



A service of the [U.S. National Library of Medicine](#)  
and the [National Institutes of Health](#)

Select 19536297

---

1: [PLoS One](#). 2009 Jun 17;4(6):e5947.



## **Modulation of angiogenic and inflammatory response in glioblastoma by hypoxia.**

[Murat A](#), [Migliavacca E](#), [Hussain SF](#), [Heimberger AB](#), [Desbaillets I](#), [Hamou MF](#), [Rüegg C](#), [Stupp R](#), [Delorenzi M](#), [Hegi ME](#).

Laboratory of Brain Tumor Biology and Genetics, University Hospital Lausanne (CHUV) and University of Lausanne, Lausanne, Switzerland.

Glioblastoma are rapidly proliferating brain tumors in which hypoxia is readily recognizable, as indicated by focal or extensive necrosis and vascular proliferation, two independent diagnostic criteria for glioblastoma. Gene expression profiling of glioblastoma revealed a gene expression signature associated with hypoxia-regulated genes. The correlated gene set emerging from unsupervised analysis comprised known hypoxia-inducible genes involved in angiogenesis and inflammation such as VEGF and BIRC3, respectively. The relationship between hypoxia-modulated angiogenic genes and inflammatory genes was associated with outcome in our cohort of glioblastoma patients treated within prospective clinical trials of combined chemoradiotherapy. The hypoxia regulation of several new genes comprised in this cluster including ZNF395, TNFAIP3, and TREM1 was experimentally confirmed in glioma cell lines and primary monocytes exposed to hypoxia in vitro. Interestingly, the cluster seems to characterize differential response of tumor cells, stromal cells and the macrophage/microglia compartment to hypoxic conditions. Most genes classically associated with the inflammatory compartment are part of the NF-kappaB signaling pathway including TNFAIP3 and BIRC3 that have been shown to be involved in resistance to chemotherapy. Our results associate hypoxia-driven tumor response with inflammation in glioblastoma, hence underlining the importance of tumor-host interaction involving the inflammatory compartment.

Publication Types:

- [Research Support, N.I.H., Extramural](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 19536297 [PubMed - in process]

PMCID: PMC2694268

---