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N-3-oxododecanoyl homoserine lactone inhibits angiogenesis by activating the angiopoietin-Tie system in human endothelial cells

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Objectives: The dysregulation of the angiopoietin-Tie system is associated with the development of sepsis-associated endothelial dysfunction. Bacterial quorum-sensing molecules act as pathogen-associated molecular patterns, however, the effect of quorum-sensing molecules on the angiopoietin-Tie system remains uncertain.

Methods: This study investigated the molecular mechanisms of endothelial dysfunction in human umbilical vein endothelial cells treated with N-3-oxododecanoyl homoserine lactone (3OC12-HSL) derived from Pseudomonas aeruginosa.

Results: Treatment with 3OC12-HSL reduced cell viability in a dose-dependent manner. Moreover, 3OC12-HSL treatment impaired the ability of tube formation even at non-lethal concentrations. The patterns of mRNA expression regarding the angiopoietin-Tie axis were assessed and the increased mRNA expressions of angiopoietin-2, Foxo-1, Tie1, and VEGFR2 were found in the 3OC12-HSL-treated cells. Western blot revealed that treatment with 3OC12-HSL increased the relative expressions of agiopoietin-2 and Foxo-1 and decreased the expression of Tie2. The study further evaluated the expression of IQGAP1 and the expressions of IQGAP1 and Rac1 decreased in cells treated with 3OC12-HSL. In addition, coimmunoprecipitation studies showed that treatment with 3OC12-HSL decreased the association between IQGAP1 and Rac1 in endothelial cells.

Conclusions: 3OC12-HSL can impair endothelial angiogenesis via the activation of the angiopoietin-Tie pathway. In addition, it may induce the dissociation of IQGAP1 with Rac1. Adjuvant therapy for blocking the quorum-sensing systems can help preserve endothelial cell integrity and prevent organ failure in patients with sepsis.