MASTER'S THESIS

Anti-tumorigenic properties of Stanniocalcins in human cancers

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Date of Award:
2011

ANTI-TUMORIGENIC PROPERTIES OF STANNIOCALCINS IN HUMAN CANCERS

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A thesis submitted in partial fulfillment of the requirements

for the degree of

Master of Philosophy

Principal Supervisor: Prof. WONG Kong Chu

Hong Kong Baptist University

August 2011

ABSTRACT

Stanniocalcin-1 (STC1) is the glycoprotein hormone found in the corpuscle of Stannius unique to the bony fish. The function of STC1 in fish is mainly regulating the plasma Ca^{2+} homeostasis, preventing the fish suffer from hypercalcemia. Later on, the mammalian stanniocalcins (STCs) were found and cloned as STC1 and STC2. The functions of STCs are still undergoing characterized; however, the recent studies indicated that mammalian STCs only take a minimal role in Ca^{2+}/Pi homeostasis. Instead, the increasing number of studies signified the involvement of human STC1 and STC2 in carcinogenesis.

Cancer developments basically associate with genetic, epigenetic, immunological and microenvironmental factors. Our previous study has demonstrated the epigenetic regulation of STC1 gene expression in apoptotic cancer cells treated with histone deacetylase inhibitors. The possible roles of STC1 in apoptosis have been demonstrated in different laboratories. The transcriptional relationship between p53 and STC1 was suggested; however the underlying regulatory mechanism is not clear. In this study, we were interested in this regulatory relationship, aiming to decipher the involvement of the transcriptional factor p53 in the regulation of STC1 expression. Using pharmacological, STC-1 promoter and western blot analyses, our data revealed the first time that p53 activated STC1 gene expression via the enhancement of trichostatin (TSA)-stimulated histone acetylation and NFκB signaling in the human nasopharyngeal cancer cells, CNE2. Lentiviral transfection with the STC1 gene induced cellular apoptosis and the effect was augmented in doxorubicin (Dox) treated cells.

STC2 has also been suggested as a putative gene for carcinogenesis.

Clinically, STC2 act as the prognostic biomarker in breast, renal, gastric and ovarian cancers. STC2 involved in cancer progressions and it possibly associated with poor prognosis. The significance of STC2 upregulation was observed in human gastric and colonrectal cancer samples. Nevertheless, the mechanism between the activity of STC2 and tumorigenesis still not fully elucidated. We sought to clarify how STC2 is involved in aggressiveness of gastric cancer. The knockdown of STC2 in human gastric cell line, MKN74 was studied by the migration and invasion assay. When compared the shSTC2 cloned cells to the parental and shCtrl cloned cells, the knockdown of STC2 significantly increased the number of migrated and invaded cells for 48 hr incubation. Additionally, the western blotting data revealed that the increasing the level of Vimentin while reducing in E-cadherin expression. This indicated that the motility of shSTC2 cells with a propensity to EMT. Our findings suggest that the reduced expression of STC2 may elevate EMT in human gastric cancers and thereby contribute to cancer metastasis.

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