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S-PROPARGYL-CYSTEINE (SPRC)-INDUCED ANGIOGENESIS AND STAT3-MEDIATED MECHANISMS

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Objectives Angiogenesis, a physiological or pathological process characterised by the sprouting of new blood vessels from existing vessels, plays a vital role in ischemic heart disease. Since before hydrogen sulphide was reported to induce angiogenesis in vitro and in vivo, we investigated the possible pro-angiogenic effect of SPRC, a novel water-soluble modulator of endogenous hydrogen sulphide, and revealed STAT3-mediated mechanisms.

Methods Cell viability assay, cell proliferation assay, cell adhesion assay, wound healing assay, Transwell migration assay and tube formation assay were carried out to determine the pro-angiogenic effect of SPRC on endothelial cells in vitro. Matrigel plug assay, rat aortic ring assay, CAM assay and sponge implantation assay were carried out to determine the pro-angiogenic effect of SPRC in vivo. Western blot and immunofluorescence were used to detect the level and location of proteins, respectively. EMSA and CHIP were performed to determine the activation of STAT3 and its downstream promoter.

Results SPRC promoted cell proliferation, adhesion, migration and tube formation of primary HUVEC and increased angiogenesis ex vivo and in vivo. In SPRC-induced angiogenesis, phosphorylation of STAT3 was elevated significantly, followed by activation of some signal molecules, such as MAPK family and Akt pathway. The pro-angiogenic effect of SPRC mediated by STAT3 was confirmed by RNA interference of STAT3. The interaction between VEGFR2 and STAT3 was enhanced after SPRC-treatment. Meanwhile, SPRC induced translocation of STAT3 to nucleus, followed by activation of transcript, especially the promoter of vegf.

Conclusions Based on the proved pro-angiogenic effect of hydrogen sulphide, we proposed and tested a possible SPRC-mediated angiogenesis in vitro and in vivo. More important, we investigated the relative mechanisms of STAT3, including the activation of transcript and interaction with other signal molecules, in SPRC-induced angiogenesis in human umbilical vein endothelial cells.

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ABSTRACTS

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