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Immunomodulatory Effects of Paclitaxel.

Woo H. Choi[1], Ho S. Moon[2], Kyu H. Cho[3], Cheng-Z. Jiang[4],
Michael Lee and Woo S. Koh
Korea Institute of Toxicology

Paclitaxel, a chemotherapeutic agent, has also been shown to retain immunosuppressive characteristics. In this study, the immunomodulatory effects of paclitaxel were further characterized. Paclitaxel suppressed the lymphoproliferation following both Con A and LPS stimulation in a dose-dependent manner. T-cell proliferation induced by Con A was significantly decreased by treatment at 50 nM and higher, while B-cell proliferation by LPS was inhibited from 12.5 nM of paclitaxel. Splenocyte populations at S and G2/M phase increased from 5 and 1% to 34 and 10%, respectively, after the Con A stimulation for 48 hours. Co-treatment of paclitaxel with Con A to spleen cells decreased cell population at S phase but increased cell population at G1 and G2 phase, indicating that the inhibition of lymphoproliferation by paclitaxel treatment occurred in G2 phase as well as G1 phase during cell cycle progression. Paclitaxel also affected the lymphokine production. We measured five representative lymphokines, IL-2, IL-4, IL-5, IFN-γ, and TNF-α, at 24 and 48 hours after Con A stimulation. All of the lymphokines in the culture medium at 24 and 48 hours were significantly and dose-dependently depressed by the paclitaxel treatment except for IL-2 levels at 48 hour, which were dose-dependently enhanced by paclitaxel. On the other hand, paclitaxel had no effect on the phagocytic activity of macrophage when measured with RAW 264.7 cells and fluorescent beads. These results suggest that the immunosuppression by paclitaxel treatment may be mediated by the attenuation of cell cycle progression at G1 and G2 phases as well as by the diminishment of lymphokines responsible for immune responses.

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