INHIBITING CRD-BP POTENTIATES THE ANTI-GROWTH EFFECT OF DRUGS ON COLORECTAL CANCER CELLS

Nicole Betson[1], Felicite K. Noubissi[1] and Kenneth Ndebele Duma[2]

[1]Cancer Biology Research Laboratory, Jackson State University, 1400 Lynch Street, Box 18540, Jackson, MS 39217, USA
[2]Molecular Biology Research Laboratory, Jackson State University, 1400 Lynch Street, Box 18540, Jackson, MS 39217, USA

Abstract: Colorectal cancer is the fourth most common cancer in both men and women. An estimated 135, 430 new cases will be diagnosed in 2017 and approximately 50,260 people will die of colorectal cancer. Based on the 2012- 2014 data from NIH approximately 4.3 % women and men at some point during their life will be diagnosed with colon and rectum cancer. Colorectal cancer can be regarded as a model of health disparity and has been the subject of growing concern in the United States. Advanced colorectal cancers are resistant to treatment due to activation of anti-apoptotic pathways and induction of the multidrug resistance (MDR) membrane transporters that pump drugs out of the cells. Targeting factors involved in these mechanisms should aid in the sensitization of colorectal cancer cells to drugs. The coding region determinant-binding protein (CRD-BP) was shown to activate anti-apoptotic pathways and to regulate the multidrug resistance-1 (MDR-1) membrane transporter. We hypothesize that inhibition of CRD-BP in colorectal cancer cells will overcome their resistance to chemotherapeutics. To test our hypothesis we used the colorectal cancer cells HCT116 and RKO, and the chemotherapeutic drug Irinotecan. We used the MTT assay to assess cell proliferation, Caspase assay to assess cell apoptosis, and β-galactosidase assay to assess cell senescence. We observed that inhibition of CRD-BP significantly reduced the proliferation of HCT116 cells when they were treated with Irinotecan. A significant increase in apoptosis was also observed in those cells. No change in senescence was observed in HCT116 cells. CRD-BP inhibition had no effects on the proliferation, apoptosis, or senescence of RKO cells when they were treated with the drug. Our data suggest inhibition of CRD-BP potentiates the anti-growth effect of irinotecan in HCT16 cells by promoting apoptosis.

Key words: Colorectal cancer; CRD-BP; drug resistance; Irinotecan.

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