

Sphingosine Kinase 1 (SK1-43kDa) isoform expression may contribute to cancer aggressiveness

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Introduction: Sphingosine kinase 1 (SK1) is a signaling enzyme that phosphorylates the lipid sphingosine to form sphingosine-1-phosphate (S1P), leading to enhanced cell proliferation. Overexpression of SK1 is causally associated with the progression and metastasis of many cancer types, hence making SK1 inhibitors promising anti-cancer therapies. Two major SK1 isoforms (SK143kDa and SK51kDa) have been identified in breast cancer cells, both exhibiting similar S1P activation. Each SK1 isoform interacts with both common and unique signaling partners and they have been shown to perform different cellular functions. Interestingly, the SK1-51kDa isoform is susceptible to protease degradation whereas the SK1-43kDa isoform is more stable (Yagoub et al., 2014). To date there are no reports on whether one, or both, of the isoforms are expressed in normal and cancer cells of different types. **Aims:** The aim of this project was to determine the SK1 isoform expression profile of different cancer cell types to determine the level of variation or similarity of isoform expression. **Methods:** Specific PCR primers were designed to identify a unique region of the 51kDa isoform and a region common to both isoforms. RNA was isolated from a number of human cancer cell lines including MCF-7 and T-47D breast cancer cells, U2OS osteosarcoma cells, U87-MG glioblastoma, DU-145, LNCaP, PC3 and VCaP prostate cancer cells and HCT-116 colon cancer cells. MCF-7 cells stably expressing the SK1-43kDa and -51kDa isoforms were used as controls. **Results:** All cancer cell lines tested to date show expression of the 43kDa isoform. Only the MCF-7 cells expressed both isoforms. Semi-quantitative analysis of SK1 expression revealed high 43kDa isoform expression in the highly aggressive glioma cells. **Conclusion:** In this report we have shown differential SK1-43kDa isoform expression levels dependent on cancer type, with only MCF-7 breast cancer cells expressing both isoforms. Given that the SK1-43kDa protein is less susceptible to degradation, and has constitutively high SK1 activity, it is speculated that the high levels of the SK1-43kDa isoform may contribute to the more aggressive cancer phenotype.

References

Yagoub, D., Wilkins, M. R., Lay, A., Kaczorowski, D. G., Hatoum, D., Bajan, S., Hutvagner, G., Lai, J. H., Wu, W., Martiniello-Wilks, R. McGowan EM. (2014). Sphingosine kinase 1 isoform-specific interactions in breast cancer. *Mol Endocrinol*, me20131423.