736 TREATMENT WITH DECITABINE (DAC) INDUCES THE EXPRESSION OF STEMNESS MARKERS, PD-L1 AND NY-ESO-1 IN COLORECTAL CANCER

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Background Colorectal cancer (CRC) is a leading cause of cancer related deaths. Epigenetic silencing of numerous tumor suppressor genes by promoter region hypermethylation has been found in a variety of cancers including CRC. The chemotherapeutic drug decitabine (DAC) is a strong inducer of DNA demethylation. Primary cancer cells are known to express stemness markers as an escape pathway of treatment. Moreover, immunoregulatory genes can be inactivated in these cells by methylation of promoter CpG islands. Both mechanisms are known to play crucial roles in tumor progression. In this study, we investigated the effect of DAC on the expression of stemness markers, Programmed cell death ligand (PD-L1) and New York esophageal squamous cell carcinoma 1 (NY-ESO-1) in a metastatic (1872 Col) and a primary (1076 Col) colorectal cancer cell lines isolated from patients' tumor tissues.

Methods The 1076 Col and 1872 Col cell lines were treated with 5 μM of DAC for 48 hours. Differential expression of a panel of stemness and immunoregulatory markers before and after treatment was analyzed by Flow cytometry (FACS), Western Blotting (WB) and quantitative real time PCR (qRT-PCR).

Results

The following stemness markers: CD44, Nanog, KLF-4, CD133 and MSI1 were up-regulated in both 1076 Col and 1872 Col cell lines after treatment. However, significant up-regulation of the immunoinhibitory PD-L1 marker was recorded after treatment only in the metastatic 1872 Col. Interestingly, the NY-ESO-1 tumor antigen was significantly upregulated in both 1076 Col and 1872 Col cell lines after treatment.

Conclusions Treatment of colon cancer cells with DAC induces chemotherapeutic resistance as evidenced by the induction/upregulation of the stemness markers; and immune escape mechanism through the induction/upregulation of PD-L1. However, such treatment resulted in the induction/expression of the most immunogenic NY-ESO-1 tumor antigen. Our data suggest the importance use of a combined treatment strategy utilizing chemotherapy (DAC) with anti-PD-L-1/PD-1treatment in colon cancer patients.

Ethics Approval The study obtained ethical approval from Hamad Medical Corporation, Medical Research Center Ethic Board: Grant ID : IRGC-04-SI-17-142.

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