Pericyte and Glioblastoma

How pericytes contribute to brain tumor infiltration is not known. In a study Caspani et al. investigated the underlying mechanism by which the most lethal brain cancer, Glioblastoma Multiforme (GBM) interacts with pre-existing blood vessels (co-option) to promote tumor initiation and tumor progression.

Using mouse xenografts and laminin-coated silicone substrates, they showed that GBM malignancy proceeds via specific and previously unknown interactions of tumor cells with brain pericytes. Two-photon and confocal live imaging revealed that GBM cells employ novel, Cdc42-dependent and actin-based cytoplasmic extensions, that we call flectopodia, to modify the normal contractile activity of pericytes. This results in the co-option of modified pre-existing blood vessels that support the expansion of the tumor margin. Furthermore, this data provide evidence for GBM cell/pericyte fusion-hybrids, some of which are located on abnormally constricted vessels ahead of the tumor and linked to tumor-promoting hypoxia. Remarkably, inhibiting Cdc42 function impairs vessel co-option and converts pericytes to a phagocytic/macrophage-like phenotype, thus favoring an innate immune response against the tumor. Our work, therefore, identifies for the first time a key GBM contact-dependent interaction that switches pericyte function from tumor-suppressor to tumor-promoter, indicating that GBM may harbor the seeds of its own destruction. These data support the development of therapeutic strategies directed against co-option (preventing incorporation and modification of pre-existing blood vessels), possibly in combination with anti-angiogenesis (blocking new vessel formation), which could lead to improved vascular targeting not only in Glioblastoma but also for other cancers [1)].

1)
Caspani EM, Crossley PH, Redondo-Garcia C, Martinez S. Glioblastoma: a pathogenic crosstalk between tumor cells and pericytes. PLoS One. 2014 Jul 17;9(7):e101402. doi: 10.1371/journal.pone.0101402. eCollection 2014. PubMed PMID: 25032689; PubMed Central PMCID: PMC4102477.