

# Serbian Biochemical Society

**President:** Marija Gavrović-Jankulović

**Vice-president:** Suzana Jovanović-Šanta

**General Secretary:** Jelica Milošević

**Treasurer:** Milica Popović

## Organization Committee

Vladimir Mihailović

Aleksandar Ostojić

Nevena Đukić

Jelena S. Katanić Stanković

Marko Živanović

Nikola Srečković

Stefan Marković

Slađana Đorđević

Nataša Simin

Milan Nikolić

Milica Popović

Jelica Milošević

## Scientific Board

Marija Gavrović-Jankulović

Suzana Jovanović-Šanta

Marina Mitrović

Tatjana Jevtović Stoimenov

Ivan Spasojević

Snežana Marković

Melita Vidaković

Natalija Polović

Aleksandra Zeljković

Romana Masnikosa

Radivoje Prodanović

## Proceedings

**Editor:** Ivan Spasojević

**Technical support:** Dragana Robajac

**Cover design:** Zoran Beloševac

**Publisher:** Faculty of Chemistry, Serbian Biochemical Society

**Printed by:** Colorgrafx, Belgrade

Serbian Biochemical Society

Tenth Conference

with international participation

24.09.2021. Kragujevac, Serbia

***“Biochemical Insights into Molecular Mechanisms”***

---

# The effect of novel rosmarinic acid derivative on the pathogenesis of experimental autoimmune encephalomyelitis in rats

---

Milica Lazarević<sup>1\*</sup>, Goran Stegnjaić<sup>1</sup>, Dimitris Diamantis<sup>2</sup>, Christina Papaemmanouil<sup>2</sup>, Neda Đedović<sup>1</sup>, Bojan Jevtić<sup>1</sup>, Andreas G. Tzakos<sup>2</sup>, Đorđe Miljković<sup>1</sup>

<sup>1</sup>Department of Immunology, Institute for Biological Research „Siniša Stanković“, University of Belgrade, Belgrade; Serbia

<sup>2</sup>Section of Organic Chemistry & Biochemistry, Department of Chemistry, University of Ioannina, Ioannina; Greece

\*e-mail: milica.laza93@gmail.com

Rosmarinic acid is a polyphenolic compound, abundantly present in herbs of the Lamiaceae family. The aim of the study was to evaluate a recently developed rosmarinic acid derivative (RAD), with an enhanced ability of diffusion through biological membranes<sup>1</sup>, in preclinical settings of the central nervous system autoimmunity. To this extent, experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis was used. EAE was induced in DA rats by subcutaneous injection of autologous spinal cord homogenate<sup>2</sup>, while treatment with RAD (30 mg/kg) started at 7 day post immunization and lasted for 15 days. Subcutaneous RAD administration successfully ameliorated EAE, leading to abbreviation of the disease duration and reduction of maximal, cumulative and mean clinical score. Also, RAD effects on draining lymph node cells (DLNC) isolated in the inductive phase of EAE and spinal cord immune cells (SCIC) obtained at the peak of the disease were evaluated. *In vitro* treatment with RAD (5 μM) reduced production of major encephalitogenic cytokines, *i.e.* interferon (IFN)-γ and interleukin (IL)-17, both in DLNC and SCIC. The reduction of IFN-γ and IL-17 production under the influence of RAD was also detected in the CD4<sup>+</sup> T cells purified from DLNC, thus suggesting that RAD had a direct effect on CD4<sup>+</sup> T cells. Additionally, the effects of *in vitro* treatment with RAD were examined on macrophages (Mφ), immune cells with important role in EAE pathogenesis. Treatment of peritoneal Mφ, obtained from non-immunized DA rats, with RAD (25 μM) led to reduction of NO and IL-6 production, exerted no effect on IL-1β production, and elevated tumor necrosis factor production in Mφ. Expression of MHC II and co-stimulatory molecule CD80, the phagocytic ability and the production of reactive oxygen species in RAD-treated Mφ were also downregulated. Our results imply that RAD possesses anti-inflammatory and anti-encephalitogenic properties. Thus, further studies on the mechanisms behind the observed effects and their relevance for the therapy of multiple sclerosis are warranted.

## **Acknowledgements**

This study was supported by Ministry of Education, Science and Technological Development of the Republic of Serbia No. 451-03-9/2021-14/200007; Hellenic Foundation for Research and Innovation “First Call for H.F.R.I. Research Projects to support Faculty members and Researchers and the procurement of high-cost research equipment grant” (No. 991)

## **References**

1. Gerogianni PS, Chatziathanasiadou MV, Diamantis DA, Tzakos AG, Galaris D. Lipophilic ester and amide derivatives of rosmarinic acid protect cells against H<sub>2</sub>O<sub>2</sub>-induced DNA damage and apoptosis: The potential role of intracellular accumulation and labile iron chelation. *Redox Biol* 2018;15:548-56.
2. Lazarević M, et al. Complete Freund's adjuvant-free experimental autoimmune encephalomyelitis in Dark Agouti rats is a valuable tool for multiple sclerosis studies. *J Neuroimmunol* 2021;354:577547.