

*“Analysis of MSH2 and EPCAM Gene Silencing and their effect in the Wnt/ $\beta$ -catenin pathway”*

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Small interfering RNA (siRNA) mediated gene silencing approach has potential benefit as a therapeutic strategy against selective pathways in colorectal cancer. *EPCAM*, a transmembrane glycoprotein mediating cell adhesion, was known to be involved in suppressing the *Wnt/ $\beta$ -catenin* pathway, one of vital pathway for tumour progression in colon cancer cells. *EPCAM* deletions caused a transcriptional read-through that may silence its neighbouring gene, *MSH2*. This study aims to investigate the synergistic effect of co-siRNA targeted genes, *MSH2* and *EPCAM*, in colon cancer cell line, HCT116, and their effect in modulating the *Wnt/ $\beta$ -catenin* pathway. Pre-designed siRNAs of *MSH2* and *EPCAM* were transfected into HCT116 cells. The cells were divided into six groups: untreated cells, cells treated with negative control siRNA, *MSH2*-siRNA treated cells, *EPCAM*-siRNA treated cells, cells treated with both *EPCAM* and *MSH2*-siRNAs, and cells treated with transfection reagent (mock control). The mRNA and protein expression following the individual and combined siRNA treatments were evaluated by two-step reverse transcription quantitative polymerase chain reaction (RT-qPCR) and Western blot. Based on morphological observation, few cells in the siRNA treated samples were seen to be detached and aggregated. The mRNA and protein expression levels of *MSH2*, *EPCAM* and  $\beta$ -*catenin* were reduced in the individual *MSH2* and *EPCAM*-siRNA treated samples as compared to the untreated sample. Further reduction of mRNA and protein expressions for *MSH2*, *EPCAM* and  $\beta$ -*catenin* were detected in combined siRNA treatments. The synergistic effect of *MSH2* and *EPCAM* in reducing the level of  $\beta$ -*catenin* expression by siRNA has suggested that these genes may play a role in suppressing the *Wnt/ $\beta$ -catenin* pathway in colon cancer cells.

**Keywords:** Small interfering RNA (siRNA), colorectal cancer, *MSH2*, *EPCAM*,  $\beta$ -*catenin*

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