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Session IV: Biology, Host-Pathogen-Interaction and Immunology

Do extracellular vesicles from *Trichinella spiralis* muscle larvae harbor the potential to induce regulatory T cells?

Sofija Glamočlija[1], Natasa Ilić[2], Alisa Gruden-Movsesijan[1], Ljiljana Sabljić[1], Sergej Tomić[1], Ljiljana Sofronić-Milosavljević[1], Maja Kosanović[1]

[1]Institute for the Application of Nuclear Energy – INEP, University of Belgrade, Belgrade, Serbia
[2]Institute for Biological Research "Sinisa Stankovic", National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia
*Correspinding author: maja@inep.co.rs

During the chronic phase of the infection, *Trichinella spiralis*, through its excretory-secretory products (ES L1), induce Th2 and regulatory immune responses, thus creating nonpermissive environment for the development of autoimmune and other chronic inflammatory diseases. Our major goal is to discover immunomodulatory components within ES L1 products, so that we can characterize them and use them to design treatment for humans. Extracellular vesicles, isolated from *T. spiralis* ES L1 products (TsEVs), may be the important players in initiation, progression and regulation of the immune response, via their impact on dendritic cells. Human monocyte derived dendritic cells (DCs) were treated with TsEVs and subsequently co-cultivated with allogenic T cells. Phenotypes and cytokine production of DCs and T cells were determined by flow cytometry. TsEVs proved to be potent inducers of stable tolerogenic DC phenotype. TsEVs treated DCs express HLA-DR, CD-40, CD-86 almost at the level of the control, untreated DCs, expression of CD-83 was slightly elevated, while the expression of ILT-3 and CCR-7 was significantly increased compared to control. Elevated production of anti-inflammatory and regulatory cytokines IL-10 and TGF-β, alongside semi-mature phenotype indicates the capacity of these cells to polarize T cell immune response towards Th2 and regulatory type. Indeed, T cells co-cultured with TsEVs stimulated DCs showed significant increase in the production of IL-4 and IL-10 with the production of IFN-γ at the level of the control. Moreover, TsEVs stimulated DCs induced expansion of CD4+CD25+Foxp3+ regulatory T cells.

We can conclude that TsEVs act in a similar way as *T. spiralis* ES L1, in terms of inducing tolerogenic phenotype of DCs and regulatory response of T cells, which means that they have the capacity to convey the immunomodulatory properties of ES L1. Further studies will be focused on the possibility of using TsEVs as potential therapeutics for inflammatory disorders. (Funded by Ministry of Science, Technological Development and Innovation, Republic of Serbia, Co. No. 451-03-47/2023-01/200019)

Keywords: *Trichinella spiralis***,** extracellular vesicles**,** regulatory T cells

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