ROLE OF p53 ON THE DIFFERENTIAL SUSCEPTIBILITY TO UV-INDUCED APOPTOSIS IN CONFLUENT AND PROLIFERATING DNA REPAIR-DEFICIENT CELLS.

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p53 activation is one of the main signals after DNA damage, controlling cell cycle arrest, DNA repair and apoptosis. We have previously shown that confluent nucleotide excision repair (NER) deficient cells are more resistant to apoptosis induced by UV irradiation. In this work, we analyzed the effect of the ATM/ATR inhibitor caffeine on apoptosis in normal and NER-deficient (XPA and XPC) cells, as well as the patterns of p53 activation in proliferating and confluent cells. Strong p53 activation was observed either in proliferating or confluent cells. Caffeine increased apoptosis levels and inhibited p53 activation in proliferating cells, suggesting a protective role for p53. However, in confluent NER-deficient cells no effect of caffeine was observed. The levels of the cyclin/Cdk inhibitor $p21^{Waf1/Cip1}$ correlated well with p53 activation in proliferating cells. Surprisingly, confluent cells also showed similar activation of $p21^{Waf1/Cip1}$. Thus, these results indicate that the reduced apoptosis in confluent cells is not associated to DNA damage removal, as this effect is observed in NER-deficient cells. Moreover, the strong activation of p53 in confluent cells, which barely respond to apoptosis, suggests that this protein, in these conditions, is not linked to UV-induced cell death signaling.