

Characterization of telomere maintenance and chromosomal integrity in human fibroblasts and keratinocytes

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In spite of the significant progress in cancer biology and modern radiation biology in the last decades, it is still an open question how exactly different human cell types respond to ionizing radiation. The majority of studies have been done on two types of human cells: skin fibroblasts and peripheral blood lymphocytes. The main reason for this is the relatively easy access to these cells in individuals. Other cell types, such as normal epithelial cells, have been used on a much smaller scale and consequently there is relatively little data on how normal epithelial cells respond to ionizing radiation in comparison with fibroblasts. The study of epithelial cells is highly relevant for the elucidation of radiation-induced carcinogenesis as the majority of human solid cancers will develop from epithelial cells. The work presented here is the characterization of karyotypes and telomere loss in non-irradiated fibroblast and keratinocyte populations from the same donor during the different stages of proliferation *in vitro* and results for the response of fibroblasts to five doses of γ -radiation spanning the range 10-2000 mGy with respect to cell proliferation and kinetics of γ H2AX foci. An increase in the incidence of telomere loss with doublings *in vitro* was noted; however, it followed different kinetics in the two cell types. An increase in clonal and *de novo* chromosomal aberrations was observed in both fibroblasts and keratinocytes as proliferation progressed into senescent phases. Clonal emergence from the second senescent plateau characterized by progressive instability of the genome and different kinetics of telomere maintenance, was observed in keratinocytes. Fibroblasts and keratinocytes showed different kinetics of γ H2AX foci, with apparent higher initial induction in fibroblasts, but faster disappearance of the induced foci. The radiosensitivity and the transmission of radiation-induced damage could largely differ according to the cell type status at irradiation (fibroblasts/ keratinocytes, young/ senescent) and their role in the long-term occurrence of radiation-induced tumours needs to be characterized.