The PI3K/Akt/mTOR Pathway Is Implicated in the Premature Senescence of Primary Human Endothelial Cells Exposed to Chronic Radiation.

Abstract:
The etiology of radiation-induced cardiovascular disease (CVD) after chronic exposure to low doses of ionizing radiation is only marginally understood. We have previously shown that a chronic low-dose rate exposure (4.1 mGy/h) causes human umbilical vein endothelial cells (HUVECs) to prematurely senesce. We now show that a dose rate of 2.4 mGy/h is also able to trigger premature senescence in HUVECs, primarily indicated by a loss of growth potential and the appearance of the senescence-associated markers β-galactosidase (SA-β-gal) and p21. In contrast, a lower dose rate of 1.4 mGy/h was not sufficient to inhibit cellular growth or increase SA-β-gal-staining despite an increased expression of p21. We used reverse phase protein arrays and triplex Isotope Coded Protein Labeling with LC-ESI-MS/MS to study the proteomic changes associated with chronic radiation-induced senescence. Both technologies identified inactivation of the PI3K/Akt/mTOR pathway accompanying premature senescence. In addition, expression of proteins involved in cytoskeletal structure and EIF2 signaling was reduced. Age-related diseases such as CVD have been previously associated with increased endothelial cell senescence. We postulate that a
similar endothelial aging may contribute to the increased rate of CVD seen in populations chronically exposed to low-dose-rate radiation.