GLYCOLIPIDOMIC CHARACTERIZATION OF ASTROCYTOMA AND ADJACENT TISSUE: A MASS SPECTROMETRY APPROACH TO GANGLIOSIDE PROFILING

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Abstract
This study highlights the use of ion mobility mass spectrometry to characterize gangliosides in peritumoral tissue of diffuse astrocytoma. The identification of specific species, such as GT1b and Fuc-GD1 variants, suggests their potential as biomarkers and contributors to tumor progression. These findings open new avenues for diagnostic and therapeutic strategies.

Introduction
Diffuse astrocytoma is a primary brain tumor marked by the subtle infiltration of cancer cells into adjacent brain tissue. Due to this invasive nature, studying the peritumoral region is crucial for understanding tumor progression [1]. The present study introduces ion mobility mass spectrometry (IMS MS) as a novel tool for analyzing gangliosides in this region. Using high-resolution nanoESI IMS MS and tandem MS, a diverse array of ganglioside species was identified. Several species, including GT1b and Fuc-GD1 variants, may serve as biomarkers or contribute to tumor infiltration. These findings create new opportunities for diagnostic and therapeutic targeting in diffuse astrocytoma.

Experimental
Peritumoral brain tissue from a 30-year-old male with WHO grade II diffuse astrocytoma was collected with informed consent and ethical approval. Gangliosides were extracted using a modified Svennerholm and Fredman method, purified by protein precipitation, Sephadex G-25 filtration, and dialysis, then reconstituted in methanol and diluted to 5 pmol/µl. Samples were ionized via nanoESI in negative ion mode and analyzed by IMS MS and MS/MS on a Synapt G2-S system (Waters, UK). Instrument settings included 1.4 kV capillary voltage, 40 V cone voltage, and source/desolvation temperatures of 100/150 °C. Collision-induced dissociation (CID) was conducted following IMS, with energies ranging from 20 to 45 eV.

Results
IMS MS profiling of gangliosides in the peritumoral tissue revealed a significantly higher diversity of structures compared to previous reports. Several species were found prominently expressed, including GT1(d18:1/18:0), GT1(d18:1/20:0), GM2(d18:1/16:2), GD1(d18:1/16:0), GD2(d18:1/20:0), Fuc-GT3(d18:1/24:4), and Fuc-GD1(d18:1/18:2). These gangliosides may contribute to the creation of a tumor-supportive microenvironment, promoting cell–cell interactions, immune modulation, and tumor invasion. Structural characterization by tandem

MS confirmed GT1(d18:1/20:0) as the GT1b isomer, highlighting the resolving power of IMS MS for isomer differentiation. Overall, the results suggest that specific ganglioside patterns in peritumoral tissue could serve as biomarkers and play functional roles in diffuse astrocytoma progression.

Conclusions

The study demonstrates that ion mobility mass spectrometry allows for detailed characterization of the complex ganglioside composition in peritumoral tissue. The identification of specific ganglioside species suggests their potential as biomarkers and their possible role in tumor progression. These results offer new insights into the aberrant molecular landscape that triggers and even facilitates diffuse astrocytoma invasion.

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Reference

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