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Proapolipoprotein A1 Demonstrates Improved Potential as a Serum Marker for Brain Metastases Without Vascular Disease Interference

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There is controversy about how the brain should be staged in individuals with lung cancer. In addition, continuous monitoring of the brain for the development of brain metastases after definitive treatment is not usually performed. A serum marker of brain metastases would thus be useful. The development of brain metastases is accompanied by disruption of the blood-brain barrier (BBB). Proteomic markers from the brain may appear in the blood when metastases develop. S100β is a well-established marker of BBB opening that has a high rate of false positives for detecting brain metastases in recovering lung cancer patients. This is due frequently to minor leakage of the BBB resulting from small vessel ischemic disease (SVID), a common cerebrovascular finding in patients suffering from hypertension, diabetes, and/or hyperlipidemia, as well as in the elderly. This work discusses a new marker that appears to have a higher positive predictive value for brain metastases compared with S100β.

Based upon initial findings produced by 2D protein electrophoretic analysis of serum from a single lung tumor patient collected both before and after the detection of brain metastases by MRI, we identified strong upregulation of a protein for brain metastases. By LC-tandem MS this protein was identified to be proapolipoprotein A1. This was investigated further by selecting several lung tumor patients screened as positive or negative by MRI with SVID present and absent, as well as control CSF as a brain protein reference. Proapolipoprotein A1 was analyzed in these samples on a 2D gel with an expanded pI range (4.7 to 5.9) by conventional staining and Western blot analysis.

2D protein staining and Western blot analysis confirmed the upregulation of proapolipoprotein in the MRI positive samples and a reference CSF sample. This protein also does not appear to be elevated by the presence of SVID.

Proapolipoprotein and its related variants appear to be potential markers for the presence of brain metastases in lung cancer patients and, unlike S100β and transthyretin, it does not appear to be elevated by the presence of SVID. Detailed findings from this research work can be found in *Cancer* (Marchi N, Mazzone P, Fazio V, et al. Cancer 2008[March]; 112[6]:1313–1324).

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