

Mitochondrial expression of TASK-3 channels in human malignant melanoma cell lines and their role in cell survival and proliferation

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TASK-3 channels are expressed in several cell types including both healthy and malignantly transformed cells. The role of channel function in tumourigenesis has been proposed in different human cancers. In this work the distribution pattern of TASK-3 channel protein was investigated in cultured melanoma malignum cells and in non-malignant HaCaT keratinocytes using immunochemical methods. Before these experiments, the TASK-3 expression of melanoma cells was confirmed on mRNA level as well. The subcellular localization of the channel protein was found to be mainly intracellular, while the labelling of cell surface membrane was not significant. Double-labelling experiments revealed that the distribution of TASK-3 channels shows strong co-localisation with mitochondria in both investigated cell types. These results were confirmed by immunohistochemical staining of wax-embedded human skin tissue sections, where the same labelling pattern could be observed in melanocytes and keratinocytes as well.

Our findings suggested that TASK-3 channels are present in the mitochondrial membrane of melanoma cells, where they might contribute to mitochondrial function. It has been proposed earlier that they might provide greater hypoxia tolerance for tumour cells, which might contribute to cell survival and tumour growth, but the exact mechanism by which these effects are exerted is still unknown.

We investigated the significance of TASK-3 mitochondrial TASK-3 channels in cell viability by interfering with the function of the channel protein. Melanoma cells were transiently transfected with shRNA cassettes, and TASK-3 knockdown cell cultures were generated. The reduced expression of TASK-3 resulted in characteristic changes of the cell morphology, reduction of DNA content, decreased metabolic activity and impaired mitochondrial function. These changes indicate that TASK-3 channels expressed in the mitochondrial membrane may have crucial roles in maintaining the viability of melanoma cells. However, further experiments are needed to clarify whether the inhibition of TASK-3 channel function could be exploited in anti-cancer therapy.

Key words:

TASK-3 channel (TASK-3-csatorna)

melanoma (melanoma)

mitochondrion (mitokondrium)