

BAG3 localizes in axonal structures during neuronal differentiation and is expressed in cellular processes of migrating cells in mouse cerebral cortex

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BAG3 protein belongs to the family of co-chaperones involved in protein quality control and in the clearance of misfolded proteins [1]. Few studies have addressed BAG3 distribution and function in the central nervous system (CNS) and little is known about the cellular localization of BAG3 during neuronal differentiation in vitro and migration in vivo. Therefore we analysed by immunofluorescence microscopy the cellular distribution of BAG3 in the PC12 cell model treated or not with NGF and in developing and adult cortex of mice brain. Our results shows that BAG3 localizes mainly in vesicle structures of the neuritic domain during cell differentiation, while in undifferentiated cells it appears confined to the cytoplasm near the nuclear membrane. These observations were corroborated by transmission electron microscopy (TEM) which revealed that in NGF-differentiated PC12 cells, BAG3 localizes into electron-dense vesicles clustered along the axon and showing the typical aspect of the large dense core vesicles (LDCVs). Interestingly, the change of BAG3 localization during neuronal differentiation was associated only to a slight increase in the total BAG3 immunoreactivity as shown by western blot analysis. In order to provide further insights on the role of BAG3 in neuronal differentiation and migration, we also analysed BAG3 localization in mice developing and adult cerebral cortex. In mouse developing cortex, BAG3 appeared to be intensely expressed in cellular processes of migrating cells, while in adult brain a low expression was detected in neuronal cell bodies and glial cells. In conclusion, our findings suggest that the presence and differential expression of BAG3 might be required for the correct development of the nervous system as well as for the maintenance of protein homeostasis.

References

[1] Merabova N et al. (2015) WW domain of BAG3 is required for the induction of autophagy in glioma cells. *J Cell Physiol* 230:831-841.

Keywords

BAG3, PC12 cells, neuronal differentiation, mouse cerebral cortex, confocal microscopy, transmission electron microscopy