

Pro- and Anti-Inflammatory miRNA Expression in Swine and Human Intracerebral Hemorrhage

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Introduction

Intracerebral hemorrhage (ICH) accounts for 10% of strokes and 50% of stroke mortality. It is known that there is a robust inflammatory response post-ICH, but the mechanistic pathways remain poorly understood. MicroRNA (miRNA) are small, non-coding RNA molecules that regulate gene expression. Therefore, miRNA have therapeutic potential as regulatory targets for gene expression implicated in disease, including post-ICH inflammation.

Hypothesis

miRNA 29a, 29b, 31, 34c, 125a, 132, 142, 150, 151a, 181a, and 186, identified as important post-ICH inflammatory mediators in a previous miRNA/mRNA integrated analysis of swine ICH, will be identified in human ICH samples. Those miRNA with known anti-inflammatory function will show decreased post-ICH expression, whereas those that have known inflammatory function will show increased post-ICH expression.

Methods

In swine (n=10), peripheral blood mononuclear cells (PBMCs) were collected just prior to and six hours following ICH induction. miRNA-seq was performed and differentially expressed miRNA were identified by comparing post-ICH with pre-ICH swine samples (false discovery rate <0.05). Blood samples from human subjects (n=11), collected between 24 and 48 hours after ICH onset, were also analyzed with miRNA-seq.

Results

Two hundred miRNA were found to overlap in both swine and human samples; For the 11 miRNA above, all were downregulated post-ICH in swine, and all were identified in the human samples; seven of were classified as anti-inflammatory and four as inflammatory based on literature review. Mean absolute miRNA counts were similar for inflammatory (2448.4) and anti-inflammatory (1218.37) miRNA.

Conclusions

For the 11 miRNA of primary interest, a small majority (64%) were anti-inflammatory; a decrease in anti-inflammatory miRNA, as found, would be expected to drive more inflammatory gene expression post-ICH. The lack of more consistency in inflammatory vs. anti-inflammatory miRNA expression post-ICH is potentially attributable to sample collection timing, variable miRNA expression between different blood cell types, the influence of other ICH-associated systemic processes, or unidentified confounding factors. Additional studies with sample collection later after ICH onset and comparison to controls are needed.

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