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Ca2+/Calcineurin mediated release of astrocytic miR-23a regulates neuron-glia cross-talk and is increased in the exosomes derived from Parkinson's patient plasma

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State of the art: Astrocyte dysfunction is well implicated in various neurodegenerative disorders associated with frontotemporal dementia, like Alzheimer's disease (AD) and Parkinson's disease (PD). Recently, Ca2+/Calcineurin signaling has been reported to induce astrocyte reactivation in AD. However, very little is known regarding its implications in PD. So we decided to explore the role of Ca2+/Calcineurin signaling in regulating neuron-glia cross-talk in PD.
Methodology: 1. MPTP mouse models; 2. Immunohistochemistry; 3. qRT-PCR; 4. Exosomes isolation; 5. 3'UTR cloning; 6. Luciferase assay; 7. Rodent astrocyte primary culture; 8. Immunoblotting; 9. Bioinformatics; 10. PD patient blood sample processing.
Results: In the MPTP mouse models, we identified activation of Calcineurin in the astrocytes using immunohistochemistry. Next, activation of Ca2+/Calcineurin pathway was confirmed in the primary rodent astrocyte cultures and in human astrocytic cell line 1321N1 treated with Rotenone (neurotoxin). Activation of Ca2+/Calcineurin further led to the release of astrocyte-enriched miR-23a via exosomes. This exosomal miR-23a was taken up by the neurons under neurotoxin-generated stress. Inside the neurons, astrocytic miR-23a uptake proved to be neuro-protective via downregulation of the pro-apoptotic PUMA. We cloned the 3'UTR of PUMA and performed luciferase assay which revealed direct binding of miR-23a to the PUMA 3'UTR. Next, our bioinformatics-based predictions from PD patient sRNA-Seq datasets revealed a high abundance of miR-23a in PD. miR-23a expression was also found to increase in the exosomes isolated from PD patient plasma.
Conclusion: Exosomal miR-23a is an important regulator of astrocyte-neuron cross-talk during PD pathogenesis and could be a potential biomarker for PD.

Conflicts of interest

N/A