



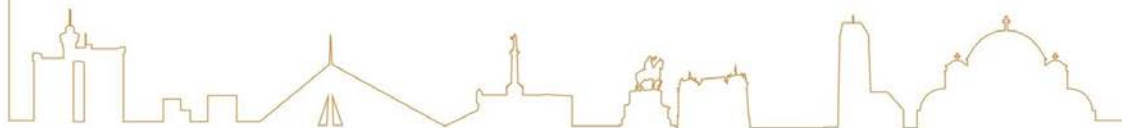
# CoMBoS

1<sup>st</sup> Congress of Molecular Biologists of Serbia

## KNJIGA SAŽETAKA BOOK OF ABSTRACTS



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Goran Brajušković  
Ana Đorđević

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Dušan Radojević  
Ivan Strahinić  
Goran Brajušković

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## PRO-INFLAMMATORY AND ANTI-INFLAMMATORY ROLE OF HMGB1 IN THE LIVER OF DIABETIC RATS

Sofija Jovanović Stojanov, Ilijana Grigorov, Anja Petrović, Desanka Bogojević, Svetlana Ivanović Matić, Vesna Martinović

*Institute for Biological Research "Siniša Stanković", University of Belgrade, Belgrade, Serbia.*

**Introduction:** Oxidative stress and chronic low-grade inflammation in diabetes leads to liver injury. During diabetes, extracellular level of high-mobility group box-1 (HMGB1) protein increases. *Considering that* extracellular HMGB1 (eHMGB1) protein functions as a pro-inflammatory mediator, triggering inflammatory responses by promoting the expression of inflammatory cytokines, *the aim of this study was to investigate its contribution to the maintenance of inflammatory condition in the liver of diabetic rats.* This may help to better understand diabetes-induced liver pathologies and potentially provide target to develop efficient therapies.

**Methods:** Diabetes was induced by a single intraperitoneal (ip) injection of STZ (65 mg/kg). Inflammatory status in the rat liver was determined in the fourth week after diabetes induction by measuring expression of pro-inflammatory cytokines (TNF $\alpha$ , IL-6) and related production of anti-inflammatory protein haptoglobin (Hp). We also studied the effects of HMGB1 on inflammation through its interaction with TLR4 and related downstream signaling pathways in terms of inhibited HMGB1 secretion in diabetic rats by ethyl pyruvate (EP) treatment (80 mg/kg/ip/daily).

**Results:** The results show that decrease in eHMGB1 expression caused by EP treatment, correlates with reduced level of TNF $\alpha$ , IL-6 and Hp in the serum and liver of diabetic rats. These changes are in accordance with significant decrease in HMGB1/TLR4 interaction and decreased activation of MAPK (p38, ERK, JNK), NF- $\kappa$ B p65 and JAK1/STAT3 signaling pathways in diabetic liver.

**Conclusion:** In diabetic liver eHMGB1 is involved in the inflammatory response dually. It acts pro-inflammatory by enhancing production of inflammatory mediators and anti-inflammatory by increasing Hp expression.

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