Mahsa Karbaschi, J Clinic Toxicol 2016, 6:5(Suppl)
http://dx.doi.org/10.4172/2161-0495.C1.018

Rescue of cells from apoptosis increases DNA repair in UVB exposed cells: Implications for the DNA damage response

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Classically, the nucleotide excision repair (NER) of cyclobutane pyrimidine dimers (CPD) is a lengthy process ($t_{1/2}$ > 48 h). Using the T4 endonuclease V-modified comet assay, we uniquely found a far more rapid repair of UVA-induced CPD ($t_{1/2}$ = 4.5 h) in human skin keratinocytes. The repair of UVB-induced CPD began to slow within 1 h of irradiation, causing damage to persist for over 36 h. A similar trend was noted for the repair of oxidatively-modified purine nucleobases. Supportive of this differential repair, we noted an up-regulation of key genes associated with NER in UVA-irradiated cells, whereas the same genes were down regulated in UVB-irradiated cells. There were no significant differences in cell viability between the two treatments over the first 6 h post-irradiation, but after 24 h apoptosis had increased significantly in the UVB-irradiated cells. The role of apoptosis was confirmed using a pan-caspase inhibitor, which increased CPD repair, similar to that seen with UVA. These data indicate that the cellular 'decision' for apoptosis/DNA repair occurs far earlier than previously understood, and that the induction of apoptosis leads to lesion persistence, and not vice versa. This also highlights a new, potential increased carcinogenic risk from UVA-induced DNA damage as, rather than undergoing apoptosis, high levels of damage are tolerated and repaired, with the attendant risk of mutation.

Biography

Mahsa Karbaschi has completed her PhD in Cancer Studies and Molecular Medicine at the University of Leicester in the UK and Post-doctoral studies from Florida International University in Florida, US. Her research interest is in formation and repair of oxidatively damaged DNA and also in development of new methodologies for the evaluation of DNA damage.

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