Abstract

53BP2 was initially identified as a protein interacting with p53 in a yeast two-hybrid screen and subsequently shown to enhance p53 transcriptional transactivation and induce apoptosis when transiently overexpressed in cell lines. In order to further study the biologically relevant effects of 53BP2, we have constructed HEK293 stable cell lines where 53BP2 expression can be regulated using an ecdysone inducible expression system. Our results indicate that the response of cells is dependent on the amount of 53BP2 that is expressed. High levels of 53BP2 expression (>or=140-fold above endogenous) impede cell cycle progression and induce apoptosis. Lower levels of 53BP2 expression (6-11-fold above endogenous) suppress colony formation but do not lead to detectable perturbations in the cell cycle or apoptosis. Lower levels of 53BP2 expression sensitized cells to apoptosis induced by DNA damaging chemotherapy agents doxorubicin, ara-C and VP16, but not microtubule active agents paclitaxel and vinblastine. Our results demonstrate that high levels of 53BP2 expression have profound biological effects ultimately leading to apoptosis, whereas lower levels of 53BP2 expression have more subtle effects on growth and sensitize cells to some chemotherapy agents.