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Plasma Extracellular Vesicle (EV) Glial Fibrillary Acidic Protein (GFAP) and Tau as biomarkers for Brain Cancer

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Introduction

Early detection of brain cancer remains a challenging proposition. We applied a novel alternating current electrokinetic (ACE) chip device that relies on the dielectrophoretic (DEP) force to isolate and analyze the proteomic content of extracellular vesicles (EV) derived from undiluted patient plasma to identify biomarkers for early detection of brain tumors.

Methods

EVs derived from cultured cells or plasma samples were isolated using the ACE chip. The concentration of intra-vesicular glial fibrillary acidic protein (GFAP) and Tau was determined using immunofluorescence staining. Improvement in model prognostication was quantified using net reclassification improvement (NRI>0) and integrated discrimination improvement (IDI).

Results

EVs secreted by cultured brain tumor cells (brain metastasis, meningioma, and glioma) harbored high levels of GFAP and Tau. We isolated EVs from plasma collected from brain tumor patients (5 meningiomas, 5 metastases, 6 gliomas) and 17 non-cancer controls. Compared to controls, plasma EVs from brain tumor patients exhibited greater fluorescence for GFAP (1.94±0.139 vs. 1.28±0.042, $p<0.0001$) and Tau (4.92±0.43 vs. 1.79±0.11, $p<0.0001$). Immunofluorescence did not differ between tumor types. Elevated EV GFAP was associated with a sensitivity of 88%, a specificity of 92%, and a AUC of 0.931 (95% CI 0.84-1.022) for brain tumor detection. Similarly, elevated EV Tau was associated with sensitivity of 94%, specificity of 94%, and AUC of 0.948 (95% CI 0.846-1.05) for brain tumor detection. The combination of EV GFAP and Tau improved test discrimination relative to GFAP alone (NRI>0 1.66, 95% CI 1.19-2.13, $p<0.001$; IDI 0.26, 95% CI 0.11-0.41, $p<0.001$) or Tau alone (NRI>0 1.54, 95% CI 1.03-2.05, $p<0.001$; IDI 0.18 0.038-0.32, $p=0.013$).

Conclusions

We have provided proof-of-principle studies to demonstrated the utility of a novel DEP-based technology for minimally invasive brain cancer detection using undiluted patient plasma.

Learning Objectives

1. Identify plasma extracellular vesicle-derived GFAP and Tau as important biomarkers of brain tumors

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