



XXV Congresso de Iniciação Científica da Unicamp

October 18 to 20 Campinas | Brazil

25 anos



2017



Energetic Metabolism in the Treatment of Prostate Cancer: Effects of P-MAPA Immunomodulator

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Abstract

The American Cancer Society estimates that 161.360 new cases of Prostate Cancer will be diagnosed in the United States of America (USA) in 2017. Faced with such alarming data, research into new therapeutic options is necessary, and the P-MAPA immunomodulator opens a new perspective for the combat of this type of cancer. Therefore, the aim of this study is to characterize the molecular effects of P-MAPA immunotherapy in Prostate Cancer treatment involving cellular energy metabolism.

Key words:

Prostate Cancer, Metabolism, P-MAPA

Introduction

The American Cancer Society estimates that 161.360 new cases of Prostate Cancer (CaP) will be diagnosed in the United States of America in 2017 and about 26.730 men will die as a consequence of this disease (1). Among the options for treatment of this disease are radical prostatectomy and radiotherapy (2). Several studies have been conducted to offer new therapeutic options for CaP, and immunotherapy represents one of the approaches. Therefore, the use of P-MAPA immunomodulator opens a new perspective for the fight against CaP (3). Moreover, a hallmark of neoplastic cells is the rapid and increased cell proliferation, which causes these cells to alter their metabolic pattern (4). Thus, the objective of this study is to characterize the molecular effects of P-MAPA immunotherapy in CaP treatment involving cellular energy metabolism.

Results and Discussion

Fifteen Fischer rats (variety 344), obtained from CEMIB / UNICAMP were used. For CaP induction, 10 animals received a daily subcutaneous dose of 100 mg/kg of Testosterone Cypionate for 3 consecutive days. Subsequently, the animals were anesthetized with 2% Xylazine Hydrochloride and 10% Ketamine Hydrochloride and performed a 0.5 cm suprapubic incision for inoculation of a 15 mg / kg dose of the N-methyl-N-nitrosurea carcinogen dissolved in (1M pH 6.0) sodium citrate and with thermosensitive copolymer (Pluronic 127) in the capsule of the ventral prostatic lobe (protocol developed and supplied by the Laboratory of Urogenital Carcinogenesis and Immunotherapy and Institute of Chemistry / UNICAMP). One week after administration of the carcinogen, the 10 animals received subcutaneous injections of 5mg / kg Testosterone Cypionate twice a week for 120 days. The other 5 animals were considered as Control Group. After the 120-day induction period, the animals were divided into 3 groups (5 animals per group): Control Group: received subcutaneous injections of 5 mL / kg of 0.9% physiological solution, three times a week for 30 days; CaP Group: received the same treatment as the Control Group; Group CaP + P-MAPA: received subcutaneous injections of 5 mg / kg of P-MAPA (Farmabrilis, São Paulo, Brazil), three times a week for 30 days. After 160 days of treatment, samples of the prostatic ventral lobe of all animals were collected and

submitted to immunohistochemical analysis (GLUT-1, LDH-A, OHADH and ATPase). There was moderate cytoplasmic immunostaining for GLUT1 and LDH-A in the CaP group, indicating that these neoplastic cells are capturing more glucose and converting pyruvate to lactate, ensuring the cell supply of ATP, even under hypoxia conditions. In addition, there was an intense cytoplasmic immunostaining of OHADH and β -F1-ATPase in the CaP + P-MAPA group, showing that the treatment with P-MAPA is able to influence the metabolism of acetyl-coA from the oxidation of fatty acids, and also, to increase the energy supply from the oxidative phosphorylation.

Conclusions

Neoplastic cells increase oxygen uptake and, when under hypoxia conditions, produce energy mainly by the conversion of pyruvate to lactate. In addition, treatment with P-MAPA increases the metabolism of acetyl-coA, increasing the production of ATP via oxidative phosphorylation.

Acknowledgement

Support by Farmabrilis-Brazil, PIBIC/SAE-Brazil (UNICAMP) and FAPESP-Brazil (Process number 2014/11866-1) are also acknowledged.

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