Suppression of LAT1 in endothelial cells of tumor tissues exhibits an anti-angiogenesis effect

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Angiogenesis plays a critical role in supporting tumor growth and metastasis. L-type amino acid transporter 1 (LAT1), a transporter for large neutral amino acids, is expressed at a high level in a wide range of cancers. LAT1 has, thus, been proposed as a promising molecular target for cancer therapy. We have recently found that, in addition to the cancer cells, LAT1 is also highly expressed in endothelial cells of human pancreatic cancer tissues and xenograft tumor models. In *ex* and *in vivo* angiogenesis assays, we found that pharmacological inhibition and genetic ablation of endothelial LAT1 exert an anti-angiogenic effect. Moreover, contribution of LAT1 in angiogenesis was verified in *in vitro* angiogenesis assays using human umbilical vein endothelial cells. As a possible mechanism underlying the upregulation of LAT1 in endothelial cells, we found that angiogenic growth factors, VEGF and FGF2, induce LAT1 expression. These results indicate that the enhanced amino acid uptake mediated by LAT1 in tumor-associated endothelial cells contributes to tumor angiogenesis. Beside the previously well-recognized inhibition of amino acids uptake of LAT1 in cancer cells, suppression of the tumor angiogenesis via the inhibition of endothelial LAT1 would therefore also contributes to the anti-tumor effect of cancer therapies targeting LAT1.