Profiling of MnSOD Interaction Proteins in Low-Dose Radiation Induced Adaptive Response

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Humans are repeatedly exposed to low doses of ionizing radiation (LDIR, <10cGy). Recent studies have shown that exposure to LDIR induces an adaptive radioresistance response to upcoming radiation and chemotherapy in healthy cells. It is thought LDIR activates specific proteins, which provide increases cellular tolerance to the oxidative damage caused by high-dose IR (HDIR). MnSOD has been shown to play a key role in providing this radioresistant effect by reducing the number of toxic superoxides formed after radiation[1, 2]. Deciphering the mechanisms of MnSOD's protective role after LDIR is necessary to utilize potential benefits of LDIR and eventually incorporating it into chemotherapy regimens. This study uses human keratinocyte cell line (HK18) to show that although MnSOD protein level was not obviously enhanced after radiation, a substantial amount of its enzymatic activity was increased after irradiation with 10cGy x-ray. This result led to the exploration of what other proteins MnSOD is able to communicate and interact with. Two proteomic experiments, using gel-based mass spectrometry for protein identification, yielded a comparative profile of MnSOD interacting partners before and after LDIR. Analysis of these two profiles revealed an increase of in the overall number and relative amount of proteins that MnSOD interacts with after receiving LDIR. Importantly, many "partners" of MnSOD after IR have functions related to cell cycle regulation, DNA repair, apoptosis regulation and mitochondrial function. These results suggest that the oxidative stress defense role of MnSOD may also be linked to its communication with other partner proteins to influence the overall cellular reactions to stress conditions.

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2. Fan M, Ahmed KM, Coleman MC, Spitz DR, Li JJ. Nuclear factor-kappaB and manganese superoxide dismutase mediate adaptive radioresistance in low-dose irradiated mouse skin epithelial cells. Cancer Res 2007;67:3220-8.