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Cell cycle and apoptosis regulator 2 at the interface between DNA damage response and cell physiology

Running Title: CCAR2 role in DDR and cell physiology.

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ABSTRACT

Cell cycle and apoptosis regulator 2 (CCAR2 or DBC1) is a human protein recently emerged as a novel and important player of the DNA damage response (DDR). Indeed, upon genotoxic stress, CCAR2, phosphorylated by the apical DDR kinases ATM and ATR, increases its binding to the NAD+-dependent histone deacetylase SIRT1 and inhibits its activity. This event promotes the acetylation and activation of p53, a SIRT1 target, and the subsequent induction of p53 dependent apoptosis. In addition, CCAR2 influences DNA repair pathway choice and promotes the chromatin relaxation necessary for the repair of heterochromatic DNA lesions. However, besides DDR,