The Role of PIWI and piRNAs in Modulating Microglial Activation

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Abstract

Chronic inflammation hampers regeneration and exacerbates neurodegenerative conditions. It is mainly caused by excessive and prolonged activation of microglia, the immune cells in the nervous system. Extensive research has elucidated the role of transcription factors and pro-inflammatory signalling pathways in the activation of microglia. Recently, small non-coding RNAs have been shown to regulate gene expression at multiple levels. Hence, we investigated the role of piRNAs and the related PIWI-like proteins in neuroinflammation. Our experiments showed that inflammatory signals can strongly induce the expression of PIWI-like homologs and piRNAs in murine microglial BV-2 cells. In loss-of-function assays, we detected a significant decrease in the induced expression of pro-inflammatory genes, the production of reactive oxygen species and nitric oxide. Accordingly, when neuronal cells were exposed to conditioned medium collected from PIWI-depleted microglia, less cell toxicity and neuronal death were observed. In addition, we identified two differentially expressed piRNA sequences in activated BV-2 cells that were potentially involved in regulating pro-inflammatory genes at the post-transcriptional level. Hence, our study has identified novel targets for suppressing excessive microglial activation to alleviate neurodegenerative conditions.

***Keywords**: PIWI, piRNAs, The activation of microglia, Transcription factor, Modulating microglial activation, Chronic inflammation*