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Proteomic profiling of exosomal biomarkers in alzheimer's disease: A path toward early diagnosis and therapeutic monitoring

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Statement of the Problem: Alzheimer's Disease (AD) lacks reliable, non-invasive biomarkers for early diagnosis and monitoring of disease progression. This study explores the proteomic profiling of brain-derived exosomes in plasma as a novel biomarker source for early-stage Alzheimer's detection.

Methodology: In this prospective study, plasma samples were collected from 40 AD patients (mild cognitive impairment to moderate stages) and 40 age-matched cognitively healthy individuals. Brain-derived exosomes were isolated using immunoaffinity techniques targeting neuronal surface markers (L1CAM). Mass spectrometry-based proteomic analysis (LC-MS/MS) was performed to identify differentially expressed proteins. Statistical analysis included false discovery rate adjustment and pathway enrichment analysis. Correlation with neuropsychological scores (MMSE, ADAS-Cog) was also assessed.

Results: A panel of 12 proteins showed significant differential expression in AD patients compared to controls ($p < 0.01$). Notably, Neurogranin, Synaptophysin, and Clusterin were consistently elevated in AD samples. The protein panel achieved a diagnostic accuracy of 91%, with an AUC of 0.94, sensitivity of 88%, and specificity of 93%. Proteins identified were associated with synaptic dysfunction and amyloid-beta clearance pathways. Correlation analysis revealed strong associations between exosomal Neurogranin levels and cognitive decline ($r = -0.74$, $p < 0.001$).

Conclusion & Significance: Brain-derived exosomal proteins represent a promising class of non-invasive biomarkers for early diagnosis and disease monitoring in Alzheimer's Disease. This novel approach holds potential for enhancing early intervention strategies and personalized treatment plans. Further validation in longitudinal and multicentric cohorts is recommended.

Biography

Charlotte E. Rowe is a leading neuroscientist specializing in biomarker discovery and neurodegenerative disease research. She holds a Ph.D. in Molecular Neuroscience from University College London and has led numerous high-impact studies on Alzheimer's disease and Parkinson's disease. Rowe currently heads the Translational Neuroproteomics Lab at King's College London and is involved in several international consortia focusing on exosome-based diagnostics. Her pioneering work in plasma-based biomarker development has been widely published and funded by the UK Medical Research Council (MRC) and the Alzheimer's Research Trust.

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