

Abstract

MST1 kinase is an internal part of the Hippo signal pathway. The Hippo pathway is an evolutionary conserved regulator of tissue and organ growth and affects proliferation and apoptosis. Active MST1 kinase phosphorylates YAP and TAZ oncoproteins, which regulate the activity of transcription factors in their unphosphorylated state, including TEAD and SMAD. Furthermore active MST1 kinase phosphorylates FOXO transcription factors and induces their translocation into the cell nucleus. Finally the activation of MST1 kinase leads to cell apoptosis or halt cell cycle in G1 phase. Activation of MST1 protein depends on its auto-phosphorylation and cleavage. Recently, there are several articles which take interest in the issue of activation of MST1. Some of them describe the activation of MST1 by the effector caspase-3 and -7, on the other hand the latest articles argue that MST1 kinase itself is responsible for the activation of caspases. The molecular mechanism of MST1 kinase activation was studied in this bachelor thesis. We used the biologically active compounds GDC-0941 for the activation of MST1 protein. The activity of caspase was inhibited by specific inhibitor Z-DEVD. Using electrophoresis and Western blot it was demonstrated that MST1 is active in the case when caspases are inhibited. This fact points to the possible role of other protease in the process of activation of MST1 kinase.

(In Czech)

Keywords: MST1 kinase, caspase, leukemia, cell death