

Critical role of phosphorylation of serine 165 of YBX1 on the activation of NF- κ B in colon cancer

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Y-box binding protein 1 (YBX1) is a multifunctional protein known to facilitate many of the hallmarks of cancer. Elevated levels of YBX1 protein are highly correlated with cancer progression, making it an excellent marker in cancer. The connection between YBX1 and the important nuclear factor κ B (NF- κ B), has never been previously reported. Here, we show that overexpression of wild type YBX1 (wtYBX1) activates NF- κ B, suggesting that YBX1 is a potential NF- κ B activator. Furthermore, using mass spectrometry analysis, we identified novel phosphorylation of serine 165 (S165) on YBX1. Overexpression of the S165A-YBX1 mutant in either 293 cells or colon cancer HT29 cells showed dramatically reduced NF- κ B activating ability as compared to that of wtYBX1, confirming that S165 phosphorylation is critical for the activation of NF- κ B by YBX1. We further show that expression of the S165A-YBX1 mutant dramatically decreased the expression of NF- κ B-inducible genes, reduced cell growth, and compromised tumorigenic ability as compared to wtYBX1. Taken together, we provide the first evidence that YBX1 functions as a tumor promoter via NF- κ B activation, and phosphorylation of S165 of YBX1 is critical for this function. Therefore, our important discovery may lead to blocking S165 phosphorylation as a potential therapeutic strategy to treat colon cancer.