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Critical Role of Jnk and P38Mapk Pathway on Sodium Butyrate-Induced Apoptosis in DU145 Human Prostate Cancer Cell

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Sodium butyrate (NaBu) is known to exhibit anticancer effects through the differentiation and apoptosis on various carcinoma cells. However, the mechanism by which NaBu induced apoptosis and the involvement of protein kinases during apoptosis is not completely understood. To gain an insight into the underlying pathways, we performed cell culture experiments in androgen-independent human prostate cancer, DU145 cells, focusing on various protein kinases. NaBu causes concentration-dependent cell detachment and growth inhibition (IC50 » 4.9 mM). The 24-hr exposure of NaBu to DU145 cells caused strong apoptotic effect with 26% nuclear fragmentation and condensation. In consistent, NaBu induced caspase 3 and poly ADP-ribose polymerase (PARP) cleavage and up-regulation of bax, apoptotic protein, suggesting that mitochondrial damage is involved in NaBu-induced caspase-dependent apoptosis. Interestingly, NaBu stimulated p38 mitogen-activated protein kinase (MAPK) and c-Jun NH2-terminal kinase (JNK) activation, but not extracellular signal-regulated kinase 1/2 (ERK1/2) activation during apoptosis. Furthermore, NaBu up-regulated total protein levels and phsopho-forms of MAPK kinase 3 (MKK3) and MKK4 as the upstream kinases of p38 MAPK and JNK independent of oxidative stress. It is suggested that NaBu can be a promising chemopreventive agent for prostate cancer and p38 MAPK and JNK pathways have critical roles on NaBu-induced apoptosis in DU145 cells.

Keyword : Sodium butyrate (NaBu)-prostate cancer- JNK- p38 MAPK- apoptosis