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MEETING ABSTRACT

A2.5

miRNA and neuroregenerative processes in a mouse model for peripheral nerve injury

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Background: microRNAs (miRNAs) are important modulators of multiple processes in health and disease, including neuropathy and neuroregeneration. Upon peripheral nerve injury, neurons residing in the dorsal root ganglia (DRGs) increase their excitability and nociceptive signalling and exhibit transcriptional alterations that promote axonal regeneration. These responses are highly complex and distinguishing the mechanisms necessary for regeneration from the ones involved in neurodegeneration and neuropathy is challenging.
Methods: To explore the potential role of miRNAs in processes initiated by a peripheral nerve injury, we employed the spared nerve injury (SNI) model in mice. DRGs of sham and SNI mice were subjected to a combined miRNA-mRNA sequencing approach. Sequencing results were further analysed for significant correlations between one candidate miRNA and mRNAs of potential target genes and protein–protein interaction and DIANA microCDS analyses were performed. The expression of the miRNA of interest was validated by RT-qPCR and *in situ* hybridization. Intrathecal injection of a miRNA inhibitor and pain-related behavioural testing (von Frey, dynamic plantar aesthesiometer, cold plate) were performed to assess the role of the miRNA in processes occurring after peripheral nerve lesion. Additionally, the outgrowth capacity of DRG neurons overexpressing the miRNA was evaluated *in vitro*.
Results: miRNA-mRNA sequencing identified a novel miRNA, which was highly upregulated in the DRGs of mice subjected to SNI. The expression of this miRNA was significantly correlated with a number of computationally predicted deregulated mRNAs (FDR < 0.05) in the same tissue samples. This miRNA was expressed predominantly in neurons, as revealed by RT-qPCR and *in situ* hybridization validation. *In vivo*, intrathecal injection of a miRNA inhibitor did not alleviate the SNI-induced mechanical and cold hypersensitivity, whereas viral miRNA overexpression increased neuronal outgrowth in primary DRG neuronal cultures.
Discussion: We propose that this novel miRNA is a potential master regulator of mRNA transcripts that are implicated in pathways inhibiting neuronal regeneration. Additional studies on this miRNA could provide insight on the different mechanistic aspects that are initiated after peripheral nerve injury, as well as novel therapeutic approaches in neuroregeneration.
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