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PAC-p53 interactions

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Tudor P Toma
Email: t.toma@imperial.ac.uk

The tumor suppressor protein p53 has a role in cellular apoptosis through the transcriptional regulation of several target genes, including PAC1 (phosphatase of activated cells 1) which inactivates mitogen-activated protein (MAP) kinases. However, the molecular mechanisms of interaction between p53 and PAC1 have been unclear. In the April 3 Nature, Yuxin Yin and colleagues at Columbia University, New York, show that under specific stress conditions, p53 regulates transcription of PAC1 through a novel p53-binding site, and that PAC1 is necessary and sufficient for p53-mediated apoptosis (*Nature*, **422:**527-531, April 3, 2003).

Yin *et al.* used a p53-inducible system comprising EB-1 cells derived from a human colon cancer with mutant p53. They observed that PAC1 transcription was induced in these cells in response to serum deprivation and oxidative stress, resulting in p53-dependent apoptosis. Using small interfering RNA they reduced PAC1 transcription and observed an inhibition of p53-mediated apoptosis. Overexpression of PAC1 increased susceptibility to apoptosis and suppressed tumor formation. In addition, they showed that activation of p53 significantly inhibits MAP kinase activity.

"We demonstrate here that p53 uses a palindromic binding site to regulate its target gene PAC1. The identification of this mechanism for p53 action will provide insights into the molecular basis of how p53 selectively regulates its target genes to eliminate cancer cells and suppress tumorigenesis", conclude the authors.

References

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