

55ASM-0112 FT | The influence of physical exercise on oestrogen and androgen receptor expression in a chemically and hormonally-induced rat model of prostate cancer

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Background: Oestrogen (ER) and androgen (AR) receptors play an important role in normal prostate development and are also implied in prostate cancer (PCa) development. Several studies suggested that physical activity may decrease the risk of PCa development and also changes sexual hormones and their receptors. This study aimed to evaluate the effects of physical exercise on ER α and AR expression in a rat model of chemically and hormonally-induced PCa.

Materials and Methods: Fifty-five male Wistar Unilever rats of 12 weeks of age were randomly divided into four groups: control sedentary ($n = 10$), control exercised ($n = 10$), induced sedentary ($n = 15$) and induced exercised ($n = 20$). Animals from exercised groups started the exercise training in a treadmill (Treadmill Control LE 8710, Harvard Apparatus, USA), at the age of 8 weeks, for 35 weeks (5 days/week). The protocol for PCa induction started at 12 weeks of age and consisted of sequential administration of flutamide (50 mg/kg, TCI Chemicals), testosterone propionate (100 mg/kg, TCI Chemicals) and *N*-methyl-*N*-nitrosourea (30 mg/kg, Isopac[®], Sigma Chemical Co.), followed by subcutaneous implants of crystalline testosterone. Animals were sacrificed at 61 weeks of age and a complete necropsy was performed. All experiments were approved by DGAV (no. 021326). Antibodies for ER α (1:500, clone 6F11, Novocastra) and AR (clone PG21, Merck Millipore) were used for the immunohistochemical study. The staining extension was evaluated in normal prostate tissue and in dorsolateral prostate lesions (hyperplasia, dysplasia, prostatic intraepithelial neoplasia (PIN) and microinvasive carcinoma) and assessed to five levels (0%, <25%, 25-50%, 50-75% and >75%), considering the extension of immunopositive tissue. Data was analysed with SPSS 25.

Results: The normal prostate tissue and dorsolateral prostate lesions of animals from all groups were immunopositive for ER α and AR. However, the groups showed high immunopositivity for AR and low positivity for ER α (<25% in all groups) with similar values between both control and induced groups ($p > 0.05$). The malignant lesions (PIN and microinvasive carcinoma) showed lower AR expression when compared with normal prostate tissue in all groups.

Conclusions: As expected, the AR expression was lower in malignant lesions. Inversely to that reported in other studies, the exercise training did not modify the ER α and AR expression, which may be related to the duration and type of exercise performed.

55ASM-0130 FT | Deciphering the Nfr2-dependent antioxidant mechanism of action behind the beneficial effects of the mitochondriotropic cinnamic acid AntiOx₄CIN₄

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Background: Mitochondria are key organelles involved in cellular survival, differentiation, and cell death induction. In this regard, alterations in mitochondrial morphology and/or function are involved in stress-induced adaptive pathways, priming mitochondria for mitophagy, or apoptosis induction. The concept of hormesis states that exposure of cells to a low-dose of a potentially harmful stressor (*e.g.* ROS) triggers an adaptive response that renders them less sensitive to subsequent exposures. Within this context, mitochondrial hormesis (“mitohormesis”) occurs when low-intensity stress triggers a retrograde cascade that induces protective (non)-mitochondrial adaptations to restore and/or maintain cellular homeostasis. Nuclear factor erythroid 2-related factor 2 (NRF2) is a master regulator of the oxidative stress response inducing antioxidant-encoding genes expression. Most diet-derived polyphenols, including hydroxycinnamic acids (HCAs), can act as inducers of NRF2 as they are Michael acceptors or can be metabolized as such. Our current hypothesis is that AntiOx₄CIN₄ can increase the cellular resistance to stress by NRF2-dependent mechanism and metabolic pathways through a process of “mitohormesis”.

Materials and Methods: Herein, we studied the time-dependent effects of the novel mitochondriotropic agent (AntiOx₄CIN₄) on human hepatoma-derived HepG2 cell line by measuring the protein expression of NRF2/KEAP1/p62 and its effects on mitochondrial physiological parameters, mainly mtDNA copy number, oxygen consumption,