# Kurarinone induced p53-independent G0/G1 cell cycle arrest by degradation of K-RAS via WDR76 in human colorectal cancer cells

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Kurarinone (KR), a naturally occurring flavonoid in Sophora flavescens Aiton and a traditional herbal medicine, reportedly has anti-cancer activity against various cancer types both in vitro and in vivo. However, the cellular mechanism of KR remains unknown. Therefore, we aimed to elucidate the mechanism of cell cycle arrest induced by KR in human colorectal cancer cells. KR not only reduced cell proliferation but also induced G0/G1 arrest of colorectal cancer cell lines. The results of western blotting analysis showed that KR reduced the protein levels of cyclin D1/D3 and CDK4/6 by downregulating signaling proteins such as K-RAS, c-MYC, and p-extracellular signal-regulated kinase. Additionally, KR arrested the cell cycle in the G0/G1 phase in a p53-independent manner, and decreased the protein level of K-RAS by proteasomal degradation dependent on WDR76, an E3 ubiquitin ligase. From these results, we propose that KR could be a potent anti-cancer agent, acting through the degradation of K-RAS dependent on WDR76, regardless of the p53 status.