Lymphangiogenesis requires Ang2/Tie/PI3K signaling for VEGFR3 cell-surface expression.

Korhonen EA, Murtomäki A, Jha SK, Anisimov A, Pink A, Zhang Y, Stritt S, Liaqat I, Stanczuk L, Alderfer L, Sun Z, Kapiainen E, Singh A, Sultan I, Lantta A, Leppänen VM, Eklund L, He Y, Augustin HG, Vaahtomeri K, Saharinen P, Mäkinen T, Alitalo K.

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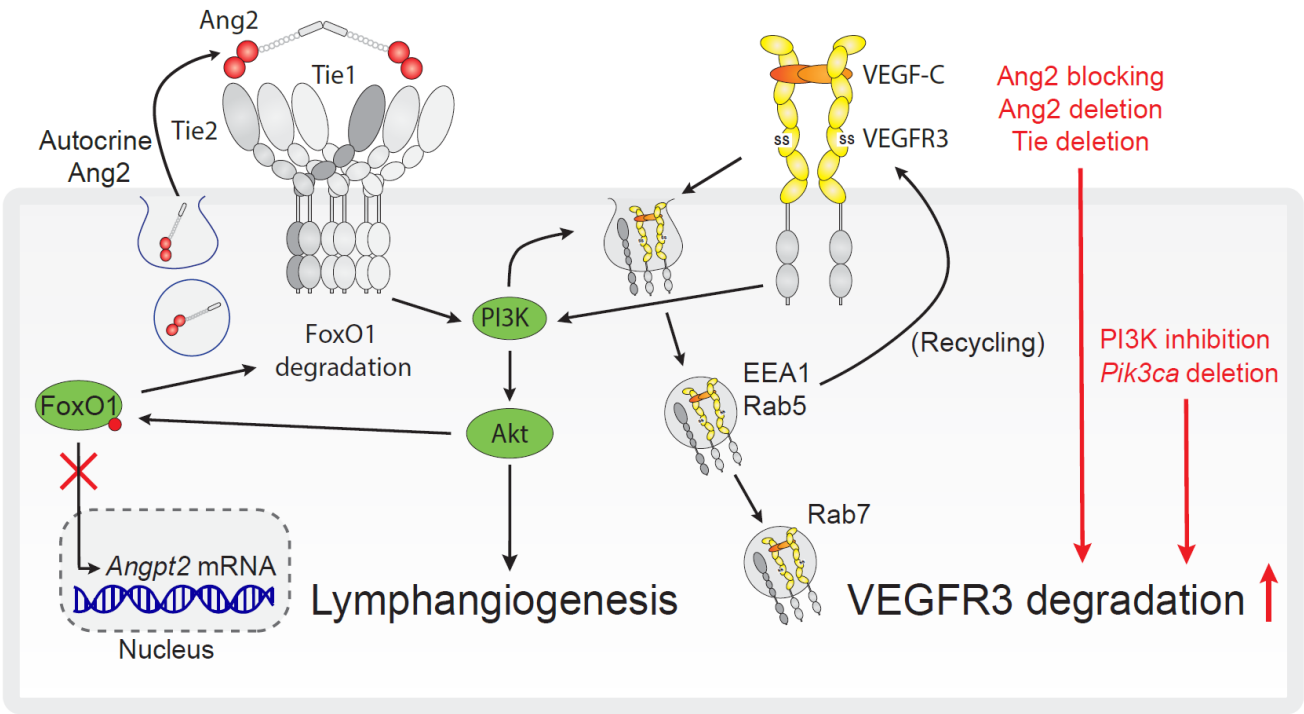

Key findings:

- Tie receptor deficiency and Ang2 inhibition leads to atrophy of lymphatic vessels in lymphatic endothelial cells (LECs).
- Ang2/Tie/PI3K signaling is required for normal postnatal lymphatic vessel development via the maintenance of VEGFR3 expression.
- Deletion of Tie1 and Tie2 receptors or treatment with Ang2-blocking antibodies inhibits VEGF-C–induced lymphangiogenesis in adult mice.
- Ang2/Tie signaling cooperates with the VEGF-C/VEGFR3 pathway involved in regulation of the development and growth of lymphatic capillaries and collecting vessels.
- These results suggest a novel approach for therapeutic modulation of lymphangiogenesis by targeting Ang2/Tie/PI3K signaling.