

P045 The VEGF/VEGFR and Ang/Tie axes have opposing roles in pericyte recruitment following eNOS-induced neovascularization

Stone OA, Harper SJ, Bates DO

Microvascular Research Laboratories, Bristol Heart Institute, Southwell Street, University of Bristol, Bristol, BS2 8EJ, UK.

Understanding the basic mechanisms of blood vessel growth may lead to the development of more effective pro- and anti-angiogenic therapies. We have previously demonstrated neovascularisation of non-ischemic tissue following eNOS overexpression. To further investigate the cellular and molecular mechanisms of eNOS induced angiogenesis, we delivered Ad.eNOS in combination with Ad.sVEGFR1 or Ad.sTie2 in the mesenteric angiogenesis assay, blocking VEGF/VEGFR and Ang/Tie signalling respectively. Ad.sTie2 significantly inhibited the Ad.eNOS induced increase in vessel density and diameter, and selectively inhibited proliferation in conduit (16-35 μ m diameter) but not exchange (<16 μ m diameter) vessels. Although no significant reduction in fractional pericyte coverage was observed, pericytes were morphologically distinct and appeared detached from the vessel wall, indicating an important role for the Ang/Tie axis in EC-pericyte interactions. Administration of Ad.sVEGFR1 also significantly decreased vessel density and overall vessel proliferation. Surprisingly, VEGF-A blockade led to a significant increase in fractional pericyte coverage, indicating that VEGF-A may have an inhibitory effect on pericyte recruitment/function. Taken together, these data reveal important mechanisms of eNOS induced neovascularisation and demonstrate the role of Angiopoietin-1 in EC-pericyte homeostasis. Furthermore, our data support the recently described inhibitory action of VEGF-A on pericyte function.