PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

pRB repression in yeast

ArticleInfo		
ArticleID	:	4158
ArticleDOI	:	10.1186/gb-spotlight-20010725-01
ArticleCitationID	:	spotlight-20010725-01
ArticleSequenceNumber	:	229
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	2
ArticleHistory	:	RegistrationDate : 2001–07–25 OnlineDate : 2001–07–25
ArticleCopyright	:	BioMed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	130592211

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The retinoblastoma protein (pRB) is a tumor suppressor protein that can act as a transcriptional repressor, but the mechanisms underlying this function are unclear and controversial. In the July 17 Proceedings of the National Academy of Sciences, Kennedy *et al.*, from the Massachusetts General Hospital Cancer Center, describe the use of a yeast model system to address the mechanism of pRB repression (*Proc Natl Acad Sci USA* 2001, **98:**8720-8725). They expressed a chimeric protein in which the large pocket domain of mammalian pRB was fused to the DNA binding (DB) domain of the yeast Gal4p factor. The DB-pRB protein could repress expression of a *HIS3* reporter gene under the control of a promoter containing Gal4p binding sites. A tumor-derived pRB mutant lacking exon 22 failed to repress *HIS3* expression. However, another mutant pRB protein that is defective in binding to LXCXE-containing proteins retained transcriptional repression in yeast. Experiments in mutant yeast strains showed that pRB repression required an intact *RPD3* histone deacetylase gene and the RbAp48 ortholog *MSI1*, but not *SIN3* or *SAP30* activities. The authors propose that, MSI1 mediates recruitment of histone deacetylases to the pRB protein for trascriptional repression.

References

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2. *Proceedings of the National Academy of Sciences*, [http://www.pnas.org]

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