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Identification of tumor-marker gangliosides for early cancer detection: A multi-platform approach.

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Background: Tumor-marker gangliosides (TMGs) have enormous potential for early-stage cancer detection as diagnostic biomarkers despite being relatively understudied in this context. AOA Dx is focused on the analytical development of three separate platforms for the quantitation of TMGs in human serum. The development of these platforms for TMG quantitation may allow for the identification of diagnostic signatures for early-stage cancer detection. **Methods:** First, we are developing a pipeline of antibody-based assays to target TMGs. To aid in development of multiple immunoassays, we collected specificity and affinity data on commercial and proprietary antibodies targeting TMGs using glycoarrays. We are also currently using two immune-based platforms to target TMGs. We have developed an enzyme-linked immunosorbent assay (ELISA) and we have implemented high-performance thin-layer chromatography (HPTLC) to detect individual and total gangliosides. Additionally, we are applying both targeted and untargeted mass spectrometry to human serum from confirmed cancer diagnoses. **Results:** The specificity and affinity data from the glycoarrays confirm that our TMG antibodies have negligible cross-reactivity and are suitable for diagnostic platform development. Additionally, our developed ELISA allows for the quantification of TMGs in diverse and complex matrices including human serum and plasma, cell lines, and exosomes. HPTLC also detects individual and total gangliosides in each of these matrices, which allows for high-throughput analysis for TMG quantitation. Finally, the application of both targeted and untargeted mass spectrometry has identified multiple TMGs characterized by unique lipid tails. Notably, MS analysis shows that the serum of melanoma and ovarian cancer patients exhibited significantly increased levels of several ganglioside species compared to age-matched healthy serum, further highlighting the potential of TMGs as a promising avenue for cancer diagnosis. Further experiments will focus on refining all platforms. We will also expand the demographic representation of our human serum sample cohort to confirm the initial findings from our mass spectrometry experiments and continue to use this platform to identify additional TMGs of interest. **Conclusions:** AOA Dx is advancing the development of a multi-platform approach for the detection of TMGs. Our objective is the identification of a diagnostic disease signature for early-stage cancer detection. The validation of this type of diagnostic panel would allow for expedited diagnosis and treatment of cancers currently diagnosed at late stages, ultimately reducing healthcare costs and increasing survival rates. Future research will aim to validate these biomarkers in independent prospective studies. Research Sponsor: None.