regulation of cell death. We have explored the effect of IF_1 expression on apoptotic cell death. HeLa cells in which IF_1 was overexpressed ($+IF_1$) or suppressed using siRNA ($-IF_1$) were exposed to staurosporine (STS, 1 μM) or etoposide (Eto, 100 μM) for up to14 h. STS- or Eto-induced cell death was significantly reduced in $+IF_1$ (by ~30%) and increased in $-IF_1$ cells. In $+IF_1$ cells, caspase activation and annexin V binding were reduced and mitochondrial morphology was better preserved. Cytochrome *c* release, measured using the redistribution of cyt-GFP, was also significantly delayed in $+IF_1$ cells. Following STS treatment, $\Delta\psi_m$ measured using TMRM, collapsed relatively rapidly in $+IF_1$ cells, while it was maintained for up to 2 h in $-IF_1$ cells. IF_1 may protect cells from apoptotic cell death by regulating changes in $\Delta\psi_m$ and ATP levels, or by regulating mitochondrial structure and limiting cyt *c* release. Thus, IF_1 upregulation may predispose tissues to tumour growth by suppressing apoptotic responses following moderate injury and may also promote resistance to anti-cancer therapies.

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S12.38 Nutrient modulation of mitochondrial function, oxidative stress and cell cycle in human colon cancer

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Mitochondria are intimately involved in the life and death of the cell, capable of integrating pro- and anti-apoptotic signals and committing the cancer cell to apoptosis. Moreover, these organelles are the main source of intracellular reactive oxygen species. Therefore, the aim of this study was to investigate the effects of dietary antioxidants and glucose deprivation on mitochondrial function, cell cycle and oxidative stress in cell lines corresponding to different stages of human colon cancer. Tocopheryl acetate, resveratrol and vitamin C caused apoptosis in a cell line derived from metastatic tumour (SW-620); however, only resveratrol increased the apoptosis in a cell line derived from primary colorectal adenocarcinoma (HT-29). Additionally, vitamin C exhibited opposite effects on cell proliferation between the studied stages. Basal differences in cytochrome *c* oxidase, lactate dehydrogenase activity and H_2O_2 production were suppressed by glucose deprivation. Glucose-deprived HT-29 cells showed an upward in oxygen consumption coupled to a decrease in pro-oxidant production and lipid peroxidation. In conclusion, antioxidant compounds might modulate cell cycle in human colon cancer cells and oxidative stress could be one of the underlying mechanisms responsible for the observed phenotypic variations between its stages.

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S12.39 Natural sunlight damage to human skin mitochondria

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The aim of this in vitro study was to assess mitochondrial damage expressed in human skin cells exposed to simulated sunlight from a Q-Sun solar simulator. Excessive or continuous exposure to ultraviolet radiation contained in sunlight can result in the initiation and promotion of skin cancers, with many of the Irish population possessing particularly sensitive skin types. Non-tumour skin keratinocytes (HaCaT) and amelanotic tumour keratinocytes (C32) were exposed to different lengths of simulated sunlight and examined for mitochondrial damage. Effects on cell proliferation, mitochondrial mass and metabolism were assessed through a range of colorimetric assays. Mitochondrial DNA was assessed for induction of deletions, genome frequency and comparison of PCR efficiency of a 16Kbp product (almost the entire genome) versus a short conserved region. Results demonstrate that exposure of human skin cells *in vitro* to simulated sunlight causes mitochondrial DNA damage and influences the regulation of mitochondrial genome copy number. A substantial increase in mitochondrial activity was observed in non-tumour cells 4 h post exposure to simulated sunlight. The $mtDNA^{4977}$, though detected, did not increase in frequency with sunlight exposure. The $mtDNA^{3895}$ deletion was observed to be induced substantially in the amelanotic tumour cells. The frequency of deletions identified in this study may provide a potential biomarker for cumulative sunlight exposure in human skin.

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S12.40 Response to metabolic stress in cybrids obtained from patients with Leber's hereditary optic neuropathy

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Leber's hereditary optic neuropathy (LHON), the first maternally inherited disease to be associated with point mutations in mtDNA, is the second prevalent mitochondrial disorder. LHON is characterized by selective loss of ganglion cells in the retina leading to central vision loss and optic atrophy. ROS overproduction has been reported in cells harbouring mtDNA pathogenic mutations. 11778/ND4, 3460/ND1, and 14484/ND6 are the three most frequent LHON pathogenic mtDNA point mutations affecting complex I, and result in decreased ATP synthesis and increased oxidative stress. We studied ROS production and GSH level in ND4, ND1 and ND6 cybrid cellular model. Cybrids were obtained by fusing a rho° cell line completely devoid of mtDNA with cytoplasts derived by enucleated cells from LHON or healthy patients. ROS production and GSH content were measured in basal condition and in experimental stress induced by glucose-deprivation galactose-replacement. Basal ROS production measured by flow cytometry was modestly more elevated in cybrids harbouring the three LHON mutations than in healthy cells. GSH content in all cybrids in basal condition were not different. LHON mutated cybrids showed decreased growth and larger increase ROS and GSSG production compared with control cybrids. The response to stress was slight different among the three mtDNA point mutations. These results indicate that this cybrid cell model is a useful tool to explain the pathogenic mechanism of LHON, and may provide convenient system to test novel therapy strategies.

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S12.41 Altered mitochondrial respiration and energy metabolism in brain cells from transgenic Alzheimer's disease mice

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