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Authors: Martina Magni, Giacomo Buscemi, Laura Zannini

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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.

Martina Magni¹, Giacomo Buscemi² and Laura Zannini^{3,*}

¹ Department of Medical Oncology and Hematology, Fondazione IRCCS Istituto Nazionale dei

Tumori, Via Venezian 1, 20133 Milan, Italy. ² Department of Biosciences, University of Milan, via

Celoria 26, 20133 Milan, Italy. ³Istituto di Genetica Molecolare, Consiglio Nazionale delle Ricerche

(IGM-CNR), via Abbiategrasso 207, 27100 Pavia, Italy.

* To whom correspondence should be addressed. Tel: +390382546363; Fax: +390382422286;

Email: laura.zannini@igm.cnr.it

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,

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