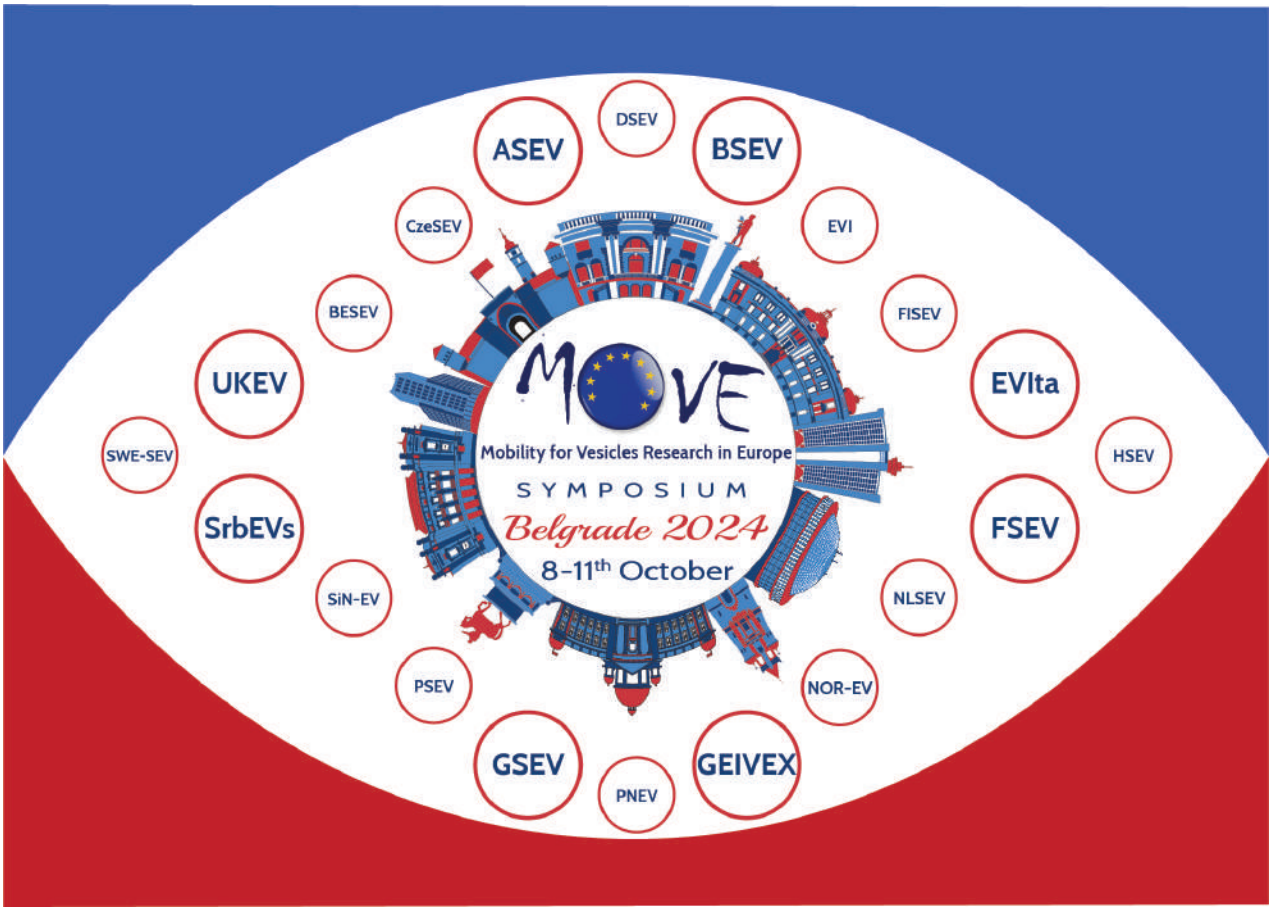
2nd MOVE Symposium



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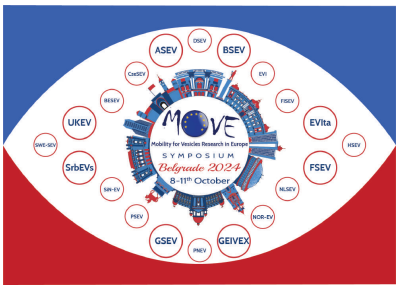

2nd MOVE Symposium

8-11 October 2024, Belgrade, Serbia

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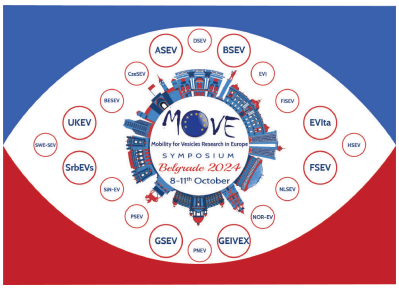

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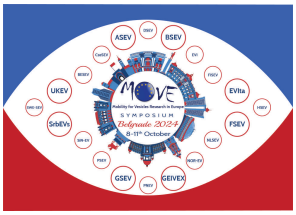

P-I-7

Interactions of Trichinells spiralis mucle larvae extracellular vesicles with target cells and their mechanisms of action

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Introduction: The parasite Trichinella spiralis induces a tolerogenic immune microenvironment in its host, which also leads to the alleviation of chronic inflammatory diseases. This effect is exerted by excretory–secretory products of the muscle larvae (ES L1), with extracellular vesicles (TsEVs) being one of their most active components. TsEVs have been shown to induce a stable tolerogenic phenotype of human monocyte-derived dendritic cells (hDC), which are then able to induce regulatory T cells (Treg). It has also been shown that TsEVs can alleviate allergic airway inflammation in a mouse model. However, the mechanisms of action TsEVs underlying the observed effects are still unknown. Therefore, the aim of this study was to investigate how TsEVs interact with human cells and which signalling pathways they employ.

Methods: TsEVs were isolated from ES L1 by differential ultracentrifugation and purified by ultrafiltration. The glycosylation of TsEVs was analysed with lectins in the ELLA assay. Uptake of TsEVs by hDC was observed with or without inhibitory sugars. The interaction of TsEVs with innate pattern recognition receptors was analysed using transfected HEK293 cells. The signaling pathways employed by TsEVs were investigated in TsEVs-treated hDC by qPCR.

Results: Glycosylation analysis revealed that TsEVs have a glycosylation pattern characteristic of helminths and uptake experiments showed that the interaction of TsEVs with hDC is partially dependent on glyco-interactions. However, TsEVs also activate the innate pattern recognition receptor TLR2. PCR results suggest that TsEVs, probably due to having multiple active molecules, activate multiple signaling pathways, such as mTOR, NF-kB2 and IDO.

Conclusion: The results obtained in this work represent the first steps towards elucidating the mechanisms of action of TsEVs as potent immunomodulators and facilitate the future development of TsEVs-based therapeutics.

Funded by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia, Co. No. 451-03-66/2024-03/200019 and No. 337-00-577/2021-09/41; the Inovation Fund of the Republic of Serbia Grant No. 5906; the Government of Lower Austria project Danube-Allergy Research Cluster (P17); the FWF project P 34867, and the OEAD projects CZ 04/2024, CZ 07/2023, CZ 15/2023, and RS 08/2022.

Publishers:
Serbian Society for Extracellular Vesicles, SrbEVs with
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ISBN 978-86-905626-1-9
Year: 2024.