

Mammalian sterile20-like kinase 1 (Mst1) exerts its tumor suppressor function through its downstream effector peroxiredoxin 1

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The mammalian Ste20-like kinase 1 (Mst1) is a serine/threonine protein kinase that plays an important role in various biological processes, such as, cell proliferation, apoptosis and cell motility. Recently, Mst1 has become a subject of intense investigation, as it has been shown to have tumor suppressor activity. Despite this interest, little is known about the mechanism by which it exerts its tumor suppressor function. Using two independent protein interaction screens, we show that Mst1 associate, in an oxidation-dependent manner, with Prdx1, an enzyme that regulates the cellular redox state by reducing hydrogen peroxide to water and oxygen. Mst1 inactivates Prdx1 by phosphorylating it at T90 and -183, leading to accumulation of hydrogen peroxide in cells. Our results suggest that by sustaining high oxidant level in cells exposed to high H2O2, Mst1 might induce apoptosis and promote its tumor suppressor function.

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