Supplemental Figure 4. Proposed Model. E2F1 and HDAC1/2 promote the expression of ATM. In the presence of DNA double strand breaks, the MRN complex (MRE11, Rad50, NBS1) promotes the autophosphorylation of ATM leading to activation of down-stream components BRCA1, CHK2, and p53. Stabilized and activated p53 induces the expression of response genes that promote cell cycle arrest and DNA repair. Pre-treatment with an HDAC inhibitor reduces the expression of DNA repair genes including ATM, limiting the cell’s ability to elicit a sufficient response to DNA double strand breaks. Aside from HDAC1/2 regulation of ATM, HDAC inhibitors also reduce the protein expression of MRE11, Rad50, and BRCA1 of this pathway in cancer cells.