N-MYC DOWNSTREAM REGULATED GENE 1 (*NDRG1*) EXPRESSION AND LOCALIZATION IS TUMOUR GRADE DEPENDENT IN OESOPHAGEAL CANCER.

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Abstract

Differentially expressed genes in oesophageal cancer tissue were identified by differential display reverse transcription polymerase chain reaction (DDRT-PCR) using malignant and corresponding normal tissue of the same patient. Differentially expressed gene fragments were isolated, cloned, sequenced and their homologous sequence identified in GenBank using BLAST. *NDRG1* was identified as one of the genes down regulated in tumour tissue and confirmed by Northern blot analysis. Immunohistochemical studies using a larger patient sample revealed that NDRG1 expression and localization was tumour grade dependent. Whereas the protein was exclusively located either in the membrane, nucleus or cytoplasm in normal oesophageal epithelial cells, it was exclusively found in the membrane in dysplastic and poorly differentiated tumour cells. Well-differentiated tumour cells exhibited membrane, cytoplasmic and mixed (cytoplasmic and nuclear) but not exclusive nuclear localization. Based on the difference on cellular localization of the protein, it is possible to distinguish normal oesophageal epithelial cells from tumour cells. In addition, the distinct localization of the protein in the different tumour grades suggests the NDRG1 protein is potentially a useful marker for distinguishing some of the tumour grades. This is the first study to report on the relationship between NDRG1 protein expression and cellular localization in cancer and provides the basis for this gene as a potential candidate biomarker in cancer of the oesophagus.