

## **Hypoxia Gene Networks in Gliomas**

John Muller<sup>1</sup>, Luke Jackson<sup>1</sup>, Elise O'Herron<sup>2</sup>, Scott Cooper<sup>2</sup>, Angela Richardson<sup>2</sup>

<sup>1</sup>Indiana University School of Medicine; <sup>2</sup>Indiana University School of Medicine, Department of Neurological Surgery

### **Background and Hypothesis:**

Gliomas are the most common primary brain tumor and range from low grade to high grade, with glioblastomas (GBM) being the most aggressive. Translation of therapies for these tumors from preclinical models to clinical practice has been limited. Preclinical studies are typically performed in ambient air (21% oxygen), while physiological oxygen tension (physioxia) is 3-5%. Extracranial tumor tissue processed in physioxia demonstrates distinct gene expression profiles and chemoresistance as compared to the same samples processed in ambient air. However, the role of varying oxygen tension in gliomas has not been well studied. GBMs often have areas of necrosis with presumed low oxygen tension, while these findings are typically absent in lower grade gliomas. In this study, we examine expression of hypoxia related genes in patient samples obtained from grade II, III and IV gliomas. We hypothesize that increasing tumor grade will be associated with differential expression of hypoxia-related genes.

### **Methods:**

Gene expression in patient brain tumor samples (glioblastoma, high grade astrocytoma, low grade astrocytoma) and normal brain samples (from epilepsy surgery) was assayed using real time PCR. Hypoxia-related gene expression was examined in cBioPortal for Cancer Genomics by comparing survival in the top-expressing and bottom-expressing quartile for these transcripts.

### **Results:**

Patient samples were screened for differences in gene expression with greater than two-fold upregulation in GBM as compared to normal brain tissue. Expression level of one of these genes, ADM, was significantly associated with survival in patients with GBM ( $p < 0.05$ ). Additional differences between grades of glioma will also be presented.

### **Potential Impact:**

This work demonstrates differential expression of hypoxia-related gene transcripts in gliomas. The next step is to assess differences between patient samples processed in differing oxygen tensions to assess efficacy of chemotherapeutics and gene expression in samples that have never been exposed to ambient air.