Irith Ginzburg

Leah Behar
Roee Atlas
Jacob Blumenthal
Evan Elliott

Tau–microtubule associated protein: Regulation of expression and axonal localization in neuronal cells

Department of Neurobiology

Tel. 972 8 934 **2799** **Fax.** 972 8 934 **4131**
E-mail: Irith.ginzburg@weizmann.ac.il
Web page: www.weizmann.ac.il

The primary determinants that govern neurite outgrowth and differntiation of neurite into axons and dendrites are yet unknown. A major question concerning differentiation relates to the cellular mechanisms responsible for the establishment of neuronal polarity in which the cytoskeleton is involved. The difference between the dendritic and axonal cytoskeleton depends on segregation of tau- MAP into the axon, which results from tau mRNA localization and local translation in the axon. Recent studies by us and others have demonstrated localization of different mRNAs in dendrites and in axons, where they are locally translated in response to various stimuli. This provides a functional mechanism for specific protein synthesis operating during development, plasticity, learning, and memory.

The tau transcript is trafficked in an RNA-protein complex (RNP) from the neuronal cell body to the distal parts of the axon and reaches as far as the growth cone. The RNP complex containing tau is anchored along the axon and at the growth cone in a non-translated state. Extracellular signals mediate the translation of the RNP complex mRNAs thus enabling the neuron an autonomous protein expression regulation at distal parts from the soma. Whereas the types of localized mRNAs vary, they share several common features. These include on cis-acting signals generally located within the 3'-untranslated region (3'UTR), the capacity to move on microtubules, and binding of trans-acting proteins thus forming RNP granules. Only a few of the granule components have so far been identified. One of the proteins situated in the RNP complex in the neuronal axon is the RNA binding protein HuD, which binds directly tau mRNA and functions in its stabilization. We have identified two new proteins associated with tau mRNA and HuD protein and are currently trying to elucidate their function in the tau RNP complex. This research will expand the knowledge on RNA regulation and protein translation control in the distal parts of the axon in neurons.

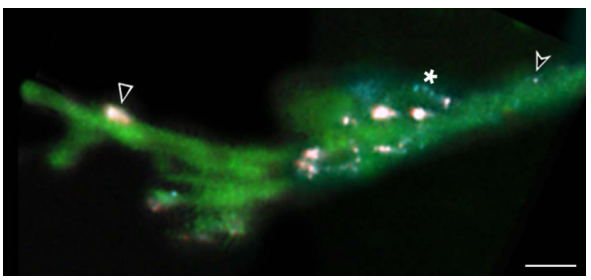

Fig. 1 *Tau RNP granules are present in growth cone and colocalize on microtubules*

Selected Publications

Aronov S., G. Aranda, L. Behar. and I. Ginzburg (2001). Axonal tau mRNA localization coincides with tau protein in living neuronal cells J. Neurosci. 21, 6577-6587.

Aronov S., G. Aranda. and I. Ginzburg (2002). Visualization of translated tau protein in the axons of neuronal P19 cells and characterization of tau RNP granules. J Cell Sci. 115, 3817-3827.

Rosenmann H. and I, Ginzburg (2003). Regulation of Localization and Phosphorylation of Tau. Alzheimer's Disease and Related Disorders: Research Advances. Editors: Khalid Iqbal, Ph.D.Bengt Winblad, M.D., Ph.D. 286-298

Atlas R., Behar L., Elliott,E., and Ginzburg., I.(2004). The Insulin-like growth factor mRNA binding-protein IMP-1 and the Ras-regulatory protein G3BP associate with tau mRNA and HuD protein in differentiated P19 neuronal cells. J. of Neurochemistry. 89, 613-626.

Acknowledgements:

I.G. is the incumbent of the Sophie and Richard S. Richards Professorial Chair in Cancer Research. United States-Israel Binational Science Foundation (BSF).

Nella and Leon Benoziyo Center for Neuroscience , Shane Joseph D.