Wnt/β-catenin signaling pathway does not regulate c-myc gene expression in 42GPA9 (mouse adult Sertoli) cell line.

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INTRODUCTION

Sertoli cells are the nutritional and metabolic support and control of germ cell proliferation and differentiation. Wnt/β-catenin signaling is important for the development of the seminiferous epithelium during embryonic age, however after birth this pathway is downregulated. Transgenic mouse where β-catenin is constantly activated have altered spermatogenesis among other adverse effects. Cx43 is the most abundant protein within gap junctions which are essential for Sertoli cell functionality. The gene of this protein is a Wnt/β-catenin target in rat cardiomiocytes. c-Myc is a transcription factor involved in transcription of genes necessary for the maintenance of the pluripotent state of stem and tumorigenic cells. The gene of this protein is a target of Wnt/β-catenin pathway in embryonic and tumorigenic cells. In the transgenic mouse models and in studies with human prostate cancer cells, c-Myc was upregulated possibly affecting Sertoli cell functionality.

OBJECTIVES

In this work, we evaluated whether LiCl treatment induce upregulation of cx43 and c-myc gene expression in 42GPA9 cells, and the possible molecular mechanism involved in the differential response of these genes.

MATERIALS AND METHODS

Nuclear translocation of β-catenin was evaluated by western blot and indirect immunofluorescence analyses. mRNA abundance was determined by RT-qPCR and histone marks and β-catenin promoter occupancy at the WRE (Wnt Response Element) was assessed by ChIP analysis.

DISCUSSION AND RESULTS

Sertoli cells (42GPA9) responded to LiCl or Wnt3a treatments, accumulating β-catenin within the nucleus, activating axin2 transcription. In mES cells cx43 and c-myc genes were upregulated under LiCl treatment, but stimulated 42GPA9 showed a 2-fold increase of cx43 mRNA, while c-myc mRNA was not affected. Both WRE showed histone marks of activation such as H3K9Ac and H3K4me3, but β-catenin was not recruited in c-myc WRE.

CONCLUSIONS

These findings suggest that c-myc gene is not a direct target of β-catenin upon activation of the Wnt/b-catenin signaling pathway compared to cx43 gene in 42GPA9 cells.

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