



**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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MULTIDISCIPLINARY APPROACHES**

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## Friday, December 6<sup>th</sup> Session: IMMUNOTHERAPY

### Poster presentation

#### TOLEROGENIC EFFECTS OF ETHYL PYRUVATE ON DENDRITIC CELLS – THE IMPORTANCE OF NRF2 AND NF- $\kappa$ B SIGNALING

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Dendritic cells (DC) are professional antigen presenting cells that are crucial for initiation, propagation, but also for regulation of immune response. Tolerogenic dendritic cells have immuno-regulatory properties and they are a promising potential therapy for multiple sclerosis, as well as for other autoimmune diseases. Ethyl pyruvate (EP) is a redox analogue of dimethyl fumarate (Tecfidera), a drug for multiple sclerosis treatment. We have recently shown that EP has the ability to direct DC towards tolDC in both murine and human DC. In order to investigate mechanisms responsible for EP-imposed tolerance in DC, we examined signal pathways responsible for anti-oxidative cell protection such as Nrf2 signalling pathway, HO-1 and NQO1 enzymes. Furthermore, pro-inflammatory transcription factor NF- $\kappa$ B was also observed. Additionally, change in morphology of DC was assessed via actin filaments staining. EP was applied on days 3 and 6 during 7 days long differentiation of C57BL/6 mouse bone marrow derived immature DC (iDC) or lipopolysaccharide induced mature DC (mDC). Afterwards, immunocytochemistry staining was performed. Results have shown that the maturation of DC led to reduction of the Nrf2 and HO-1 expression, which was successfully prevented by EP. Furthermore, the expression of NQO1 was higher in EP-treated iDC in comparison to untreated iDC. However, the expression in EP treated mDC was lower than in untreated mDC, but still higher than in iDC. Finally, EP-treated mDC had lower expression of NF- $\kappa$ B compared to EP-treated iDC. Moreover, these results are supported by morphological changes of DC after their treatment with EP. While mDC have observable dendrites, EP-treated DC have round shape and are much similar to iDC. In conclusion, these results clearly demonstrate that EP exerts its tolerogenic potential on DC through the up-regulation of anti-oxidative signalling pathways, as well as through the inhibition of pro-inflammatory transcription factor NF- $\kappa$ B.