Neovascularization

The degree of neovascularization is critical in assessing tumor grade and malignancy.

Glioblastoma (GBM) is the most lethal primary adult brain tumor and its pathology is hallmarked by distorted neovascularization, diffuse tumor-associated macrophage infiltration, and potent immunosuppression.

Neovascularization is a key therapeutic target for cancer treatment. However, Anti-angiogenic therapy have shown modest success, as tumors develop rapid resistance to treatment owing to activation of redundant pathways that aid vascularization. Shenoy et al. hypothesized that simultaneously targeting different pathways of neovascularization will circumvent the current issue of drug resistance and offer enhanced therapeutic benefits. To test this hypothesis, they used of two distinct models of tumor-neovascularization, which exhibit equally dense microvasculature but show disparate sensitivity to anti-SDF-1 treatment. Lewis lung carcinoma (LLC) is primarily a vasculogenic-tumor that is associated with Hematopoietic stem cells functioning as a hemangioblast to generate circulating Endothelial Progenitor Cells contributing to formation of new blood vessels, and responds to anti-SDF-1 treatment. B16F0 melanoma is an angiogenic-tumor that derives new blood vessels from existing vasculature and is resistant to anti-SDF-1 therapy. In this study, we observed increased expression of the angiogenic-factor, Robo1 predominantly expressed on the blood vessels of B16F0 tumor. Blockade of Robo1 by the decoy receptor, RoboN, resulted in reduced microvascular-density and tumor-growth. However, this was associated with mobilization of BM-cells into the B16F0 tumor, thus switching the mode of neovascularization from angiogenic to vasculogenic. The use of a combinatorial treatment of RoboN and the monoclonal anti-SDF-1 antibody effectively attenuated tumor-growth and inhibited both angiogenic and BM-derived microvessels [1)]

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Shenoy AK, Pi L, Ligocki AP, Hosaka K, Cogle CR, Scott EW. Targeting Redundant ROBO1 and SDF-1 Pathways Prevents Adult Hemangioblast Derived-EPC and CEC Activity Effectively Blocking Tumor Neovascularization. Stem Cell Rev Rep. 2023 Jan 18. doi: 10.1007/s12015-022-10498-7. Epub ahead of print. PMID: 36652143.