

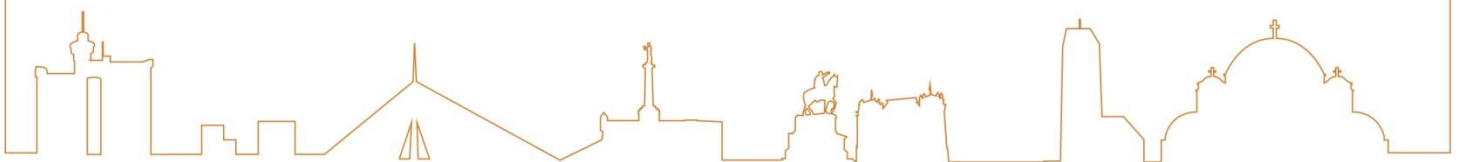
# CoMBoS

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

## KNJIGA SAŽETAKA BOOK OF ABSTRACTS



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## GLUCOCORTICOID PRERECEPTOR METABOLISM IN THE LIVER OF 5 $\alpha$ -DIHYDROTESTOSTERONE-TREATED RATS AS ANIMAL MODEL OF POLYCYSTIC OVARY SYNDROME

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**Introduction:** Polycystic ovary syndrome (PCOS) is a reproductive and metabolic disorder characterized by hyperandrogenism, ovulatory dysfunction, visceral obesity and insulin resistance. PCOS is also associated with enhanced cortisol metabolite excretion, as well as with altered peripheral glucocorticoid metabolism, which is inevitably linked to insulin resistance characteristic for women with PCOS. The main enzymes involved in glucocorticoid prereceptor metabolism are 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ HSD1) that regenerates corticosterone from its inactive precursor, and 5 $\alpha$  and 5 $\beta$  reductases (5 $\alpha$ R and 5 $\beta$ R) that inactivate corticosterone. In this study, female rats treated with nonaromatizable 5 $\alpha$ -dihydrotestosterone (DHT) were used as an animal model of PCOS and the aim was to examine whether this treatment affects hepatic glucocorticoid prereceptor metabolism.

**Methods:** We analyzed the effects of prolonged treatment of prepubertal rats with DHT on body and liver masses, and plasma and liver corticosterone levels. The expression of hepatic 11 $\beta$ HSD1, hexose-6-phosphate dehydrogenase (H6PDH), 5 $\alpha$ R, 5 $\beta$ R and glucocorticoid receptor (GR) were analyzed by real-time PCR and Western blot methods.

**Results:** DHT treatment induced an increase in body and liver masses, an elevation of hepatic 11 $\beta$ HSD1 expression and a reduction of 5 $\alpha$ R mRNA level, leading to tissue corticosterone rise and GR nuclear accumulation. In addition, H6PDH and 5 $\beta$ R mRNA levels remained unchanged.

**Conclusion:** DHT treatment affected hepatic glucocorticoid prereceptor metabolism through enhanced corticosterone availability and its decreased inactivation, which led to enhanced GR activation. Further studies should reveal possible link between enhanced hepatic glucocorticoid signaling and metabolic disturbances observed in PCOS.

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