Mitochondrial dysfunction in the aging ER-beta knockout mouse prostate

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Abstract

INTRODUCTION AND OBJECTIVE: Estrogen receptor beta (ERβ) is expressed mainly in epithelial cells of the prostate and may play a role in promoting tissue homeostasis through various mechanisms. Since preliminary data suggests that BPH tissues are characterized by mitochondrial dysfunction, we sought to determine whether ERβ could also regulate mitochondrial respiration in the prostate using an ERβ-knockout mouse model.

METHODS: Mice with conventional genome-wide deletion of ERβ were generated on a C57/BL6 background and examined at 2 mos and 16 mos of age for differences in mitochondrial respiration compared to age-matched wild type controls. Urine void spot assays were performed in both control and ERβ knockout mice at 16 mos of age immediately prior to mitochondrial respiration assays. Mitochondrial function was measured via oxygen consumption rate using lysates prepared from fresh tissue.

RESULTS: In prostate tissue lysates, mitochondrial electron transport chain complex I activity selectively in aged ERß knockout mice was reduced compared to wild type age-matched controls in both the absence (state 4) and presence (state 3) of ADP. This decrease in both basal respiration and maximal capacity for respiration of the mitochondrial tissue in animals lacking ERβ expression suggests a loss of number or function of mitochondria in the prostate compared to age-matched controls. Void spot assays were inconclusive, perhaps due to the small number of animals in the study.

CONCLUSIONS: Overall, loss of ERβ in the mouse prostate appeared to inhibit mitochondrial activity in aged ERβ knockout mice. Future studies will focus on whether ERβ deficiency contributes to bladder voiding dysfunction and will explore the potential for ERβ-selective ligands as potential BPH therapy via promotion of mitochondrial function.

Cellular Respiration - Electron Transport Chain

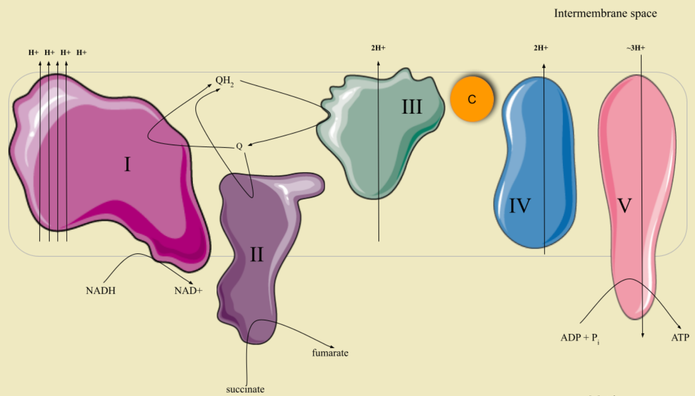
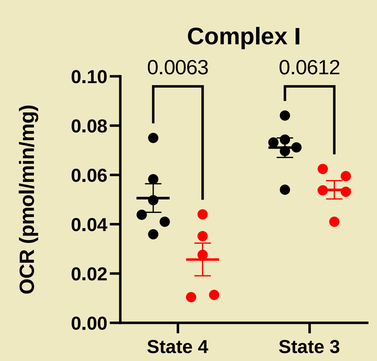
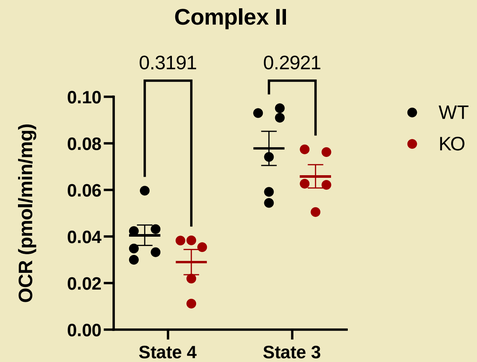
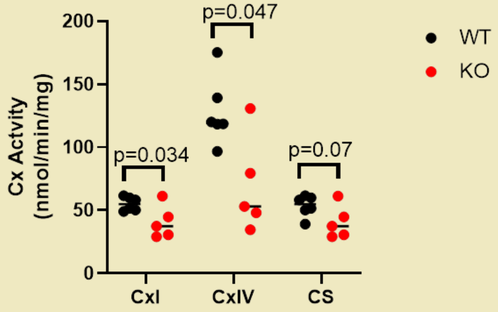


Image drawn by Alexis Adrian, University of Wisconsin

Aged, but not young, ER-beta ko mice have decreased mitochondrial complex I and complex IV function



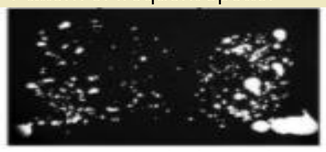




Potential impact on voiding patterns

Pattern at 9 weeks

Pattern of frequent spotter

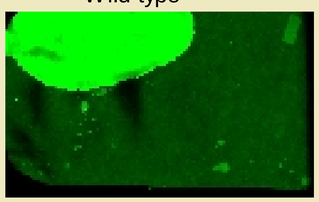


Evaluation of voiding assays in mice: impact of genetic strains and sex

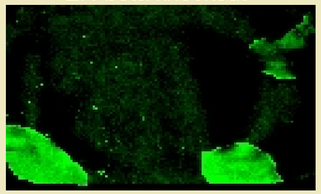
Dale E. Bjorling, Zunyi Wang, Chad M. Vezina, William A. Ricke, Kimberly P. Keil, Weiqun Yu, Lianyu Guo, Mark L. Zeidel, and Warren G. Hill Show fewer authors

Voiding pattern at 17 months of age:

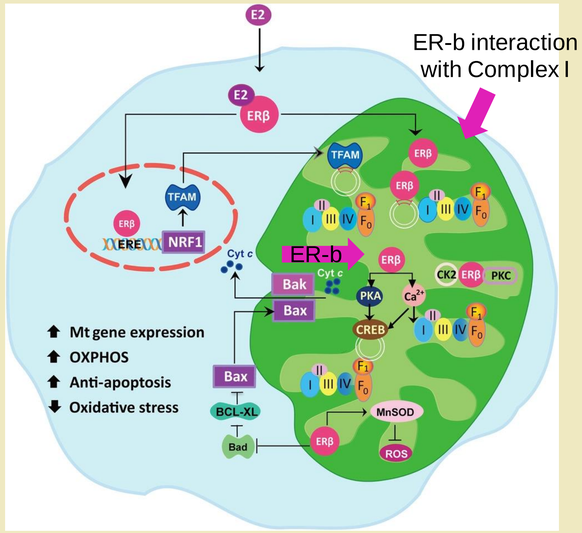
Wild-type



ER-beta knockout



ER-beta may protect mitochondrial complex 1 activity in prostate



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Estrogen receptor-β in mitochondria: implications for mitochondrial bioenergetics and tumorigenesis

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