

## MASTER'S THESIS

### The regulation of stanniocalcin-1 gene expression in rat sertoli and leydig cells

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**The Regulation of Stanniocalcin-1 Gene Expression  
in Rat Sertoli and Leydig Cells**

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**A thesis submitted in partial fulfillment of the requirements  
for the degree of  
Master of Philosophy**

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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 (P450<sub>scc</sub>) and steroidogenic 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.

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