Function of RanBP and RanGAP in the dissociation of nuclear transport complexes

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Ran•GTP is required to assemble export complexes, which are resistant to stimulated nucleotide hydrolysis by RanGAP [1]. The same applies for Ran-import receptor complexes which are recycled into the cytoplasm. This inhibition of hydrolysis is probably due to steric reasons, as it is known for import receptor complexes like Ran•Importin β and Ran•transportin [2,3]. In the presence of RanBPs, however, Ran•GTP dissociates from the transport receptor and becomes accessible to inactivation by RanGAP [4]. The structure of a Ran complex with RanBD1 has shown that RanBPs can sequester the acidic C-terminal DEDDDL motif of Ran, a function that was proposed to facilitate the dissociation of transport receptor complexes [5]. We have now solved the structure of a complex of Importin β, Ran and RanBP corresponding to a potential dissociation intermediate.

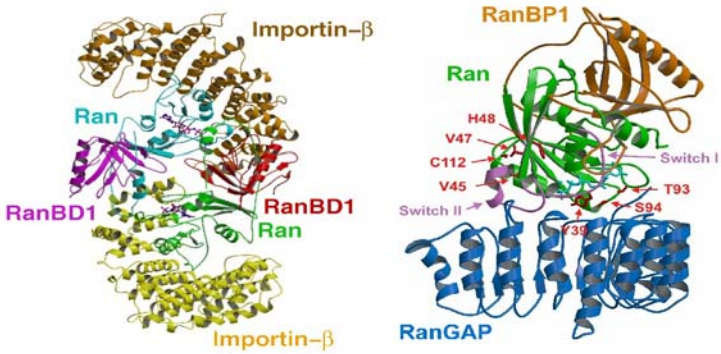

Figure 1: Structures of the Importin-β-Ran-RanBD1 complex and the RanGAP-Ran-RanBP1 complex. The latter shows the fluorescence-labelled cysteine mutations.

The next step of the dissociation process is the RanGAP-stimulated nucleotide hydrolysis in Ran. We solved the three-dimensional structure of a Ran•RanBP1•RanGAP ternary complex [7]. To address the question of the RanBP1-function and of the acidic tail of RanGAP, we re-investigated the reaction kinetics using fluorescence spectroscopy [8]. Additional genetic experiments in *S. cerevisiae* demonstrate a profound effect of the acidic tail on the microtubule organization during mitosis.

References

[1] D. Görlich & U. Kutay, Annu. Rev. Cell. Dev. Biol. **15**, 607-660 (1999).
[2] Y.M. Chook, G. Blobel, Nature **399**, 230 (1999).
[3] I.R. Vetter, A. Arndt, U. Kutay, D. Görlich, A. Wittinghofer, Cell **97**, 635-646 (1999).
[4] U. Kutay et al., Molecular Cell **1**, 359-369 (1998).
[5] I.R. Vetter, C. Nowak, T. Nishimoto, J. Kuhlmann, A. Wittinghofer, Nature **398**, 39 (1999).
[7] M.J. Seewald, C. Körner, A. Wittinghofer, I.R. Vetter, Nature **415**, 662-666 (2002).
[8] M.J. Seewald, A. Kraemer, M. Farkasovsky, C. Körner, A. Wittinghofer, I.R. Vetter, MCB **23**, 8124-8136 (2003).