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Modulation of microtubule organization, microtubule proteins



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Research topics

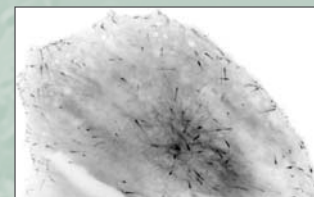
The long-term research programme of the laboratory has been focused on studying the structure-function relationships of microtubule (MT) proteins and their interactions with other cytoskeletal elements in cells under normal and pathological conditions. The organization of MT networks is controlled by microtubule organizing centres (MTOCs). One of the key components of MTOCs is γ -tubulin, which is necessary for nucleation of MT. There are cumulative data indicating that γ -tubulin could also have other functions. Current work focuses on the understanding of the function of γ -tubulin forms, modulation of MT properties by signal transduction molecules, and molecular and functional characterization of MTOC components. To address these questions, techniques of molecular biology, biochemistry and immunology are being used, as well as a variety of microscopic techniques, including live cell imaging. Our results demonstrate that non-receptor protein tyrosine kinase Fyn of the Src family and phosphoinositide 3-kinase play an important role in MT nucleation from membranes. We have also shown that ectopic cellular expression of γ -tubulin in gliomas may serve as a novel marker of anaplastic changes. Finally, we have identified class III β -tubulin, which is regarded as a neuronal marker, in primary cultures of astrocytes expressing GFAP and nestin.

Current grant support

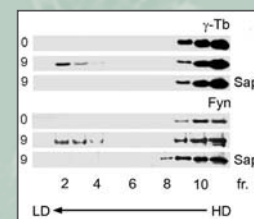
Ministry of Education, Youth and Sports (Center of Cell Functional Organization, LC545); GA CR (GD204/05/H023), GA AS CR (KAN200520701)

Selected recent papers

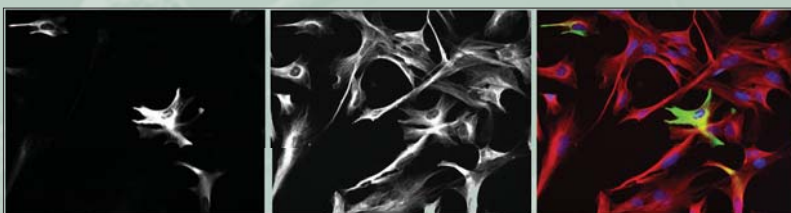
1. Sulimenko V, Dráberová E, Sulimenko T, Macůrek L, Richterová V, Dráber P, Dráber P. Regulation of microtubule formation in activated mast cells by complexes of γ -tubulin with Fyn and Syk kinases. *J Immunol.* 2006;176:7243-7253.
2. Katsetos CD, Reddy G, Dráberová E, Šmejkalová B, Del Valle L, Ashraf Q, Tadevosyan A, Yelin K, Maraziotis T, Mishra OP, Mörk S, Legido A, Nissanov J, Baas PW, de Chadarévian JP, Dráber P. Altered cellular distribution and subcellular sorting of γ -tubulin in diffuse astrocytic gliomas and human glioblastoma cell lines suggest centrosome protein amplification. *J Neuropathol Exp Neurol.* 2006;65:465-477.
3. Dráberová E, Del Valle L, Gordon J, Marková V, Šmejkalová B, Bertrand L, de Chadarévian JP, Agamanolis DP, Legido A, Khalili K, Dráber P, Katsetos CD. Class III β -tubulin is constitutively co-expressed with GFAP and nestin in midgestational human fetal astrocytes in primary culture: comparative observations in the fetal brain and implications in phenotypic identity. *J Neuropathol Exp Neurol.* 2008;67:341-354.
4. Macůrek L, Dráberová E, Richterová V, Sulimenko V, Sulimenko T, Dráberová L, Marková V, Dráber P. Regulation of microtubule nucleation in differentiating embryonal carcinoma cells by complexes of membrane-bound γ -tubulin with Fyn kinase and phosphoinositide 3-kinase. *Biochem J.* 2008;416:421-430.



Growing ends of microtubules detected by EB1-GFP in U2OS cells (TIRF microscopy)



Distribution of γ -tubulin and Fyn kinase during density gradient centrifugation of lysates from resting (0) and retinoic acid-differentiated (9) P19 cells (Sap, lysates with cholesterol-depleting agent saponin)



Distribution of glial fibrillary acidic protein (green) and class III β -tubulin (red) in primary culture of foetal astrocytes