NF-κB MEDIATED SIGNALING NETWORK IN LOW DOSE X-RAY INDUCED ADAPTIVE PROTECTION OF MOUSE AND HUMAN SKIN EPITHELIAL CELLS

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Mammalian cells received a certain low dose of ionizing radiation demonstrate an adaptive protection that reduces DNA damage and genomic instability induced by subsequent radiation. The molecular mechanism underlying the radioprotective effect of pre-exposure with low dose radiation is poorly understood. Using immortalized normal mouse and human skin epithelial cells, the present study provides the first evidence that NF-κB, a stress responsive transcription factor, is induced by a single exposure of 5 or 10 cGy X-ray that enhanced cell survival to 2 Gy γ-irradiation. NF-κB luciferase reporter activity was significantly enhanced by radiation with (in mouse skin JB6 cells) or without (human skin HK18 cells) the induction of expression of p65 (the major component of NF-κB). ERK, mitochondrial antioxidant MnSOD, 14-3-3 chaperon proteins (14-3-3s) and cell cycle regulators (cyclins) were enhanced by single dose or multiple long-term exposure of X-rays (0.5 cGy/day for 30 days). Inhibition of NF-κB blocked the induction of 14-3-3s and cyclins. In addition, substantial amount of induced 14-3-3ζ and cyclin B1 were found to be relocated to cytoplasm from nucleus after radiation with 10 cGy, and direct interaction between 14-3-3ζ and cyclin B1 was visualized in living cells using fluorescence-fusion proteins. As illustrated in the following Scheme, our present results suggest that the adaptive protection induced by low dose radiation in mouse and human skin cells is mediated by the activation of NF-κB. Mitochondrial antioxidant MnSOD and cyclins appear to play an important role in the NF-κB-initiated adaptive radioprotection.

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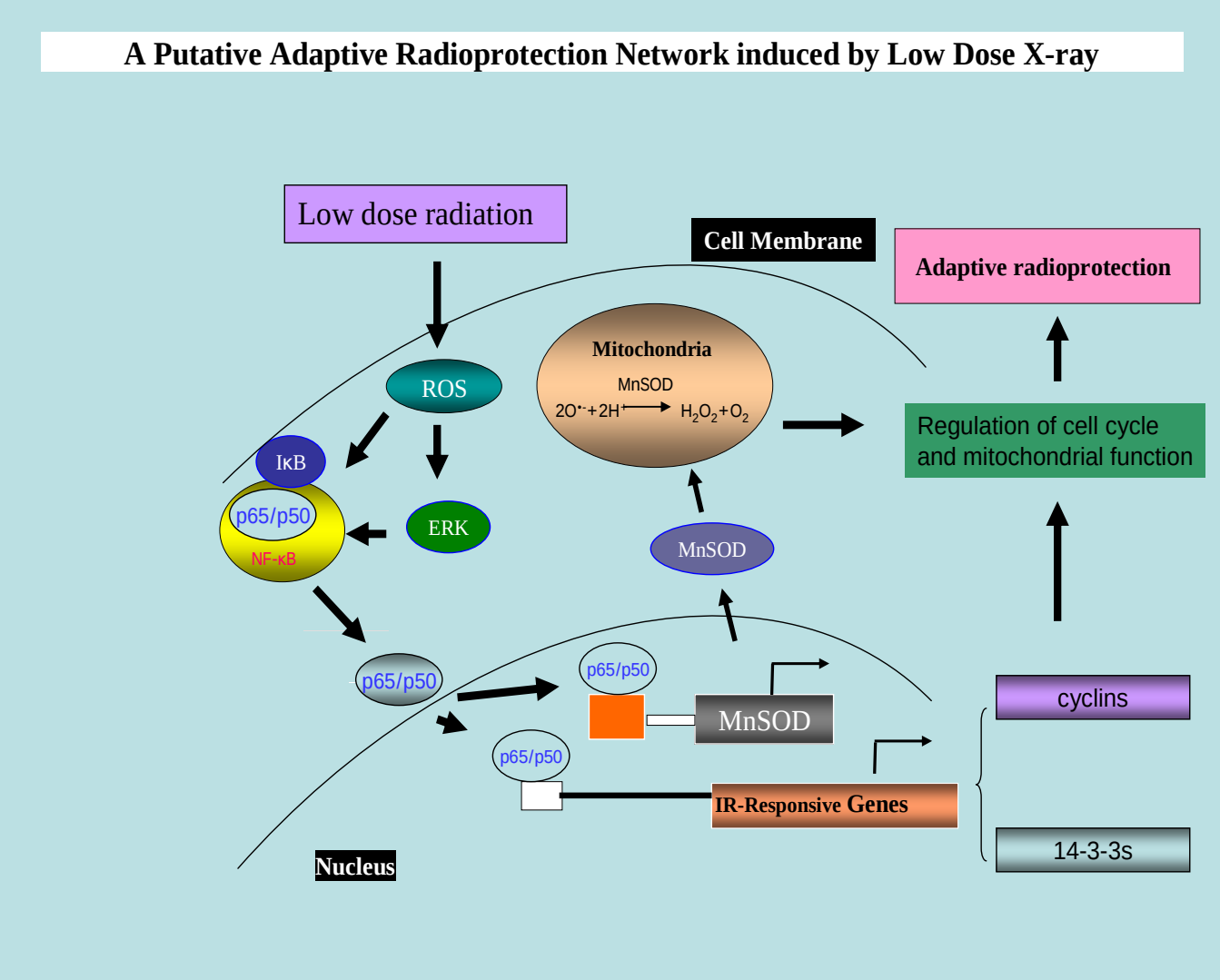
A Putative Adaptive Radioprotection Network induced by Low Dose X-ray
Low dose radiation
Cell Membrane
Adaptive radioprotection
Mitochondria
MnSOD
$2O^{\bullet-}+2H^{+} \rightarrow H_2O_2+O_2$
ROS
IκB
p65/p50
NF-κB
ERK
MnSOD
Regulation of cell cycle and mitochondrial function
p65/p50
p65/p50
MnSOD
p65/p50
IR-Responsive Genes
cyclins
14-3-3s
Nucleus