Dipyridamole induces apoptosis by inhibiting Akt activation in rat mesangial cells

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Abstract

Dipyridamole (persantin) is a nucleoside transport inhibitor and a non-specific phosphodiesterase inhibitor that increases intracellular levels of cAMP and cGMP through phosphodiesterase inhibition. Dipyridamole has been demonstrated to have an antiproliferative effect in glomerular mesangial cells. In the present study, we have confirmed that exposure of the mesangial cells to dipyridamole decreases the number of viable cells, as demonstrated by MTT assay. Dipyridamole suppressed [(superscript 3)H] thymidine incorporation into DNA and the reduction of viable cells are not due to toxicity because the LDH release from mesangial cells does not increase. Treatment of mesangial cells with dipyridamole arrests cell-cycle progression and increases the cell population at the sub G1 phase. Furthermore, incubation of mesangial cells with dipyridamole for 48 h induces characteristic features of apoptosis. The induction of mesangial cell apoptosis is correlated with Akt/PKB dephosphorylation and Bcl-2 down regulation. These data suggest that dipyridamole may block Akt/PKB phosphorylation and play a crucial role in the induction of apoptosis in rat mesangial cells.