Cyclin D1 and CDK4 translocate into mitochondria and interact with MnSOD in low dose radiation- induced adaptive radioprotection

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Although mitochondria play an essential role in radiation response, the exact mechanism underlying mitochondrial pro- or anti- apoptotic pathways in low dose radiation- induced adaptive response remain elusive. As shown in Figure 1, we have reported that Cyclin D1 up-regulated by NF-kappaB is involved in low dose radiation induced adaptive response (Ahmed, 2008). This study tested the hypothesis that Cyclin D1/CDK4 plays a key role in delivering the adaptive signaling to mitochondria to induce an anti-apoptotic response. We found that Cyclin D1/CDK4 was present in the mitochondrion of human skin keratinocytes and its mitochondrial translocation was significantly enhanced in a certain time following exposure to low dose ionizing radiation (LDR; 10-cGy x-ray). Cyclin D1/CDK4 was able to directly interact with mitochondrial antioxidant MnSOD, which may contribute to the adaptive radioresistance with reduced ROS and maintenance of mitochondria membrane potential. These results provide the evidence that cell cycle regulator Cyclin D1/CDK4 is able to regulate mitochondrial function via direct interact with mitochondrial antioxidants in low dose radiation-induced adaptive resistance. Studies on radioprotective function of Cyclin D1/CDK4/MnSOD pathway in mouse and human tissues are underway.

Ahmed KM, Fan M, Nantajit D, Cao N, Li JJ. Cyclin D1 in low-dose radiation-induced adaptive resistance. Oncogene 27:6738-6748, 2008.
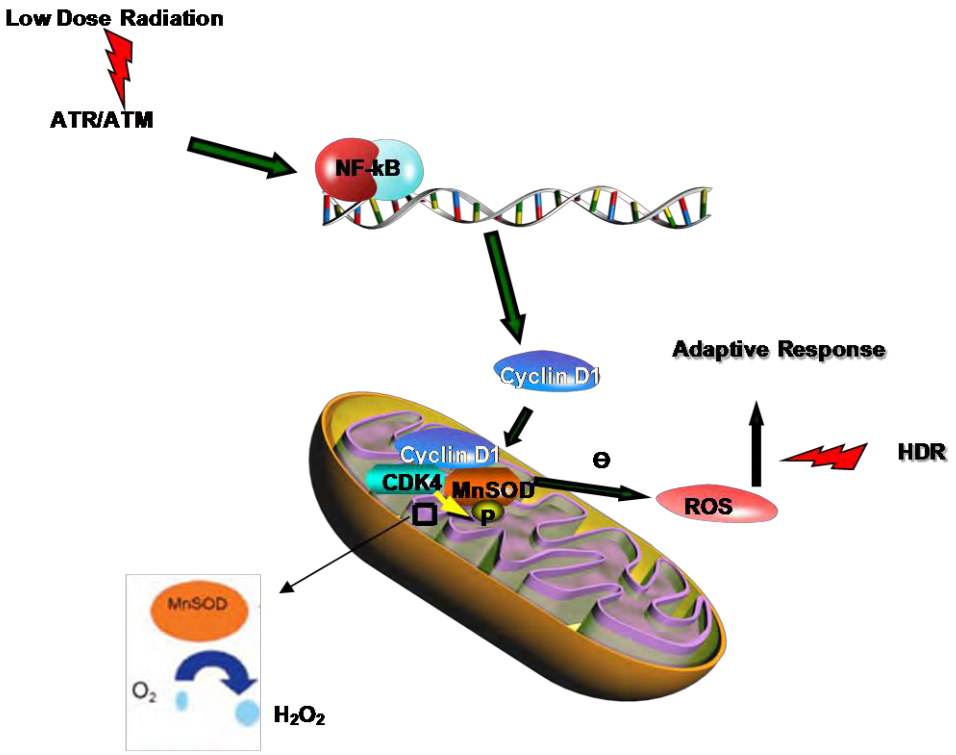
Figure 1. CDK4/Cyclin D1 mediated adaptive response by interaction with MnSOD