Highly malignant brain tumors, such as glioblastoma, are characterized by hypoxia, endothelial cell (EC) hyperplasia and hypercoagulation. However, how these phenomena of the tumor microenvironment may be linked at the molecular level during tumor development remains ill-defined. We recently provided evidence that hypoxic cancer cells release substantial amounts of tissue factor (TF), i.e. the major initiator of coagulation, associated with secreted microvesicles with exosome-like characteristics (Svensson, et al., PNAS, 2011). Further, we found that hypoxia up-regulates protease activated receptor 2 (PAR-2), i.e. a G-protein coupled receptor of coagulation dependent signaling, in ECs. Interestingly, microvesicles derived from glioblastoma cells were found to trigger TF/PAR-2-dependent activation of hypoxic ECs in a paracrine manner. Ongoing studies (Kucharzewska, et al., submitted) that expand on these findings, indicate that the molecular information (protein, mRNA and miRNA) carried by cancer cell-derived microvesicles is substantially altered by hypoxia, resulting in potent angiogenic activities in vitro and in vivo. We conclude that microvesicles constitute a novel, potentially targetable mediator of hypoxia-driven tumor development, and suggest that the hypoxic vesicle signature may serve as a non-invasive biomarker to assess the oxygenation status and aggressiveness of malignant tumors.