The Role of Ets Related Gene in the Regulation of Mitochondrial Functions in Prostate Cancer

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Background: Prostate cancer is the second most commonly diagnosed male cancer in the western world. In over half of the patients, Ets Related Gene (ERG) has been found to express in prostate epithelial cells due to chromosomal rearrangements. The biological functions of ERG in the initiation and/or progression of prostate cancer are not clearly understood. Mice that are genetically engineered to express ERG in prostate epithelium displayed increased cell death due to apoptosis. Apoptosis is a cell suicide mechanism that is mediated via mitochondria when the cell is exposed to stress through various biological, physical and chemical agents. To examine the role of ERG in mitochondrial functions, we utilized LNCaP cell culture model with doxycycline-inducible ERG expression. Methodology: Mitochondrial quantitation and functional differences were analyzed by Flow cytometry and confocal microscopy using MitoTracker (green), MitoSoxRed dyes. Mitochondrial Oxygen Consumption Rate (OCR) and Extracellular Acidification Rate (ECAR) were measured by Seahorse Bioscience XF24 analyzer. Analysis of stress and energy metabolic proteins in LNCaP cell lysates were analyzed by Western blot analysis. Results and Conclusions: Quantitation and functional analysis by Flow cytometry and Confocal microscopy revealed increased MitoSox Red staining. ERG-expressing LNCaP cells fail to respond to uncoupler of oxidative phosphorylation (FCCP) and complex I ETC inhibitor Rotenon. Molecular analysis of certain proteins involved in glycolysis, TCA cycle and fatty acid metabolism such as PDH, PDHK, LDHA, AceCS1, ACSL1 and FAS revealed increased expression in the in these metabolic enzymes. Overall, our results suggest that ERG interferes with mitochondrial functions.

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