Abstract

Cervical cancer is the fourth most common cancer among female in Malaysia and worldwide which is linked to thousands of deaths in women every year. Human papilloma virus (HPV) is a major risk factor of cervical cancer. However, the molecular mechanism of HPV-induced carcinogenesis in cervical cancer is poorly understood. The nuclear receptor co-repressor (N-CoR), a protein essential for the transcriptional repression mediated by various transcription factors, has been linked to the pathogenesis of leukaemia and lung cancer through its misfolded conformation dependent loss in tumour cells. In this study, the role of misfolding induced loss of N-CoR, its relationship with HPV induced cervical cancer cells, and the possible genes deregulated due to the loss of N-CoR was investigated. Western blotting assay, protein solubility assay and immunocytochemistry were performed to identify the conformation of N-CoR protein in HPV induced cervical cancer cells. The cells were treated with selective inhibitor of autophagy Bafilomycin A1 (BA1) to identify the relationship between misfolding induced loss of N-CoR and cell autophagy. Finally, reverse transcription-PCR (RT-PCR) was performed to identify the possible target genes of N-CoR to study the relationship between cervical cancer progression and epidermal-mesenchymal transition (EMT) pathway. As the result shown in this thesis, there was no significant correlation between N-CoR misfolding and HPV induced cervical carcinogenesis. However, EMT was found to be a potential pathway of cervical cancer progression whereas EMT regulators *Twist* and *Slug* were found to be expressed in both HPV positive and negative cervical cancer cell lines, while HOXA10 was found to be expressed in the HPV positive but not in HPV negative cervical cancer cells. This difference marks a possible interaction between HPV oncogene and HOXA10 which could be a novel target of HPV in cervical cancer progression.

Keywords: ***Cervical Cancer, N-CoR, HPV, Protein Misfolding, Autophagy, EMT***