Activation of the Nuclear ATM Pathway by Low Dose Radiation

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Ionizing radiation has been thought to have detrimental effects on chromatin structure, since radiation-induced DNA double strand breaks result in discontinuity of nucleosomes. Recetly, it has been shown that ATM protein, the product of the ATM gene mutated in ataxia-telangiectasia, recognizes alteration in the chromatin structure, and they are activated through intermolecular auto-phosphorylation at serine 1981. Here, we examined activation of ATM protein in response to low dose ionizing radiation in normal human diploid cells.

Activated and phosphorylated ATM protein is detected as discrete foci in the nucleus by using antibodies recognizing phosphorylated ATM protein at serine 1981. We found that the number of the sites where chromatin structure is disorganized increases linearly in a dose-dependent manner, and the average number of phosphorylated ATM foci per Gy is approximately 50. Although the initial foci can be detected immediately after irradiation, the size of the foci increases as increasing the time after irradiation. It should be noted that the size of the foci induced by 50 mGy was equivalent to the foci induced by 500 mGy. These results indicate that the initial signal is amplified through foci growth, and cells evolve a system by which they can respond to a small number of DNA double strand breaks.