5-(N-methylmaleimid-3-yl)-chromone, a novel microtubule inhibitor, exerts anti-proliferative effects in MDR cancer cells and cancer stem cells

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Abstract

Background and Purpose: The success of cancer chemotherapy is limited by multidrug resistance (MDR), which is mainly caused by P-glycoprotein (P-gp) overexpression. In the present study, we describe a novel microtubule inhibitor, 5-(N-methylmaleimid-3-yl)-chromone (SPC-160002), that can be used to overcome MDR. Experimental Approach: Key Results: A synthetic chromone derivative, SPC-160002, showed a broad spectrum of anti-proliferative effects on various human cancer cells without affecting P-gp expression and its drug efflux function. Treatment with SPC-160002 arrested the cell cycle at the M phase, as evidenced using fluorescence-activated cell sorting analysis, and increased the levels of mitotic marker proteins, including cyclin B, pS10-H3, and chromosomal passenger complex. This mitotic arrest by SPC-160002 was mediated by promoting and stabilizing microtubule polymerization, similar to the mechanism observed in case of taxane-based drugs. Furthermore, SPC-160002 suppressed the growth and sphere-forming activity of cancer stem cells. Conclusion and Implications: Our data herein strongly suggest that SPC-160002, a novel microtubule inhibitor, can be used to overcome MDR and can serve as an attractive candidate for anticancer drugs.

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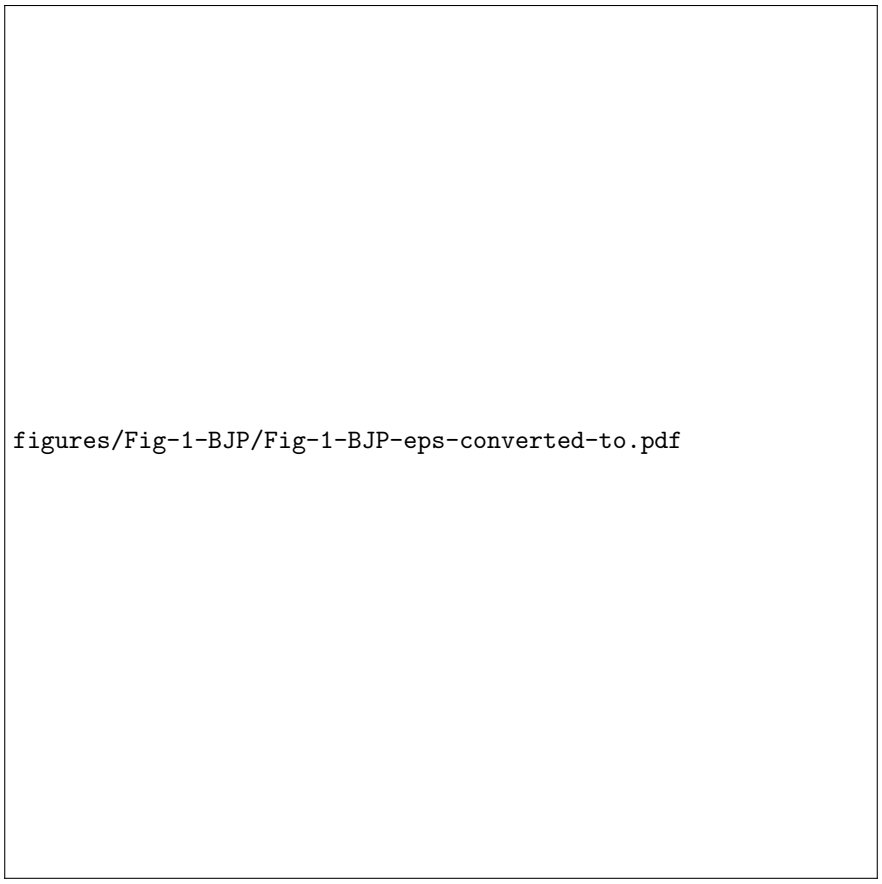

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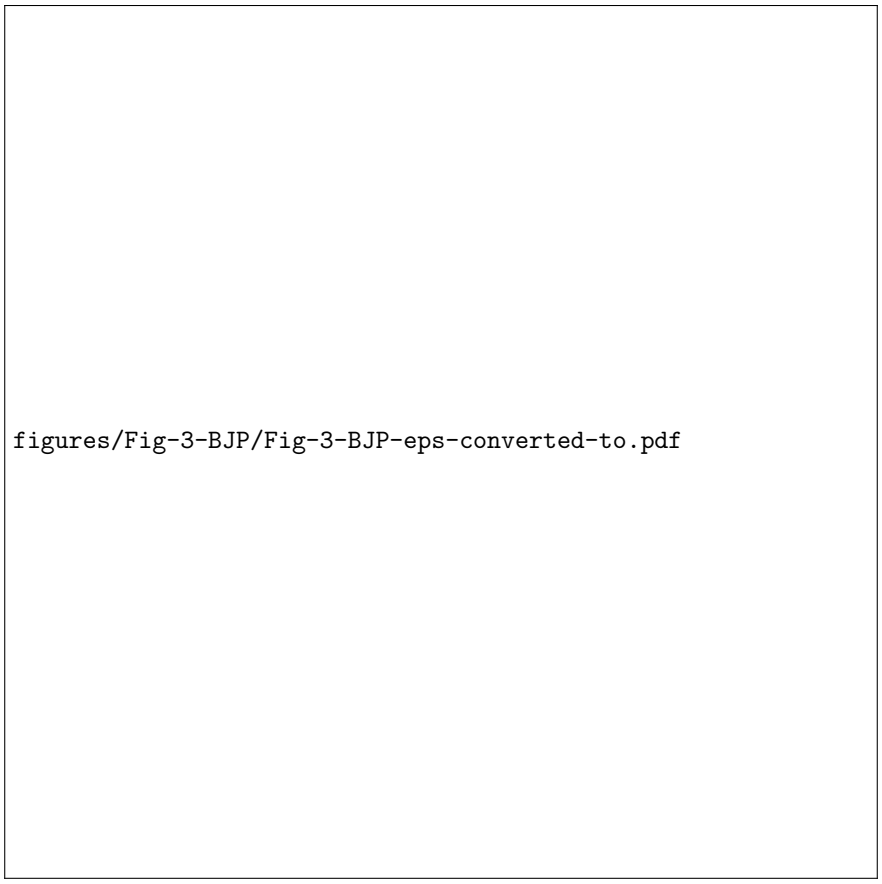

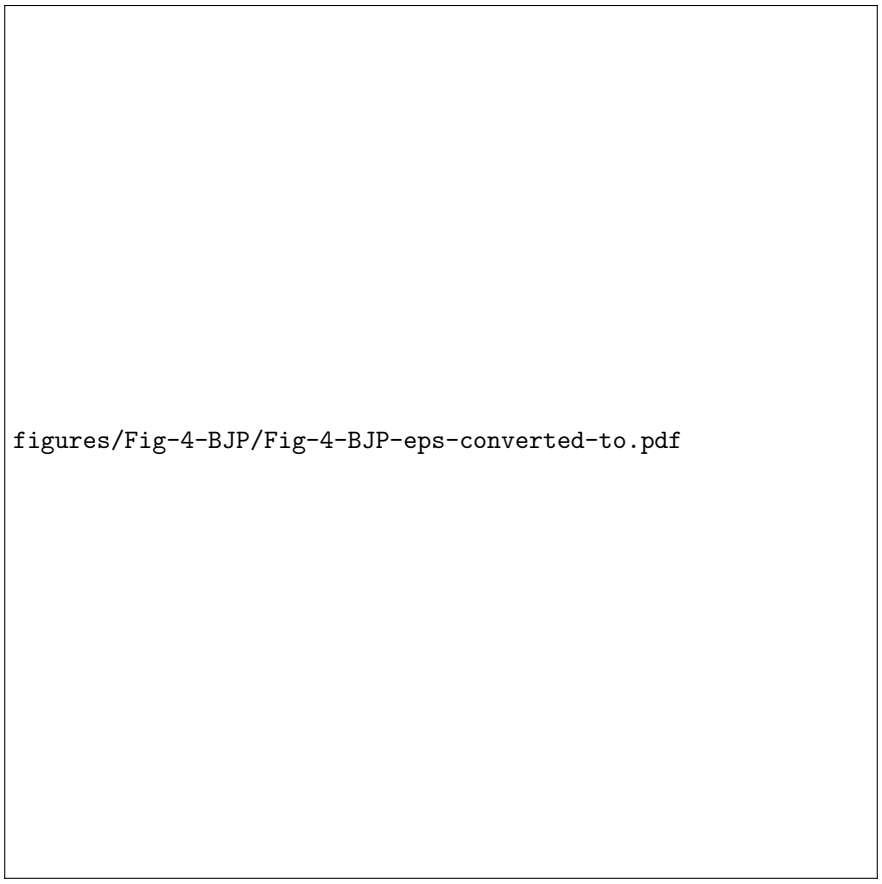

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