Nanoparticle delivery of miR-146 altered the expression of macrophage/microglia maker genes in traumatic injured rat brain

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Abstracts will be considered for both poster and platform presentations

Neurotrauma (TBI, spinal cord injury, etc.)

Traumatic brain injury (TBI) results in significant morbidity and mortality and is a major public health burden around the world. Advancement in understanding the pathophysiology and biochemical mechanisms associated with secondary injury events is encouraging but far from complete. Secondary brain injury arises hours to days after the primary insult and leads to further damage due to a cascade of biochemical events, including excitotoxicity, inflammation, oxidative stress, apoptosis, and compromised mitochondria function. These secondary biochemical and pathophysiological events occur at different time points following the initial injury and the outcome could significantly impact the fate of neuronal tissue repair or further deterioration. MicroRNAs (miRNAs) regulate widespread biochemical and molecular events and are associated with secondary brain injury events. We previously reported a dynamic alteration of hippocampal mitochondria-associated, inflammatory related miRNAs following a controlled cortical impact (CCI) injury in the rat. Here we report the expression of a subset of inflammatory miRNAs in hippocampal mitochondria and cytosol at 24-, 72-hours and 7 days following CCI, and their impact on the overall expression of pro- and anti-inflammatory macrophage/microglia marker genes. While mitochondria-enriched miR-142-3p, miR-142-5p, and miR-146a display a shift in abundance from mitochondria to cytosol, the association of other inflammation related miRNA including miR-155 and miR-223 with the mitochondria fraction was elevated. TaqMan Low Density Array analysis of macrophage/microglia phenotypic gene expression suggested a high activity of these genes up to 24 hours and subsequence reduction after 72 hours post TBI. We further demonstrate that hippocampal delivery of miR-146 effectively reduces the levels of its targets-TRAF6 and IRAK1 and alters the landscape of M1 and M2 gene expression. The manipulation of macrophage/microglia responses with miRNA targeting inflammatory signaling events may provide an interventional strategy for the treatment of TBI pathogenesis.