THE ROLE OF THE TUMOR SUPPRESSOR GENE *THY1* IN SUPPRESSION OF EPITHELIAL-MESENCHYMAL TRANSITION (EMT) IN NASOPHARYNGEAL CARCINOMA

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BACKGROUND AND AIMS: THY1 has been successfully identified as a tumor suppressor gene (TSG) in nasopharyngeal carcinoma (NPC) in our laboratory. The frequency of down-regulated THY1 protein expression was found to be significantly associated with NPC lymph node metastases. However, direct functional evidence is still lacking for THY1 being anti-metastatic in NPC. Epithelial-Mesenchymal Transition (EMT) is well-known as a closely associated process for stem cells as well as tumor cells to invade to other part of the body. We aim to study the association of EMT with the THY1 in NPC. METHODS: Functional analysis of restoration of THY1 expression in the NPC cell lines was studied. The RhoA negative regulator, p190 Rho GTPase-activating protein (p190RhoGAP) and the E-cadherin/beta-catenin cell junction was examined in the THY1-expressing NPC cells. RESULTS: Both real-time and conventional invasion chamber assays clearly showed that the invasive ability of the THY1 transfectants was consistently lower than vector-alone control. The reverse transcription-polymerase chain reaction (RT-PCR) results show that the gene expression of cell invasion-associated gelatinase MMP-9 was significantly down-regulated in the THY1-transfectants compared with the vector-alone control. The p190RhoGAP was greatly activated by phosphorylation in the THY1 transfectants, when the THY1 gene was switched on in the absence of doxycycline (dox, an analogue of tetracycline). In the presence of dox when THY1 was switched off, the phosphorylation of p190RhoGAP was reduced. It appears that the phosphorylation status of p190RhoGAP is positively regulated by THY1 in NPC cells. The immunofluorescence (IF) confocal microscopy results show that beta-catenin and E-cadherin were much more frequently translocated to the cell-cell junction in the THY1 transfectants than the vector-alone. CONCLUSIONS: These findings suggest that THY1 inhibited NPC cell invasion via the formation of adherens junction and up-regulation of p190RhoGAP. The enhanced formation of cell adherens junction by THY1 is likely to be one of the possible mechanisms to suppress EMT in NPC.