Cellular and Molecular Life Sciences

January 2013, Volume 70, Issue 2, pp 357-371

Autoinhibition of TBCB regulates EB1-mediated microtubule dynamics

Gerardo Carranza (1), Raquel Castaño (1), Mónica L. Fanarraga (1), Juan Carlos Villegas (9), João Gonçalves (2,3,4,8), Helena Soares (2,3,4), Jesus Avila (5), Marco Marenchino (6), Ramón Campos-Olivas (6), Guillermo Montoya (7), Juan Carlos Zabala (1)

Abstract

Tubulin cofactors (TBCs) participate in the folding, dimerization, and dissociation pathways of the tubulin dimer. Among them, TBCB and TBCE are two CAP-Gly domain-containing proteins that together efficiently interact with and dissociate the tubulin dimer. In the study reported here we showed that TBCB localizes at spindle and midzone microtubules during mitosis. Furthermore, the motif DEI/M-COO− present in TBCB, which is similar to the EEY/F-COO− element characteristic of EB proteins, CLIP-170, and α-tubulin, is required for TBCE–TBCB heterodimer formation and thus for tubulin dimer dissociation. This motif is responsible for TBCB autoinhibition, and our analysis suggests that TBCB is a monomer in solution. Mutants of TBCB lacking this motif are derepressed and induce microtubule depolymerization through an interaction with EB1 associated with microtubule tips. TBCB is also able to bind to the chaperonin complex CCT containing α-tubulin, suggesting that it could escort tubulin to facilitate its folding and dimerization, recycling or degradation.

Topics: Cell Biology; Biomedicine general; Life Sciences, general; Biochemistry, general

Cover Date – 2013-01-01

DOI: 10.1007/s00018-012-1114-2

Print ISSN 1420-682X

Online ISSN 1420-9071

Publisher: SP Birkhäuser Verlag Basel

Author Affiliations

1. Departamento de Biología Molecular, Facultad de Medicina, IFIMAV-Universidad de Cantabria, 39011, Santander, Spain

9. Departamento de Anatomía y Biología Celular, Facultad de Medicina, IFIMAV-Universidad de Cantabria, 39011, Santander, Spain

2. Centro de Química eBioquímica, Faculdade de Ciências, Universidade de Lisboa, 1749-016, Lisbon, Portugal

3. Instituto Gulbenkian de Ciência, Ap. 14, 2781-901, Oeiras, Portugal

4. Escola Superior de Tecnologia, Saude de Lisboa, 1990-096, Lisbon, Portugal

8. Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Room 1070, Toronto, ON, M5G 1X5, Canada

5. Centro de Biología Molecular (CSIC-UAM), Universidad Autónoma de Madrid, 28049 Cantoblanco, Madrid, Spain

6. Spectroscopy and NMR Unit, Structural Biology and Biocomputing Program, Spanish National Cancer Research Center (CNIO), Melchor Fdez. Almagro 3, 28029, Madrid, Spain

7. Macromolecular Crystallography Group, Structural Biology and Biocomputing Program, Spanish National Cancer Research Center (CNIO), Melchor Fdez. Almagro 3, 28029, Madrid, Spain