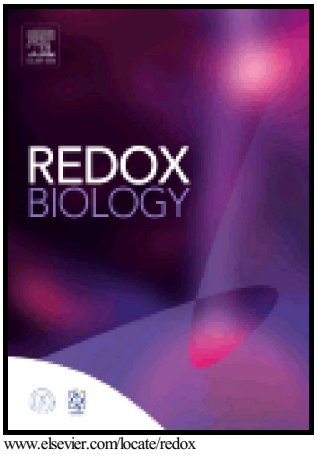

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Reduced levels of methyltransferase DNMT2 sensitize human fibroblasts to oxidative stress and DNA damage that is accompanied by changes in proliferation-related miRNA expression

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Abstract

Methyltransferase DNMT2 is suggested to be involved in the regulation of numerous processes, however its biological significance and underlying molecular mechanisms remain elusive. In the present study, we have used WI-38 and BJ human fibroblasts as an *in vitro* model system to investigate the effects of siRNA-based DNMT2 silencing. DNMT2-depleted cells were found to be sensitive to oxidative stress conditions as judged by increased production of reactive oxygen species and susceptible to DNA damage that resulted in the inhibition of cell proliferation. DNMT2 silencing promoted upregulation of proliferation-related and tumor suppressor miRNAs, namely miR-28-3p, miR-34a-3p, miR-30b-5p, miR-29b-3p, miR-200c-3p, miR-28-5p, miR-379-5p, miR-382-5p, miR-194-5p, miR-193b-3p and miR-409-3p. Moreover, DNMT2 silencing induced cellular senescence and DNMT2 levels were elevated in replicatively senescent cells. Taken together, we found that DNMT2 may