Yoshio Miki

１.Topic in Research Achievements in the Year 2006

The p53 tumor suppressor is activated in the cellular response to genotoxic stress. Transactivation of p53 target genes dictates cell cycle arrest and DNA repair or induction of apoptosis; however, a molecular mechanism responsible for these distinct functions remains unclear. Recent studies revealed that phosphorylation of p53 on Ser46 was associated with induction of p53AIP1 expression, resulting in the commitment of the cell fate into apoptotic cell death. Moreover, upon exposure to genotoxic stress, p53DINP1 was expressed and recruited a kinase(s) to p53 that specifically phosphorylated Ser46. Here, we show that the pro-apoptotic kinase, protein kinase C (PKC), is involved in phosphorylation of p53 on Ser46. PKC -mediated phosphorylation is required for the interaction of PKC with p53. The results also demonstrate that p53DINP1 associates with PKC upon exposure to genotoxic agents. Consistent with these results, PKC potentiates p53-dependent apoptosis by Ser46 phosphorylation in response to genotoxic stress. These findings indicate that PKC regulates p53 to induce apoptotic cell death in the cellular response to DNA damage. Inhibition of PKCd is associated with attenuation of p53 expression. Analysis of the deletion mutant demonstrates that p53 core promoter element (-70-46) is responsible for PKCd-mediated induction of p53 expression in response to DNA damage. PKCd may regulate p53 expression at a transcriptional level by activation of an unidentified transcription factor through p53 core promoter element.

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３. Abstracts in the year 2006

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