Correlation between apoptosis and DWNN expression in lung cancer.

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DWNN (domain with no name) is a novel gene that has been linked previously to apoptosis as one of ubiquitin protein ligases which play a significant role in the pathogenesis of many human diseases through deregulation of targeted proteolysis, of which lung cancer is no exception. Lung cancer is the leading cause of cancer in South Africa and worldwide, accounting for 17% of all cancer death. The pathogenesis of lung cancer involves the accumulation of multiple molecular abnormalities which resulted from DNA mutations. These mutations result in the activation of proto-oncogenes (such as k-ras and c-myc), Rb and p53 genes which are involved in apoptosis. Since the DWNN gene has been linked to apoptosis this study was designed to determine a possible correlation between DWNN expression and apoptosis levels in lung cancers.

Materials and methods: RNA probes complimentary to all DWNN transcripts were synthesized and labelled with (Digoxigenin) DIG. For mRNA localization, flourimetric in situ hybridization (FISH) was performed on Paraffin-embedded sections of normal and cancerous lung tissues. Imunocytochemistry (ICC) was carried out on sections that were coated with a primary antibody raised against the DWNN protein, and counterstained with Mayers hematoxylin. TUNEL was labelled in order to identify sites of apoptosis. The results were viewed under brightfield microscopy, and the images captured with a Zeiss camera.

Results: The overall results of FISH showed DWNN mRNA localization in both the cytoplasm and to a lesser extent in the nuclei of the small cell, poorly differentiated and pulmonary adeno- carcinomas. DWNN 1.1 kb and 6.1 kb mRNA were localized in the mainly in the cytoplasm of the glandular tumour cells of adenosquamous carcinomas, in the alveolar columnar cells of the bronchioloalveolar carcinomas and in the bronchial mucosa cells of giant cell and squamous cell carcinomas. ICC showed upregulation of the DWNN protein in the bronchial mucosa of adenosquamous, and giant cell carcinomas, and carcinoma *in situ*. In the normal bronchial mucosal cell there was localization of the mRNA in the both nuclei and cytoplasm but the protein expression was not upregulated. TUNEL showed increased levels of apoptosis in squamous-, giant- and the small-l cell carcinomas.

Discussion: DWNN mRNA and protein were upregulated in lung cancer as compared to normal tissues (too vague you state the cells that are involved; the upregulation was mostly seen in the cytoplasm and less in the nuclei (of which cells?) because large amount of both mRNA and the protein are localized in the cytoplasm. The regulation levels of DWNN mRNA and proteins correlated with the levels of apoptosis.

Conclusion: This study provides descriptive evidence for the involvement of the DWNN gene in tumourigenic apoptosis.