Emerging evidence implicates sphingosine-1-phosphate signaling in the pathobiology of glioblastoma and angiogenesis, but its role in glioblastoma-endothelial crosstalk remains largely unknown. In a study, Hadi et al., from Department of Medical Biotechnology and Translational Medicine, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico Milan, Laboratory of General Physiology, Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy, sought to determine whether the crosstalk between glioblastoma cells and brain endothelial cells regulates sphingosine-1-phosphate signaling in the tumor microenvironment. Using human glioblastoma and brain endothelial cell lines, as well as primary brain endothelial cells derived from human glioblastoma, they report that glioblastoma-co-culture promotes the expression, activity, and plasma membrane enrichment of sphingosine kinase 2 in brain endothelial cells, leading to increased cellular level of sphingosine-1-phosphate, and significant potentiation of its secretion. In turn, extracellular sphingosine-1-phosphate stimulates glioblastoma cell proliferation, and brain endothelial cells migration and angiogenesis. They also showed that, after co-culture, glioblastoma cells exhibit enhanced expression of S1P1 and S1P3, the sphingosine-1-phosphate receptors that are of paramount importance for cell growth and invasivity. Collectively, the results envision glioblastoma-endothelial crosstalk as a multi-compartmental strategy to enforce pro-tumoral sphingosine-1-phosphate signaling in the glioblastoma microenvironment [1)].

1)
Hadi LA, Anelli V, Guarnaccia L, Navone S, Beretta M, Moccia F, Tringali C, Urechie V, Campanella R, Marfia G, Riboni L. A bidirectional crosstalk between glioblastoma and brain endothelial cells potentiates the angiogenic and proliferative signaling of sphingosine-1-phosphate in the glioblastoma microenvironment. Biochim Biophys Acta. 2018 Jul 26. pii: S1388-1981(18)30177-X. doi: 10.1016/j.bbalip.2018.07.009. [Epub ahead of print] PubMed PMID: 30056170.