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Bromocriptine Reverses P-Glycoprotein-mediated Multidrug Resistance in Tumor Cells

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This strudy evaluated whether bromocriptine, a D_2 dopaminergic receptor agonist, influenced anticancer drug cytotoxicity and P-glycoprotein activity in a P-glycoprotein-expressing cell line compared to a non-expressing subline. The Ki values for P-glycoprotein of cyclosporine and verapamil were 1.09 and 540 μM, respectively, and that of bromocriptine was 6.52μM in a calcein-AM efflux assay using porcine kidney epithelial LLC-PK1 and L-MDR1 cells, overexpressing human P-glycoprotein. Bromocriptine at 10 μM reduced the IC_{50} of doxorubicin in K562-DXR from 9000 to 270 ng/ml and that of vincristine in K562-VCR from 700 to 0.30 ng/ml, whereas the IC_{50} values of doxorubicin and vincristine in the K562 subline were only marginally affected by these drugs. These observations suggest that bromocriptine has the potential to reverse tumor multigrug resistance involving the efflux protein P-glycoprotein in the clinical situation.