Effect of Oxygen Tension on Glioblastoma Cell Growth

Luke Jackson[1], Jack Muller[1], Elise O'Herron[1], Scott Cooper[1], Angela Richardson[1]

[1]Department of Neurological Surgery, Indiana University School of Medicine

Background and Hypothesis

Glioblastoma (GBM) is an aggressive primary malignancy of the CNS with a dismal prognosis (~15-20 months) despite standard of care therapies. The poor prognosis of GBM despite ongoing research may be due to inaccuracies in preclinical models of the disease. Cell lines typically used to study GBM are exposed to ambient air containing 21% oxygen (normoxia compared to physiologic oxygen tension, physoxia, ~5%). In extracranial tumors, exposure to the oxygen in ambient air triggers epigenetic changes that alter cell growth, metabolism, and treatment responsiveness. The aim of this study is to obtain preliminary data on the impact of physiologic oxygen tensions on primary glioma cell growth in vitro.

Experimental Design

Growth of primary glioma cell lines (GB43, GB10, GB001) and one immortalized cell line (293T HEK) was assessed in normoxia and physoxia. All cell lines were plated at 10,000 cells per well. Cells were harvested and counted in triplicate on days 2, 4, 6, 8, 10, 12. On each day the cells were counted, the media in the remaining wells was changed. This experiment was repeated three times. Wound healing assays with all cell lines were also performed at normoxia and physoxia.

Results

Cells line growth curves were plotted and showed consistent exponential growth after counting on day two. From these graphs, the cell doubling time was calculated over a period of four days during which the cells were undergoing exponential growth.

Conclusions

Current results indicated that primary glioblastoma cell lines grow at different rates at differing oxygen tensions. In ongoing studies, we are exploring the effect of low oxygen tensions on functional assays such as wound-healing. Future work will assess rates of growth and functional consequence of physoxia in tumor samples never exposed to ambient air to most accurately recapitulate the in-situ environment.