# Apoptosis signal-regulating kinase 1 mediates denbinobin-induced apoptosis in human lung adenocarcinoma cells

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摘要

**Abstract**

In the present study, we explore the role of apoptosis signal-regulating kinase 1 (ASK1) in denbinobin-induced apoptosis in human lung adenocarcinoma (A549) cells. Denbinobin-induced cell apoptosis was attenuated by an ASK1 dominant-negative mutant (ASK1DN), two antioxidants (N-acetyl-L-cysteine (NAC) and glutathione (GSH)), a c-Jun N-terminal kinase (JNK) inhibitor (SP600125), and an activator protein-1 (AP-1) inhibitor (curcumin). Treatment of A549 cells with denbinobin caused increases in ASK1 activity and reactive oxygen species (ROS) production, and these effects were inhibited by NAC and GSH. Stimulation of A549 cells with denbinobin caused JNK activation; this effect was markedly inhibited by NAC, GSH, and ASK1DN. Denbinobin induced c-Jun phosphorylation, the formation of an AP-1-specific DNA-protein complex, and Bim expression. Bim knockdown using a bim short interfering RNA strategy also reduced denbinobin-induced A549 cell apoptosis. The denbinobin-mediated increases in c-Jun phosphorylation and Bim expression were inhibited by NAC, GSH, SP600125, ASK1DN, JNK1DN, and JNK2DN. These results suggest that denbinobin might activate ASK1 through ROS production to cause JNK/AP-1 activation, which in turn induces Bim expression, and ultimately results in A549 cell apoptosis