Cell cycle and chromatin control by nuclear small G protein Ran

Naoyuki Hayashi and Ken-ichi Yamamoto

The Ran GTPase system regulates the direction and timing of several cellular events, such as nuclear-cytosolic transport, centrosome formation, and nuclear envelope assembly in telophase. Most nuclear Ran localizes to chromatin, by both RCC1-dependent and independent mechanisms. However, Ran's functions on chromatin and for cell cycle are poorly understood. To gain insight into the Ran system's involvement in chromatin formation, we investigated gene silencing at the telomere in several mutants of the budding yeast, which had defects in genes involved in the Ran system. A temperature-sensitive (Ts) mutation of the RanGAP gene, *rna1-1*, caused reduced silencing at the telomere, assessed by observing the expression of a *URA3* marker inserted at the telomere, and Ts mutations of yeast Ran homologue, *gsp1-1268* and *gsp1-1757*, increased this silencing. In the *rna1-1* mutant, hyperphosphorylated Sir3 protein accumulated. This reduced telomere silencing in *rna1-1* cells was suppressed by a high dosage of the *SIR3* gene. These results suggest that active Ran GTPase opens the heterochromatin structure at the telomere in yeast.
In cell cycle studies using *gsp1* mutants, we found suppression to the hydroxyurea (HU) and ultra violet (UV) sensitivities of the *mec1* mutant, which lacks one of the two ATM family kinases. In UV-irradiated *mec1 gsp1* cells, Rad53 was phospholyrated despite the lack of Mec1. This suppression of the *mec1* phenotype depended on the *TEL1* gene, which encodes the other of the ATM family kinases, given that the triple mutant, *mec1 gsp1 tel1*, was unable to grow. These results indicated that Rad53 was activated by Tel1 in *mec1 gsp1* cells, suggesting that Gsp1 helps regulate the role switching of the ATM family kinases Mec1 and Tel1.

Reference

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