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p53-dependent Protective Response from DNA-Damaging Agent Oxaliplatin and Thio-TEPA

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p53 mediates protective responses including DNA repair in many epithelial cancer cell types being more sensitive to DNA damage, antithetical to the situation in Burkitt lymphoma and other apoptosis-prone cell types. We have used matched isogenic pairs of p53 wild-type or deficient cell lines from breast cancer, colon cancer, and MEF to show a role for the tumor suppressor p53 in regulation of DNA repair responses to UV-radiation, cisplatin, carboplatin, and melphalan-induced DNA damages. Here we show the sensitivity of oxaliplatin, relatively new derivatives of platinum compound in p53-defective cells. Moreover, we employed the same cell lines from our prior work on nucleotide excision repair (NER) to investigate a related, yet distinct DNA repair pathway, known as base excision repair (BER). Here, we explore the sensitivity of the chemotherapy agent thio-TEPA (N, N', N'', triethylenethiophosphoramide), which largely induces base damage. p53-deficient cells were more sensitive to thio-TEPA, suggesting that this chemotherapeutic agent could benefit from knowledge of BER pathways and their regulation. Overall, we suggest that the contribution of p53 temporally correlates with DNA repair pathways to produce a resistant phenotype, while the p53-defective cells are more sensitive to certain DNA-damaging chemotherapeutic agents.

Keyword : *p53, chemotherapeutic agent, DNA repair*