# IMMUNOLOGY AT THE CONFLUENCE OF MULTIDISCIPLINARY APPROACHES

# ABSTRACT BOOK

**Institute for Biological Research "Siniša Stanković" National Institute of Republic of Serbia**
**University of Belgrade**

**Immunological Society of Serbia**

# IMMUNOLOGY AT THE CONFLUENCE OF MULTIDISCIPLINARY APPROACHES

## ABSTRACT BOOK

**Hotel Mona Plaza Belgrade**

**December 6th-8th, 2019**

**Belgrade, 2019**

**PUBLISHERS**

**Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade**
**Immunological Society of Serbia**

**For publishers**
**Dr Mirjana Mihailović, director of the Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade**
**Dr Nada Pejnović, president of the Immunological Society of Serbia**

**EDITORS**
**Tamara Saksida**
**Suzana Stanisavljević**
**Đorđe Miljković**

**Printed by: Interprint, Kragujevac**
**Circulation: 200**
**ISBN 978-86-80335-12-4**

**This publication is printed by support of the Ministry of Education, Science and Technological Development, Republic of Serbia**

**Congress President**

Nada Pejnović, Immunological Society of Serbia

**Scientific Committee**

Chairman: Đorđe Miljković, Immunological Society of Serbia
Alisa Gruden-Movsesijan, Immunological Society of Serbia
Biljana Božić-Nedeljković, Faculty of Biology, University of Belgrade
Branka Bonači-Nikolić, Serbian Association of Allergologists and Clinical Immunologists
Branka Vasiljević, Serbian Genetic Society
Gordana Leposavić, Faculty of Pharmacy, University of Belgrade
Gordana Matić, Serbian Society for Molecular Biology
Irena Lavrnja, Serbian Neuroscience Society
Ivan Spasojević, Serbian Biochemical Society
Ivana Mirkov, Immunological Society of Serbia
Ivana Novaković, Serbian Genetic Society
Jelena Drulović, School of Medicine, University of Belgrade
Ljiljana Sofronić-Milosavljević, Institute for Application for Nuclear Energy (INEP), University of Belgrade
Marija Gavrović-Jankulović, Serbian Biochemical Society
Melita Vidaković, Institute for Biological Research „Siniša Stanković“, University of Belgrade
Nevena Arsenović-Ranin, Immunological Society of Serbia
Sanvila Rašković, Serbian Association of Allergologists and Clinical Immunologists
Slađana Andrejević, Serbian Association of Allergologists and Clinical Immunologists
Slavko Mojsilović, Institute for Medical Research (IMI), University of Belgrade
Stanislava Stanojević, Institute of Virology, Vaccines and Sera "Torlak"
Vera Pravica, Immunological Society of Serbia
Vesna Tomić-Spirić, Serbian Association of Allergologists and Clinical Immunologists
Vladimir Jurišić, Faculty of Medical Sciences University of Kragujevac

**Organizing Committee**

Chairman: Tamara Saksida, Immunological Society of Serbia
Aleksandra Jauković, Institute for Medical Research (IMI), University of Belgrade
Aleksandra Popov Aleksandrov, Immunological Society of Serbia
Ana Đorđević, Serbian Society for Molecular Biology
Biljana Bufan, Faculty of Pharmacy, University of Belgrade
Goran Čuturilo, Serbian Genetic Society
Marijana Stojanović, Institute of Virology, Vaccines and Sera "Torlak"
Nataša Ilić, Institute for Application for Nuclear Energy (INEP), University of Belgrade
Nataša Lončarević-Vasiljković, Serbian Neuroscience Society
Romana Masnikosa, Serbian Biochemical Society
Suzana Stanisavljević, Immunological Society of Serbia
Željka Stanojević, School of Medicine, University of Belgrade

Short oral presentation

## ATRA- AND TGF-β-LOADED MICROPARTICLES AMELIORATE TYPE 1 DIABETES IN MICE

Ivan Koprivica[1], Dragica Gajić[1], Tamara Saksida[1], Eugenio Cavalli[2], Dominick Auci[3], Sanja Despotović[4], Nada Pejnović[1], Stanislava Stošić-Grujičić[1], Ferdinando Nicoletti[5], Ivana Stojanović[1]

*[1]Department of Immunology, Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia; [2]IRCCS Bonino Pulejo, Messina, Italy*

*[3]TherapyX, Buffalo, USA; [4]Institute of Histology and Embryology, School of Medicine, University of Belgrade, Belgrade, Serbia; [5]Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy*

Type 1 diabetes (T1D) is an autoimmune disease in which a strong inflammatory response causes the death of pancreatic β-cells. Attempts to induce anti-inflammatory/regulatory immune mechanisms that would attenuate disease progression have shown little or no beneficial effects. We introduced microparticles (MPs) loaded with Transforming Growth Factor β (TGF-β) and All-Trans Retinoic Acid (ATRA), both known stimulators of T regulatory cell (Treg) differentiation and stabilization. Male C57BL/6 mice were treated with multiple low doses of streptozotocin to induce T1D, and orally treated with vehicle, empty MPs, or ATRA- and TGF-β-loaded MPs for 10 days (every other day). T1D incidence and immune cell infiltration into the pancreatic islets were lower in ATRA/TGF-β-MPs-treated mice. In Peyer's patches (PP), ATRA/TGF-β MPs up-regulated tolerogenic dendritic cells (tolDC). Additionally, IL-1β expression was reduced in PP, as was the ratio of iNOS/Arginase expression, reflecting a less inflammatory environment. This was accompanied by reduced proportion of Th1 and Th17 cells and up-regulation of Treg. IL-17 expression within $CD4^+$ T cells from PP was also lower and was accompanied by down-regulation in the expression of RORγt, a key transcription factor of IL-17. In the pancreatic lymph nodes (PLN), the situation was similar to PP regarding the down-regulation of Th1 cells. Additionally, in response to ATRA/TGF-β MPs treatment, the proliferation of T effector cells was reduced in PLN, while Treg proliferated more. The presence of $CTLA\text{-}4^+PD1^+$ and $CD39^+IL\text{-}10^+$ Treg populations was also increased, indicating higher suppressive activity. In conclusion, ATRA and TGF-β released from MPs successfully ameliorated T1D by potentiating tolDC and Treg and inhibition of Th1 cell differentiation in gut-associated lymphoid tissue and the draining lymph nodes, thus blocking the entrance of immune cells into the pancreatic islets and protecting β-cells from further destruction.