# 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**

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**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**

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Poster presentation

## SEXUAL DIMORPHISM IN THE SEVERITY OF RAT COLLAGEN-INDUCED ARTHRITIS: THE RELEVANCE OF T FOLLICULAR CELL HELP TO B CELLS

Mirjana Dimitrijević[1], Nevena Arsenović-Ranin[2], Duško Kosec[3], Biljana Bufan[2], Mirjana Nacka-Aleksić[4], Ivan Pilipović[3], Gordana Leposavić[4]

*[1]Department of Immunology, Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia; [2]Department of Microbiology and Immunology, Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia ; [3]Immunology Research Center "Branislav Janković", Institute of Virology, Vaccines and Sera "Torlak", Belgrade, Serbia; [4]Department of Pathobiology, Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia*

Collagen-induced arthritis (CIA) is a well-established experimental model mimicking many immunopathogenic and clinical aspects of rheumatoid arthritis (RA), including sexual dimorphism in the clinical presentation. Our previous study showed that a more severe disease in female compared with male rats correlated with more robust Th17 response reflecting sexual dimorphism in Th17/Treg axis plasticity. Given that autoantibodies play a significant role in the immunopathogenesis of RA and CIA, in the present study the germinal center (GC) reaction in the lymph nodes draining inflamed joints and adjacent tissue (dLNs) was examined for putative sexual dimorphism. Female rats mounted greater serum collagen II-specific IgG response than their male counterparts. This dimorphism correlated with the higher frequency of GC B cells in female compared with male dLNs. Consistently, the frequency of activated/proliferating Ki67+ cells among dLN B cells was higher in females than in males. This was associated with the shift in dLN T follicular regulatory (Tfr)/T follicular helper (Tfh) cell ratio towards Tfh cells in females, and greater densities of CD40L and CD40 on their dLN T and B cells, respectively. The higher Tfh cell frequency in females was consistent with the greater dLN expression of mRNA for IL-21/27, the key cytokines involved in Tfh cell generation and help to B cells. Additionally, in collagen II-stimulated female rat dLN cell cultures, IFN-γ/IL-4 ratio was shifted towards IFN-γ. Consistently, serum ratio between pathogenic IgG2a and protective IgG1 collagen II-specific antibodies was shifted towards the former in females. Thus, the study suggests that targeting T/B cell interactions should be considered in further translation research aimed to design sex-specific therapies for RA.
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