Meta-Analysis of Ischaemic Stroke Patient Blood Samples Reveal miR-199a-3p as a Putative Diagnostic Biomarker

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Introduction: Ischemic Stroke (IS) is a leading cause of morbidity and mortality—accounting for ~2.7 million of total stroke-related deaths. Rapid diagnosis and treatment of IS are paramount for optimal recovery and to prevent mortality. This meta-analysis study aims to analyze previously published miRNA expression cohorts generated from blood samples extracted from IS patients to uncover new and robust miRNA biomarkers. Given the utility of miRNAs in blood, they serve as robust modalities as biomarkers.
Methods: Four independent cohorts were systematically analyzed for statistically significant, differentially-expressed miRNAs. The first cohort consisted of 48-72 hours post-stroke patient brain tissue samples (n=8) to find target genes that are being repressed by miRNAs. The expression of these miRNAs were subsequently investigated in two miRNA transcriptomes (n=35 plasma samples; n=6 serum exosome samples) and one qRT-PCR–based miRNA expression cohort (n=302 plasma samples) sampled at 5 days, 15 days, and 30 days.
Results: From the post-stroke brain tissue samples, we found that miR-199a-3p target genes were significantly repressed. Within the patient plasma and serum cohorts, miR-199a-3p was surprisingly underexpressed ($LFC < -1$, $p < 0.05$), but became overexpressed over the next 30 days ($FC > 2$, $p < 0.05$). This slow temporal increase in miR-199a-3p expression may be attributed to the lagging transcriptional response of cells. Over-representation analysis of the miR-199a-3p gene targets revealed its potential role in cellular response to hypoxia (Fold Enrichment (FE): 4.08, FDR: 8.01E-03) and neurogenesis (FE: 2.25, FDR: 2.43E-07).
Conclusion: Overall, we report that miR-199a-3p is a potential diagnostic biomarker for Ischemic Stroke that may play a role in the brain's response to stroke-induced hypoxia and in possible recovery.

Keywords: Ischemic Stroke, Blood biomarkers, circulating miRNAs