

STRATEGIES FOR THE UTILIZATION OF PLASMA-DERIVED EXTRACELLULAR VESICLE CONTENT IN BIOMARKER DISCOVERY FOR NEURODEGENERATIVE DISEASES

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“Liquid biopsies” have emerged as an exciting new technique in the field of biomarker discovery. These non-invasive techniques, utilizing plasma-derived extracellular vesicles (EVs), are especially promising and increasingly reliable in diagnosing dementia and neurodegeneration where brain biopsies are not practical. Neuron-derived EVs, which can be isolated from patient blood plasma, have been reported to contain proteins and miRNAs that may represent potential Alzheimer’s Disease (AD) biomarkers which can be useful in the context of AD diagnosis and treatment. However, one current and limiting challenge of the field is optimal, reliable isolation of neuron-derived EVs, hindered in particular because by their low abundance in blood plasma and lack of unique brain-specific surface markers that can be used for purification. Importantly, definitive evidence of their brain and neuronal origin or specificity in published reports is still lacking. Hence, there is an unmet need for alternative strategies that can provide more conclusive support for brain-derived neuron-specific and glia-specific EV-based biomarkers. We are pursuing 3 avenues of research to identify EV-based biomarkers of brain origin. (1) Identification of cell-type specific EV surface receptors that can aid in the enrichment of brain specific EVs populations from patient plasma. (2) Multi-omic characterization of EVs that can aid in the identification of cell-type specific biomarkers signatures. (3) We have developed a versatile lentivirus-based tool kit utilizing proximity-based protein biotinylation (BioID), that will allow us to identify plasma EV-derived biomarkers of neuronal and glia origin in mouse models of neurodegeneration. We hypothesise that combining these approaches will increase the likelihood of identifying disease relevant EV-based biomarkers for the diagnosis of neurodegenerative diseases in humans.