Characterization of the Domain With No Name gene in colon cancer

Charleen Rupnarain and Zodwa Dlamini

School of Molecular and Cell Biology, University of the Witwatersrand

Knockouts of the Domain With No Name (DWNN) gene showed resistance to apoptosis in CHO cell lines. In humans it expresses two mRNA transcripts of 1.1 and 6.1kb, respectively encoding for the 13kD and 200kD proteins, with the 6.1kb mRNA showing alternative splicing at exon 16.

The objectives were to determine expression patterns and levels of the three mRNA transcripts in normal and cancerous colon tissues. Apoptosis and proliferation assays were performed to establish the genes role in apoptosis. *Helicobacter pylori* has a significant relationship with colon cancer, and localization studies were done to examine this relationship with DWNN.

From colorimetric and fluorimetric in situ hybridization using Dig-labeled probes, and immunocytochemistry using antibodies against the DWNN proteins, the mRNA and protein showed upregulation in cancerous tissue structures, implicating DWNN in cancer progression. TUNEL showed higher levels of apoptosis in cancer tissue compared to normal tissue, directly proportional to DWNN upregulation, suggesting that DWNN is pro-apoptotic. The Ki-67 assay showed that proliferation has an inversely proportional relationship to DWNN localization, as did the Bcl-2 apoptosis suppressor, and this validates the suggestion that DWNN is pro-apoptotic. Immunocytochemistry using antibodies against *H. pylori* showed highly localization in adenocarcinomas and less or not at all in adenomatous glands, with localization also in the normal tissues. Therefore it may be involved in colon cancer progression, but not initiation.

Conclusion: The results suggest that DWNN may be involved in the pathogenesis of colon cancer. *H. pylori* is involved in the progression of non-invasive colon cancer to the invasive state. Further experiments are required to confirm the apoptotic nature of the DWNN gene products.