CDB SEMINAR

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Ran-GTP dependent microtubule stabilization which is involved in spindle assembly

Summary

In mitosis, proper spindle assembly is crucial for exact chromosome segregation into two daughter cells. The GTP bound form of small GTPase Ran has been shown to be important for spindle assembly. Because the guanine nucleotide exchange factor for Ran is localized on chromosomes, Ran-GTP is locally generated around chromosomes in mitosis and induces several local effects. Ran-GTP is known to stabilize and elongate microtubules. We are analyzing how Ran-GTP stabilizes microtubules and found that the complex of importin alpha and beta is the specific inhibitor for the microtubule stabilization effect. The stabilization factor is expected to be a protein bearing NLS (Nuclear Localization Signal) domain. We originally established an affinity purification method to prepare the NLS-proteins. Because the fraction of NLS-proteins has microtubule stabilization activity, the activity was purified by conventional chromatography. The proteins in the purified active fraction were identified by mass spectrometry. RGAMSF (Ran-GTP activated microtubule stabilization factor) 1 was found in it. Recombinant RGAMSF1 showed microtubule stabilization activity and the activity could be regulated by Ran-GTP and importins. When RGAMSF1 was depleted from Xenopus mitotic extracts, however, proper spindle still could be assembled in the depleted extract. Therefore, we propose that RGAMSF1 is one of the microtubule stabilization factors activated by Ran-GTP.

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