The Regulation of Stanniocalcin-1 Gene Expression

in Rat Sertoli and Leydig Cells

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ABSTRACT

Stanniocalcin-1 (STC1) is a glycoprotein hormone that is first discovered in fish and has also been identified in mammals. Mammalian stanniocalcin-1 (STC1) is widely expressed in a broad spectrum of tissues and is basically acting in autocrine and/or paracrine fashion. The expression pattern of STC1 is sexually dimorphic at embryonic and adult stages in rodent model. Considerable number of studies has been conducted using ovarian models to demonstrate the involvement of STC1 in female reproduction. Comparative information of STC1 function in testicular model is lacking. In this study, we attempted to study the possible regulation and biological function of STC1 in mammalian male reproduction. The temporal expression pattern of STC1 in postnatal testes was first mapped, which showed a decreasing trend of both STC1 gene expression and STC1 protein expression. Then the regulation of STC1 expression in two primary rat testicular cell culture models was studied. In primary rat Sertoli cell culture, our data indicated that the exogenous glucocorticoids, dexamethasone (DEX), via glucocorticoid receptor could stimulate STC1 gene expression in Sertoli cells. On the contrary suppressive effect of dbcAMP to STC1 gene expression was observed. The suppression was mediated by PKA, as the suppressive effect can be rescued by co-treatment with cAMP-dependent protein kinase inhibitor, H89. We also suggested that the de novo synthesis of other protein(s) and mRNA might be involved in the regulation of the steady-state levels of STC1 mRNA on the basis of cotreatment with translational inhibitor, CHX and transcriptional inhibitor, Act D. In primary rat Leydig cell culture, both hCG and dbcAMP suppressed STC1 gene expression and induced testosterone secretion. These effects were via PKA pathway as demonstrated through co-treatment with H89. Besides, hypoxia treatment up-regulated STC1 mRNA level in Leydig cells, at the same time suppressed testosterone production through inhibitory effect on steroidogenesis, as demonstrated by the suppression of mRNA levels of steroidogenic acute regulatory protein (StAR), cytochrome P450 side-chain cleavage enzyme (P450scc) and steroidalogenic factor-1 (SF1). This study provides the first evidence in the regulation of STC1 expression in male reproductive system. The data provide a molecular basis that may associate with specific biological function of STC1 in testicular cells. Taking all together, our study showed that STC1 expression level decreased along with the development of testicular system in postnatal growth; in Sertoli cells, STC1 gene was up-regulated by DEX, which is well-known to have inhibitory effects over testicular function such as suppressing testosterone secretion or inducing germ cell apoptosis; in Leydig cells, STC1 gene up-regulation correlated with the suppression of testosterone production after treatments of hCG, dbcAMP and hypoxia. All these might imply a possible inhibitory role for STC1 in testicular function.
Table of Contents

Declaration.................................................................................................................... i
Abstract ....................................................................................................................... ii
Acknowledgements............................................................................................................... iii
Table of contents ............................................................................................................... iv
List of figures ................................................................................................................ vi
List of abbreviation ........................................................................................................ viii

CHAPTER 1: LITERATURE REVIEW............................................................................. 1

Fish Stanniocalcin (STC) ........................................................................................................ 1
  Corpuscles of Stannius (CS).......................................................................................... 1
  Isolation of STC from Bony Fish CS ........................................................................... 3
  STC Gene and Protein in Fish ...................................................................................... 5
  STC and Fish Calcium Regulation ............................................................................. 7
  STC beyond Calcium Regulation or CS ....................................................................... 10
Stanniocalcin (STC): From Fish to Mammals .............................................................. 11

Mammalian Stanniocalcin-1 (STC1) ........................................................................... 14
  Developmental Studies of STC1 in Mammals ........................................................... 14
  STC1 and Mammalian Mineral Homeostasis ............................................................. 19
  STC1 and Mammalian Bones .................................................................................... 24
  Mammalian STC1 and Neuronal Function ............................................................... 26
  STC1 and Mammalian Reproduction ....................................................................... 28
  Mammalian STC1 and Cancer .................................................................................. 36
Working Hypothesis for the Present Study ................................................................. 39

CHAPTER 2: POSTNATAL DEVELOPMENTAL STUDY ON
STANNIOCALCIN-1 IN RAT TESTIS, OVARY AND KIDNEY................................. 40

Abstract ............................................................................................................................... 40
Introduction ............................................................................................................................... 41
Materials and Methods ......................................................................................................... 43
Results and Discussion ....................................................................................................... 47
Figures ................................................................................................................................. 52

CHAPTER 3: STANNIOCALCIN-1 EXPRESSION AND REGULATION IN
RAT PRIMARY SERTOLI CELL CULTURE ............................................................. 62

Abstract ............................................................................................................................... 62
Introduction ............................................................................................................................... 64
Materials and Methods ......................................................................................................... 67
Results ................................................................................................................................. 73
Discussion ............................................................................................................................. 80
Figures ................................................................................................................................. 85

CHAPTER 4: STANNIOCALCIN-1 EXPRESSION AND REGULATION IN
RAT PRIMARY LEYDIG CELL CULTURE .............................................................. 99