Expression of Tissue Factor and Alternatively Spliced Human Tissue Factor in Gliomas

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Introduction

It has long been recognized that cancers, including gliomas and related brain tumors, are associated with thromboembolic diseases and activators of the coagulation cascade. Accumulating evidence has shown that tissue factor (TF), a trans-membrane activator of the blood coagulation pathway, is involved in the regulation of angiogenesis, cell migration, tumor growth and inflammation. A soluble form of TF, known as alternatively spliced human tissue factor (asHTF), is believed to promote cell proliferation and tumor growth. This project examines the expression levels of TF and asHTF in human gliomas, correlates expression levels with tumor grade and begins to assess whether these proteins may be suitable for use as diagnostic markers in the future.

Methods

Glial tumors were collected from consenting patients who were undergoing surgical resection at Northwestern Memorial Hospital. Primary cell lines were established from these tumors and RNA was extracted. TF and asHTF RNA levels were analyzed by quantitative RT-PCR and correlated with tumor grade. In this study, 28 samples of varying histological grade (WHO Grade II, III and IV) were used, including astrocytoma, oligodendroglioma and mixed glioma. Samples and controls are shown in Table 1. All outlined approaches and tissue collections were IRB approved.

Learning Objectives

1. To determine the RNA expression levels of TF and asHTF in gliomas.
2. To correlate the mRNA expression levels of TF and asHTF with the histological grade of the tumor.

Table 1: List of Samples

Table 1: List of Samples and Their Diagnosis or Description

Name of Sample	Diagnosis or Description of Sample
Control	
MiaPaCa-2	Human pancreatic cell line that does not natively express TF or asHTF
MP256	Human pancreatic cell line transfected with TF-expressing vector
SNB78	Human glioblastoma cell line expressing both TF and asHTF
WHO Grade II	
MB009	Infiltrating Astrocytic Neoplasm
MB015	Fibrillary Astrocytoma
MB024	Mixed Oligoastrocytoma
MB027	Oligodendroglioma
MB028	Oligodendroglioma
BTI047	Diffuse Astrocytoma (protoplasmic type)
BTI058	Recurrent/Residual Oligodendroglioma
WHO Grade III	
MB002	Anaplastic Astrocytoma
MB006	Anaplastic Astrocytoma
MB030	Anaplastic Oligodendroglioma
BTI044	Anaplastic Oligodendroglioma
BTI064	Anaplastic Oligoastrocytoma
BTI070	Anaplastic Oligodendroglioma
WHO Grade IV	
MB001	Recurrent Glioblastoma
MB003	Glioblastoma, with sarcomatous differentiation
MB008	Glioblastoma
MB010	Glioblastoma
MB014	Recurrent Glioblastoma
MB017	Glioblastoma
MB026	Oligodendroglioma
BTI049	Glioblastoma
BTI051	Glioblastoma
BTI056	Glioblastoma (lower spectrum)
BTI059	Glioblastoma
BTI062	Glioblastoma With Mixed Features of Oligodendroglial and Astrocytic Differentiation
BTI065	Glioblastoma
BTI068	Recurrent/Residual High Grade Glioma
BTI069	Recurrent/Residual High Grade Glioma

Note: All diagnoses were determined following review by a neuropathologist.

Figure 1: TF RNA Expression Level

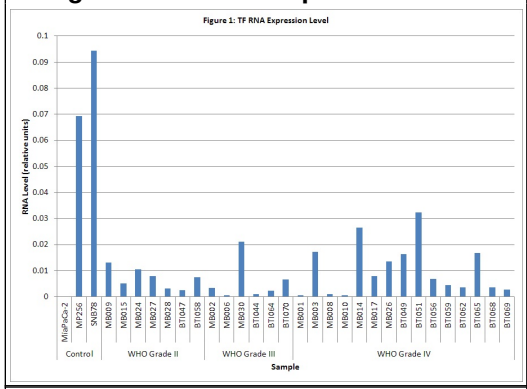
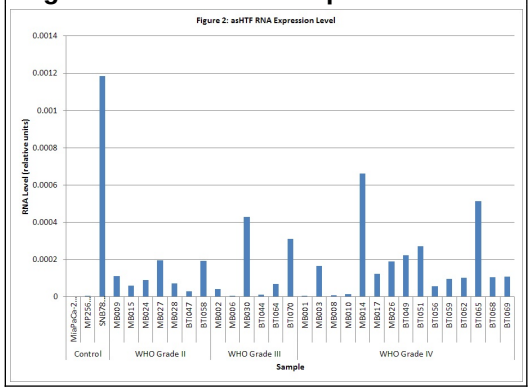


Figure 2: asHTF RNA Expression Level



Results

These results demonstrate the RNA expression levels of TF (Figure 1) and asHTF (Figure 2) in primary glioma cell lines. TF and ashTF expression was not detected in all samples, yet in samples that expressed TF and/or asHTF the expression levels were modest in those diagnosed as Grade II, higher in Grade III and highest expression levels were mainly observed in glioblastomas. Also, the TF expression level correlate closely with asHTF expression level in the same sample.

Conclusion

TF and asHTF have been shown to be associated with cancer progression and angiogenesis. Thus it is important to evaluate their expression levels in glioma. Here, we have screened glioma samples for TF and asHTF RNA expression levels. Further studies will help to elucidate their role in tumor development. Future analyses will examine TF and asHTF protein levels and localization as well as participation in the regulation of cell proliferation and migration. Future studies will also include examinations that will attempt to correlate corresponding patient data and therapeutic responses with TF and asHTF levels. This preliminary data coupled with planned future experiments will help to better understand how TF and asHTF may be used as a prognostic marker and for decisions related to glioma therapies.

Acknowledgements

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References

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