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Semaphorin 3E and Plexin-D1 Control Vascular Pattern Independently of Neuropilins

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The development of a patterned vasculature is essential for normal organogenesis. We find that signaling by semaphorin 3E (Sema3E) and its receptor plexin-D1 controls endothelial cell positioning and the patterning of the developing vasculature in the mouse. Sema3E is highly expressed in developing somites where it acts as a repulsive cue for plexin-D1-expressing endothelial cells of adjacent intersomitic vessels. Sema3E-plexin-D1 signaling did not require neuropilins, presumed obligate Sema3 co-receptors. Moreover, genetic ablation of Sema3E or plexin-D1, but not neuropilin-mediated Sema3 signaling, disrupted vascular patterning. These findings reveal an unexpected semaphorin signaling pathway and define a mechanism for controlling vascular patterning.

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