Gadd45a-dependent Base Excision Repair in response to the Alkylating Agent MMS & Thio-TEPA

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p53 tumor suppressor protein has been identified as a transcription factor that regulates many genes involved in mediating cellular responses to DNA damage. As one of a number of p53-regulated genes, Gadd45a has known to regulate nucleotide excision repair (NER) in response to UV-radiation. Recently, the base excision repair (BER) has been reported to be partially deficient in cells lacking functional p53 status. Here we statement a novel role for Gadd45a in base excision repair (BER). Gadd45-deficient cells exhibited slow BER after treatment with methyl methane sulfonate (MMS), a pure base-damaging agent. Our data showed that base-damaging therapeutic agent, Thio-TEPA (N, N, N, triethylenethiophosphoramide) induced the critical sensitivity in Gadd45a-deficient cells. We suggest that p53-regulated genes inducing Gadd45a contribute to the BER response. Gadd45a may be a key component gene of the p53 pathway involved in protection from carcinogenic base damage and maintenance of genomic stability as well as a potential therapeutic target for eliminating p53-mutant cancer cells.