The GEF Trio controls endothelial cell size and arterial remodeling downstream of Vegf signaling in both zebrafish and cell models.

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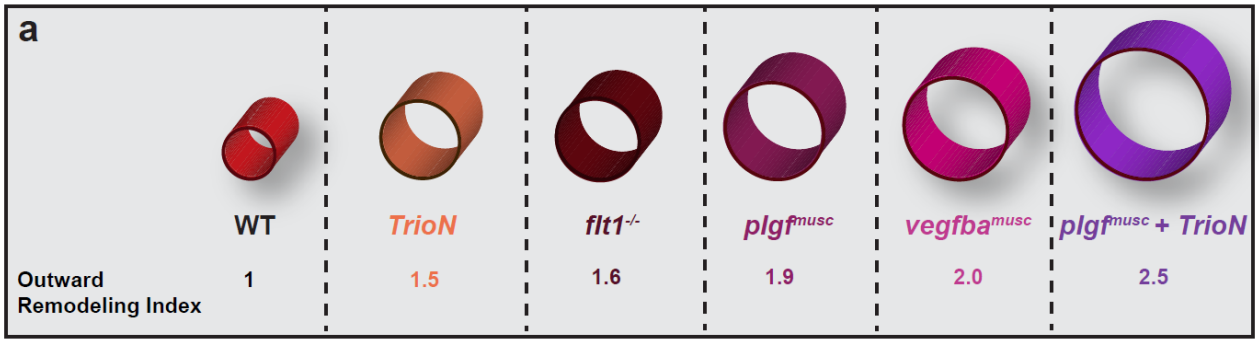
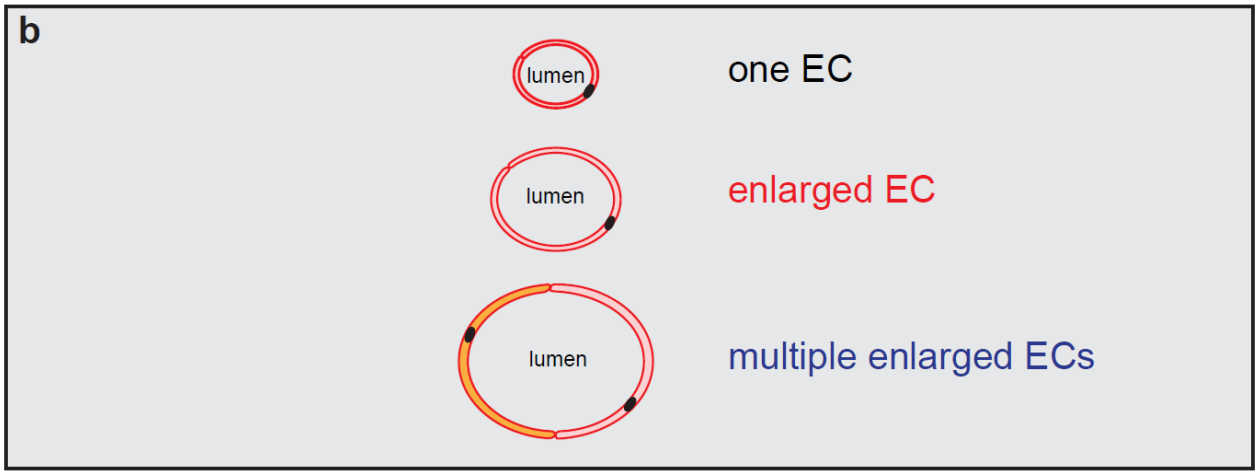
Nat Commun. 2020 Oct 21;11(1):5319. doi: 10.1038/s41467-020-19008-0.





Key findings

1. Arterial endothelial cells can dynamically enlarge resulting in the formation of large diameter arteries, independent of blood flow.

2. Endothelial enlargement requires guanine nucleotide exchange factor Trio and activation of the Trio-GEF1 targets Rac1 and RhoG at the cell periphery.

3. Activation of Trio in developing arteries involves precise titration of the VEGF signaling strength which is controlled by the soluble VEGF receptor Flt1.

4. Increasing VEGF—Trio signaling and augmenting both arterial endothelial size and number allows a 2.5-fold structural increase of arterial diameter.

5. Activation of VEGF-Trio as a means to augment arterial diameter shows promise to improve perfusion in the ischemic cardiovascular disease setting.

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