

Identification and validation of MicroRNA-mRNA Networks in Dorsal Root Ganglia after Peripheral Nerve Injury

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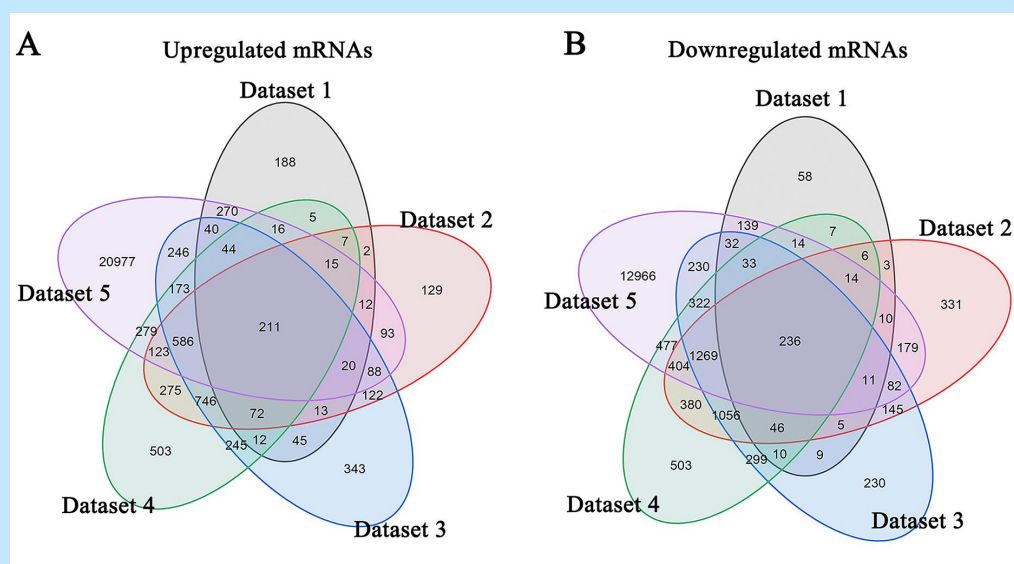
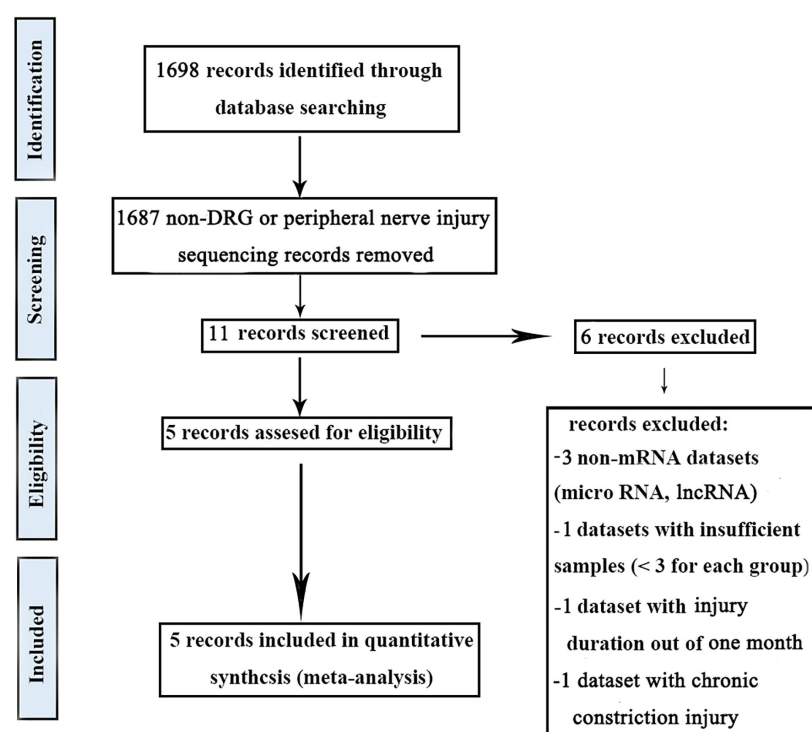
Introduction

Changes in DRG after nerve injury involve neuronal damage, apoptosis, pain transmission, and activation of regenerative programs. It is unclear which genes and microRNAs may play a major role in this process. Therefore, this study performed a meta-analysis of previously published gene expression data to reveal the potential microRNA-mRNA network in dorsal root ganglia (DRG) after peripheral nerve injury.

Methods

- We searched 5 mRNA and 3 microRNA expression data sets, obtained differentially expressed genes (DEGs) and miRNAs, determined the biological pathways.
- We predicted new microRNA-mRNA interactions.
- We verified these hub mRNA and miRNA in rats by qRT-PCR

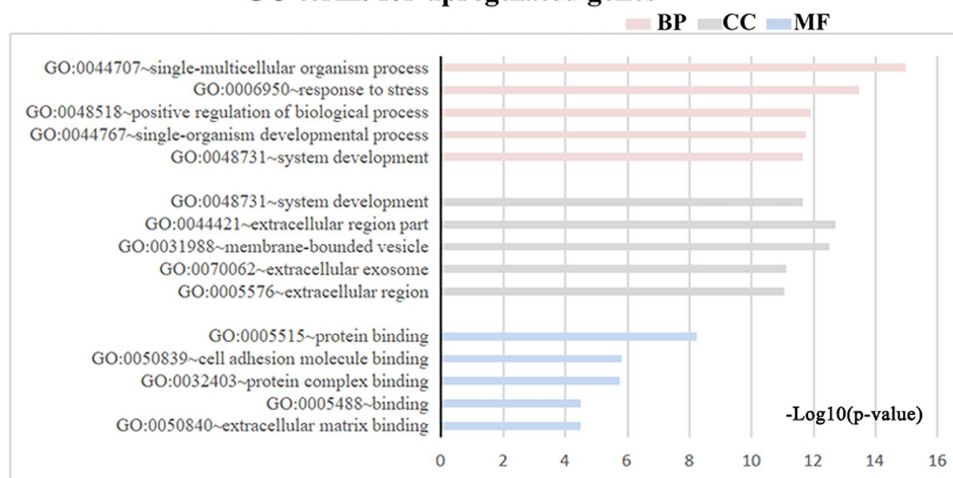
Results



Five gene expression databases of DRG after PNI were included, and Meta-analysis of five DRG gene expression databases revealed 211 upregulated mRNAs and 236 downregulated mRNAs.

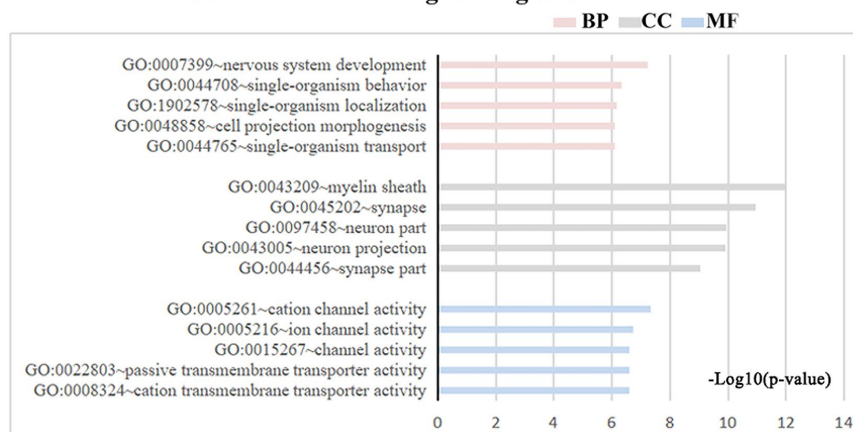
A

GO terms for upregulated genes

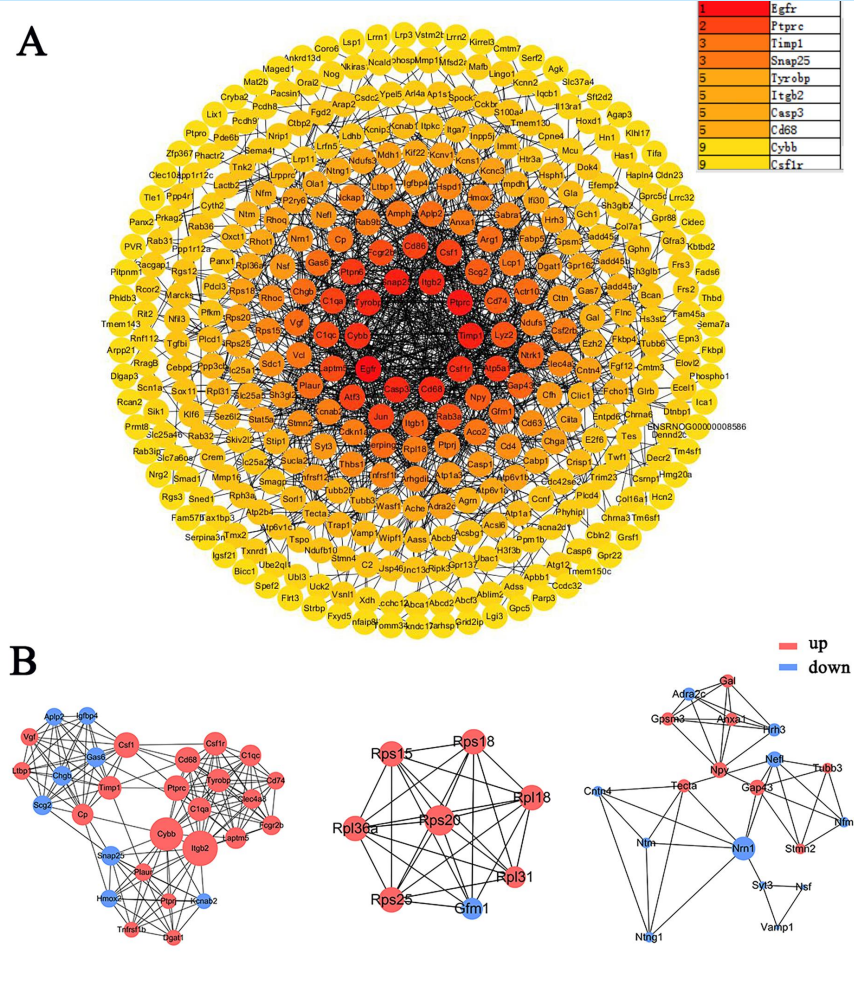


B

GO terms for downregulated genes



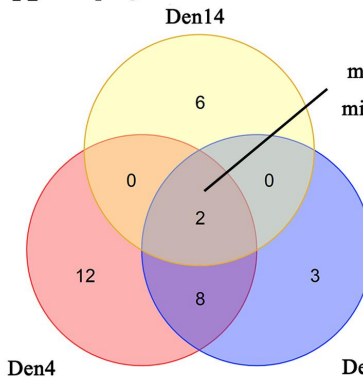
GO analysis of these DEGs showed that functions of the upregulated genes in DRG after PNI were mainly concentrated in protein activity and cell secretion. The downregulated gene functions were mainly concentrated in the activity of ion channels as well as synaptic and neuronal development.



The DEGs obtained from the meta-analysis were used to construct the protein-protein interaction (PPI) network, the depth of color was proportional to the degree of protein interaction. The core proteins of the top3 functional modules clustered in PPI were Cybb, Rps20, and Nrn1. Most of these proteins function in apoptosis, immunity, inflammation, and neurotransmitters.

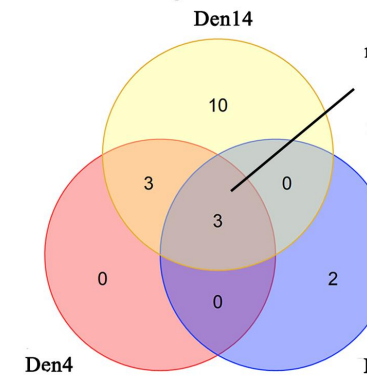
A

Upregulated microRNAs



B

Downregulated microRNAs



| Up-MicroRNA / Down-gene | Down-MicroRNA / Up-gene |
|-------------------------|-------------------------------------|
| miR-21 / Hmg20a | miR-30c-1 / Rhoq |
| miR-21 / Slc25a46 | miR-30c-1 / Crem |
| miR-21 / Etv1 | miR-500 / Sema3c |
| miR-21 / Adss | miR-551b / Cdc42se2 |
| miR-21 / Mat2b | miR-551b / Agm |
| miR-21 / Frs2 | miR-551b / Nln |
| miR-21 / Hs3st2 | miR-551b / Btg1 |
| miR-221 / Ube2ql1 | miR-551b / Marcks |
| miR-221 / Hmg20a | |

After taking the intersection of microRNA expression databases, we found two upregulated microRNAs (miR-21, miR-221) and three downregulated microRNAs (miR-30C-1, miR-500, miR-551b). We revealed 9 pairs of up-microRNA/down-gene interactions and 8 pairs of down-microRNA/up-gene interactions.

Conclusion

- We identified several genes playing an important role in the regulation of neuropathic pain and nerve regeneration, including Egfr, Ptpre, Timp1, Snap25, Tyrobp, Itgb2, Casp3, Cd68, Cybb, and Csf1r.
- We further predicted new microRNA-mRNA interactions, such as miR-21/Hmg20a, miR-221/Ube2ql1, miR-30c-1/Rhoq, miR-500/Sema3c, and miR-551b/Cdc42se2, which may be important regulatory nodes.
- We verified these hub mRNA and miRNA in rats by qRT-PCR.