Non-Invasive Blood-Based Early Alzheimer's Detection Using Sex-Specific Brain-Blood Graph Reinforcement Learning

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Alzheimer’s disease (AD) affects 1 in 9 individuals aged 65+ in the U.S., with females twice as likely as males. As AD pathology begins decades before symptoms appear, early detection and intervention are critical. I developed NeuroPlasmaNet, an AI system that identifies early-stage blood-based biomarkers using graph neural networks (GNNs) to simulate the sex-specific brain-blood multi-omics gene networks guided by neural pathology. Since AD is defined in the brain and to be detected in the blood, I first constructed biotype-stratified brain gene graphs based on cell types and layers, controlling for confounding biases such as age, APOE genotype, and education. I deployed reinforcement fine-tuning with cosine-based similarity reward function to optimize each learning iteration and align predicted genes with AD biological relevancy. This approach revealed distinct male vs. female molecular signatures. I then refined non-invasive blood-based gene selection and identified NeuroPlasma12 gene panel (e.g., C1QB, TXNIP, TREM2, GFAP, PLCG2, CD163, CAMK1D, LRP10). This brain-first analysis grounded blood markers in AD neural pathology, avoiding systemic noise. I introduced the NeuroPlasma Score (NPS) to quantify the gene panel profile, achieving 92.03% accuracy (AUC=0.9410, $p < 0.001$) for early AD detection. I also identified potential therapeutic targets (e.g., GRIN2B, PLCG2, GRM5, CAMK1D), some novel and others published in Nature and JAMA. Beyond gene markers, the results highlight modifiable cognitive risk factors, such as substance use, infections, circadian disruption, and nutrition deficiencies, and promote personalized, preventive brain health strategies to the largely overlooked preclinical population.

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