Sulfonylurea Receptor 1 Expression is Variable in Adult and Pediatric Brain Tumors

Eric M. Thompson MD; Kyle Gregory Halvorson MD; Roger McLendon MD
Duke University Medical Center

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Introduction

Edema is a significant cause of neuromorbidity in children and adults with brain tumors. Agents used to control this effect, such as corticosteroids, have their own associated morbidities. Sulfonylurea receptor 1 (SUR1) is a transmembrane protein that regulates the activity of ion channels in neurons, glia, and endothelial cells. SUR1 expression is upregulated in neuroinflammatory conditions. Inhibition of SUR1 with glyburide decreases edema and neuroinflammation by countering cytotoxic edema and apoptosis in rodent models of subarachnoid hemorrhage, stroke, trauma, and cerebral metastases. However, the expression of SUR1 in human brain tumors has not been elucidated. The purpose of this study was to determine SUR1 expression and cellular colocalization in a variety of human brain tumor specimens.

Methods

Fourteen GBM, 12 cerebral metastases, 12 medulloblastoma, 4 anaplastic ependymoma, and 13 ependymoma specimens were analyzed using immunofluorescence. SUR1 expression and colocalization with blood vessels, neurons, and glial cells was analyzed and compared using ANOVA.

Results

SUR1 expression was found in all specimens examined as a percentage of the total tissue area (mean±SD): GBM 3.9±4, Mets 4.1±3.1, MB 10±7.9, ependymoma 7.8±8.4, anaplastic ependymoma 13.6±5.7. SUR1 expression was greater in medulloblastoma and anaplastic ependymoma compared to GBM and metastases ($p<0.05$). SUR1 colocalized most reliably with the neuronal marker, NeuN, in GBM and metastases samples ($p<0.05$). SUR1 colocalized most reliably with the endothelial cell marker, CD31, in medulloblastoma and ependymoma samples ($p<0.05$).

Conclusions

SUR1 is a putative therapeutic target to reduce neuroinflammation in adult and pediatric brain tumors. Inhibition of SUR1 may result in neuronal stabilization in GBM and cerebral metastases and reduced edema in medulloblastoma and ependymoma.

Learning Objectives

Describe the differential expression of SUR1 in brain tumors.

Describe implications for future clinical trials of SUR1 inhibition to treat tumor-related vasogenic edema.

References

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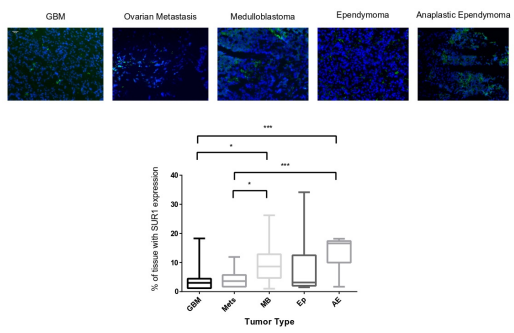
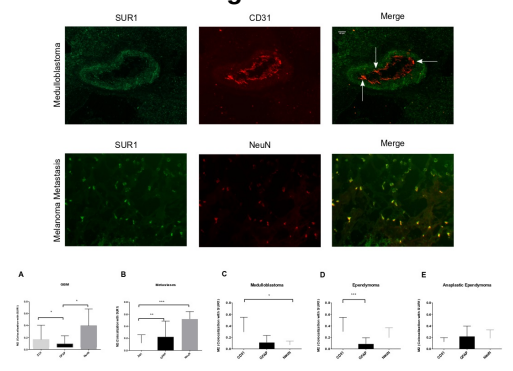
Figure 1.



Expression of SUR1 by tumor type.

Figure 2.



Colocalization of SUR1