Grant Awardees

Sat. Sep 27, 2025 9:50 AM - 10:50 AM JST | Sat. Sep 27, 2025 12:50 AM - 1:50 AM UTC Session Room 1 (Main Hall A)

WACP Grant Award Session

[GA-1-04] AI-Driven Multi-Omics Integration of Functional Connectomics and Biomarkers to Decode Resilience Mechanisms in Treatment-Resistant Depression

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Keywords：Treatment-Resistant Depression (TRD)、Resilience Mechanisms、AI-Driven Multi-Omics、Functional Connectomics、Circulating miRNA Biomarkers

Background/Aim: Treatment-Resistant Depression (TRD) affects up to 30% of major depressive disorder (MDD) patients, presenting a significant challenge in psychiatry. Resilience, the ability to maintain psychosocial functioning despite TRD, is poorly understood. This study leverages AI to integrate functional connectomics and circulating miRNA biomarkers, aiming to identify resilience mechanisms and develop precision psychiatry interventions. **Methods:** Functional MRI (fMRI) data were obtained from the UK Biobank (n=2,500; TRD cases, n=900), and circulating miRNA profiles from the exRNA Atlas (n=1,100 participants). Resilience was operationalized as high psychosocial functioning despite TRD, assessed via validated mental health scales. Functional connectomics were analyzed using a graph neural network (GNN) to map and evaluate disruptions in the default mode network (DMN), salience network (SN), and fronto-limbic circuits. Differential expression analysis identified resilience-associated miRNAs influencing synaptic remodeling and neuroinflammation. A multi-modal variational autoencoder (VAE) integrated fMRI connectivity and miRNA expression patterns into unified resilience signatures, validated using 10-fold cross-validation. An ensemble AI model predicted resilience, with critical features ranked by SHAP values. **Results:** The prediction model achieved an AUROC of 0.86 (95% CI: 0.83–0.89) and an accuracy of 78.3% (95% CI: 76.2–80.4%). DMN-SN connectivity disruptions were the strongest predictors of resilience (SHAP value: 0.62). Resilient individuals showed significantly elevated miR-124 and miR-146a expression (log2 fold change: 2.1; adjusted $p<0.001$). Integrating fMRI and miRNA features improved prediction by 22% over single-modality models, with resilient patients scoring 10.4 points higher in psychosocial functioning ($p<0.01$). **Conclusions:** This study provides a robust framework for decoding resilience in TRD using AI-driven multi-omics integration, offering novel perspectives for targeted interventions in precision psychiatry.