ABSTRACT

DWNN-deficient Chinese Hamster Ovary cells have been found to be resistant to staurosporine-induced apoptosis. The human DWNN gene is located on chromosome 16p21, with 18 exons and is 36 kb long. It is alternatively spliced at exon 16 and makes two major mRNA transcripts, 1.1 and 6.1 kb, encoding 13 kDa and 200 kDa proteins respectively. The purpose of the study was to elucidate the possible role of DWNN in cervical cancer and apoptosis, to establish tissue distribution and expression levels of DWNN at protein and mRNA levels in cervical cancer.

In situ hybridization studies showed elevated levels of the three mRNA transcripts in cervical cancer as compared to the normal tissues. The transcripts were localized in the nuclei of invaded stroma, moderately differentiated islands of tumours, dysplastic epithelium and some infiltrating lymphocytes. Immunocytochemistry showed that DWNN proteins were highly expressed in the dysplastic epithelium, dysplastic endocervical glands, moderately and well differentiated islands of tumours and the invaded stroma. Image analysis indicated elevated expression levels in the islands of tumours. Apoptosis detection by TUNEL revealed high apoptotic levels in the invaded stroma and moderately differentiated islands of tumours and this significantly correlated with DWNN localization. Proliferation assay using Ki67 antibody was found to be indirectly directly proportional to DWNN expression. Antiapoptotic Bcl-2 expression levels were found to be inversely proportional to the expression levels of DWNN.

The up-regulated levels of DWNN in cervical cancers in contrast to normal tissues suggest DWNN to be proapoptotic, as there were elevated levels of apoptosis in the same sites where there were high levels of DWNN expression and Bcl-2 was down-regulated in the same sites. DWNN expression significantly correlated with apoptotic levels and was indirectly proportional to ki67 in human cervical cancers. Real Time PCR also confirmed the up-regulation in levels of DWNN in cervical cancer.

This study suggests that the DWNN gene may be involved in apoptosis. Further characterization of this gene could lead to its manipulation as a diagnostic marker and a potential therapeutic target for cancer treatment.