for both the angiogenic vascular endothelial growth factor A (VEGF-A) and repulsive class 3 semaphorins (SEMA3). For VEGF-A signalling, NRP1 interacts with the receptor tyrosine kinase KDR, instead, upon SEMA3 binding, NRP1 recruits a cytoskeletal regulator of the plexin family. Even though Sema3a restricts vascular sprouting in the zebrafish larval trunk via Plxnd1, mouse studies showed that both SEMA3A and any SEMA3 signalling through NRP1 are dispensable for developmental angiogenesis in both the embryonic hindbrain and the postnatal retina. Zebrafish Nrp1 is encoded by two *nrp1* homologues, termed *nrp1a* and *nrp1b*. Although *nrp1a* null mutants generated by genome editing nucleases were reported to lack obvious vascular defects, the morpholino-mediated knockdown of *nrp1a* or both homologue genes impairs vessel sprouting in the larval trunk. Here, we refined the morpholino knockdown strategy and also generated a double mutant zebrafish line lacking both *nrp1* homologues (*nrp1a*$^{sa1485/sa1485}$*;nrp1b*$^{fh278/\ fh278}$) to show that Nrp1 prevents ectopic vessel sprouting in the somites, which are known to be avascular due to the repulsive Sema3a ligand and Plxnd1 signal transduction. This finding suggests that Nrp1 can serve as a receptor that links repulsive Sema3a ligand to signal transducing Plxnd1 during physiological vascular patterning in zebrafish.