conferenceseries.com

Daniele Musiani et al., J Proteomics Bioinform 2016, 9:11(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.091

PRMT1 modulates gene expression during DNA damage response, through R-methylation of histones and non-histone targets

Daniele Musiani, Alessandro Cuomo, Sriganesh Jammula and **Tiziana Bonaldi**
European Institute of Oncology, Italy

The DNA damage response (DDR) is a complex regulatory network triggered in the cells by DNA-damaging agents and ensures genome stability. We found that the major protein-arginine (R)-methyltransferase PRMT1 is induced by cisplatin (CDDP) in ovarian cancer cells and is required for the anti-apoptotic response to the drug, sustaining CDDP-triggered ATM activation. Subcellular fractionation of cells treated with CDDP or UV indicates that PRMT1 is recruited to chromatin during DDR, where it triggers methylation of R3 on histone H4, and a known transcriptional activating mark. Accordingly, RNA-seq analysis, it shows that PRMT1 mediates the transcriptional activation of 125 genes upon CDDP, while it is not implicated in the downregulation of the CDDP-repressed genes. Gene ontology analysis of the genes up-regulated via PRMT1 shows an overrepresentation of the Nf-kB-dependent transcriptional program, which regulates the senescence-associated secretory phenotype (SASP), a stress response pathway accompanying DDR. We hypothesize that the PRMT1 increased activity dictates a dynamic response of the protein-R-methylome beyond histones. SILAC MS-based proteomic analysis of cells treated with CDDP reveals a strong impact of the drug on the R-methylome with 23% out of the 206 accurately quantified R-methyl sites significantly regulated. Interestingly, the proteins containing the affected methyl-sites are known PRMT1 targets RNA and shuttling binding proteins (RBPs) that accumulate into cytosolic stress granules (SG) when the cell is exposed to stress. Based on these results, we proposed a dual function for PRMT1 in DDR: on one hand, PRMT1 emerges as a novel co-activator for the transcriptional control of the DDR-dependent SASP; on the other hand, PRMT1 re-localization results in a change of RBPs R-methylation that likely affects their accumulation in SGs where they act as mRNA chaperones to ensure efficient translation of vital mRNAs during stress.

Biography

Daniele Musiani has completed his PhD in 2012 from the University of Turin and Post-doctoral studies from the Experimental Oncology department at the European Institute of Oncology, Milan. He has published 6 papers in peer-reviewed scientific journals.

daniele.musiani@ieo.eu

Notes: