The vacuolar ATPase subunit E controls apoptosis and is down-regulated in breast cancer

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Background:

Vacuolar H+ATPase (V-ATPase) is a multi-subunit proton pump involved in the acidification of a wide variety of organelles. Dysfunction of the V-ATPase has been associated with several diseases, including cancer. Increased V-ATPase activity is reported to be critical for invasion of highly metastatic breast cancer cells and its expression at the plasma membrane correlates with the invasive characteristics of various malignant cells. Functional expression cloning identified V- ATPase subunit E (ATP6V1E) as a potential apoptosis regulatory gene. The aims of this study were to examine the effects of modulating ATP6V1E expression on the survival of breast cancer cells. In addition, we have examined the expression level of ATP6V1E in breast cancer samples.

Materials and methods:

MCF7 and MDA-MB-231 cells were transfected either with a mammalian expression plasmid encoding ATP6V1E transcript, control cells received empty vector. Culture growth, cell viability, apoptosis, and long term survival were assessed. The level of ATP6V1E transcripts in breast cancer cDNA samples, from commercial Breast Cancer cDNA Arrays, was determined by qRT-PCR TaqMan® analysis.

Results:

Over-expression of ATP6V1E levels in both cell lines resulted in an increase in basal apoptosis level and a reduction in short and long term survival. ATP6V1E expression was found to be significantly down-regulated in breast cancer samples.

Conclusion:

The present data suggest that the ATP6V1E regulates apoptosis and cell survival in breast cancer cells. The pro-apoptotic effect exerted by a single subunit of V-ATPase is a novel observation. The reduced expression of ATP6V1E in breast cancer samples suggests that a decrease in the expression levels may be significant in oncogenesis.