

**INOSITOL HEXAPHOSPHATE (IP6): MODULATION OF CELL CYCLE AND PROLIFERATION OF BLADDER CANCER IN VITRO**

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**INTRODUCTION AND OBJECTIVE:** Inositol Hexaphosphate (IP6), is a polyphosphorylated carbohydrate that is found in foods high in fiber content. We hypothesized that IP6 would modulate cell cycle and cellular growth in bladder cancer in vitro after a mere 2 hour exposure.

**METHODS:** TCCSUP, HTB9 and T24 bladder cancer cell lines were cultured using standard techniques and incubated for 2 hours with 2.5 or 4.5mM/well IP6. Cell viability was measured by MTT at 24 and 48 hours thereafter. Cell cycle analysis was measured by DNA staining and quantified by FACS analysis. Statistical analysis was performed by ANOVA.

**RESULTS:** Cell Growth/Proliferation: Reductions in cell growth were observed in the TCCSUP (Range 24.4% to 66.8%), HTB9 (Range -8.8% to 33.5%) and T24 (Range 11.4% to 43.9%) ( $P < 0.001$ ) with the exception of the HTB9 cells at 24 hours.

Cell/Cycle: IP6 2.5 and 4.5mM increased G1 phase fractions in both the TCCSUP and HTB9 cells compared to control (49.3% and 51.4% vs. 45.9%,  $P < 0.001$ ; 64.8% and 63.7% vs. 60.2%  $P < 0.001$  respectively). A significant decrease in G2 phase was observed in the TCCSUP cells (1.9% and 1.6% vs. 5.7%,  $P < 0.001$ ). No such change was observed in the HTB9 cells in respect to the G2 phase. However, a decrease in the S phase fraction was observed by both doses tested compared to control (31.6% and 32.3% vs. 35.8%,  $P < 0.001$ ) In the T24 line a decrease in the G1 phase fractions was observed with 4.5mM IP6 compared to control (55.8% vs. 63.6%,  $P < 0.001$ ). A significant increase in the S phase was observed in the T24 cells (38.9% vs. 32.6%,  $P < 0.001$ ).

**CONCLUSIONS:** The highly significant reduction in cellular proliferation exhibited by IP6 with a clinically relevant 2 hour incubation period, suggests that IP6 has the potential to become a highly effective treatment modality for carcinoma of the bladder.