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# Induction of G2/M Arrest by *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine, an alkylating agent, in Human Prostate Carcinoma Cells

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The alkylating agent *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG) is a widely spread environmental carcinogen that causes DNA lesions leading to cell killing. MNNG is a potent direct-acting carcinogen that induces tumors at the site of administration. However, under aqueous conditions, it undergoes hydrolytic decomposition and releases alkylating moieties that can bind DNA. The aim of the present study was to further elucidate the possible mechanisms by which MNNG exerts its anti-proliferative action in cultured human prostate PC-3 and DU145 cancer cells. We observed that the proliferation-inhibitory effect of MNNG was due to the induction of both cell cycle arrest and apoptosis, which was associated with gross morphological changes. DNA flow cytometric analysis revealed that MNNG arrested the cell cycle progression at the G2/M phase. The Western blotting analysis revealed that MNNG treatment causes a dose-dependent induction of cyclin-dependent kinase (Cdk) inhibitor p21(*WAF1/CIP1*) without alteration expression levels of cyclin A, cyclin B, Cdc2 and Cdk2. Our study suggests that MNNG treatment of the cells cause induction of p21 that inhibit cyclin A-Cdk2 and cyclin B-Cdc2 complexes, thereby imposing an artificial checkpoint at the G2/M transition of the cell cycle. Thus, our findings suggest that MNNG may be a potential chemotherapeutic agent for the control of human prostate cancer cells.