

## Can circulating microRNAs act as molecular biomarkers in trauma-hemorrhagic shock?

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Trauma remains a significant public health issue in all age groups. Hemorrhagic shock (HS) is the leading cause of death after trauma. More than 50% mortality is due to the Trauma-hemorrhagic shock (T/HS), a condition with no immunotherapeutic option till now. HS leads to suppressed immune system which results in patients' increased susceptibility to infection, sepsis, and multi-organ failure.<sup>[1]</sup>

MicroRNAs (miRNAs/miRs) are small (20-22 nucleotides), noncoding functional RNAs that regulate the gene expression in a sequence-specific manner at the post-transcriptional level. miRNAs play a crucial role in the regulation of acute inflammation and can influence the expression of numerous genes.<sup>[2]</sup>

A previous study showed microRNAs regulate the immune system via T cell receptor and antigen presenting signalling. Dysregulation of miRNAs lead to systemic inflammation response syndromes (SIRS) and sepsis.<sup>[3]</sup> Mira et al., 2016 showed that a total of 10,426 genes significantly differed in their expression from control among murine models of T/HS.<sup>[4]</sup> Uhlich et al., 2014 showed direct correlation of miR-221 with TLR4, MyD88 and TRAM in patients of T/HS.<sup>[5]</sup> Increase in expression of these genes causes activation of nuclear factor kappa-B and increase in circulating TNF.<sup>[5]</sup> Different research groups studied the expression of miRNAs after severe trauma. Lei et al., 2011 reported the increase in miR-21 expression in mouse cerebral cortex after traumatic brain injury.<sup>[6]</sup> Izumi et al., 2011 showed altered expression of mir-233 in neutrophils after spinal cord injury in a mouse model.<sup>[7]</sup> Although regulation of miRNAs in patients with trauma has been previously reported by some research groups, it is not well-studied.

However, regulation of miRNAs is well-studied in sepsis. Vasilescu et al., 2009 did genome-wide miRNA profiling in peripheral blood

leucocytes.<sup>[8]</sup> They observed altered expression of miR-150, miR-182, miR-342-5p and miR486 in patients with sepsis. They found that plasma levels of miR-150 were significantly reduced. Also, this reduction in expression level correlated with the level of severity of sepsis.<sup>[8]</sup> Puskarich et al., 2015 showed that higher levels of miR-150 were linked with inflammation, severity of illness, and mortality.<sup>[2]</sup> In a recent study in septic patients, serum miR-146a and miR-223 were found to be significantly reduced in septic patients compared with SIRS patients and healthy controls.<sup>[9]</sup>

MicroRNAs can serve to diagnose many pathologies responsible for a high death rate worldwide. Currently, circulating miRNAs are the most extensively studied biomolecules for a faster and cheaper analysis.<sup>[5]</sup> Based on the studies mentioned above, the author feel that miRNAs might serve as molecular biomarkers in T/HS with both high specificity and selectivity.

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