

The DWNN (RbBP6) gene in Health and Disease

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DWNN deficient cells have been found to be resistant to apoptosis induced by chemical inducers and this directly links DWNN to apoptosis. The DWNN gene is 36 kb long and contains 18 exons. It is transcribed to two mRNA transcripts, 1.1 kb and 6.1 kb and the latter is alternatively spliced in exon 16. The two mRNA species are translated into a 13 kD and a 200 kD proteins respectively. The 13 kD protein contains the DWNN domain only whereas the 200 kD proteins have the RING Finger, Rb and p53 binding domains linked to the DWNN domain.

The aim of the study is to determine the expression pattern and tissue distribution of DWNN gene products in normal and diseased human tissues. We have studied several cancers and other kidney disorders and compared the expression pattern and levels of expression to normal tissues. We have also compared the levels of expression and apoptosis in these tissues.

We have found that in most if not all cancers, DWNN, is found upregulated and in some cancers we found that it accumulates in the cytoplasm like the mutated p53. In a normal kidney DWNN is localized in the cytoplasm but it was found that in diseases like HIV associated nephropathy, Chronic Allograft Nephropathy and Acute Transplant Rejection, the DWNN was highly up-regulated and DWNN seemed to translocate to the nucleus. In Diffuse Proliferative Glomerulonephritis it was found to be downregulated. The DWNN expression levels correlated with apoptosis and was found to be inversely proportional to proliferation as it was shown by TUNEL and Ki67 respectively

The DWNN 200 cDNA had previously been cloned by detecting its interaction with tumour suppressor proteins p53 and Rb, which have a major role in apoptosis and cancer development. Accumulation of these proteins, p53 and DWNN, suggests that DWNN may be involved in a p53 dependant apoptotic pathway.