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Characterisation of p53 isoforms

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We recently established that p53 gene, like its family members p63 and p73, can express multiple mRNA variants. As a result at least nine different p53 protein isoforms can be produced due to alternative splicing, alternative initiation of translation and alternative internal promoter usage.

Using novel specific antibodies to p53 isoforms, we detect significant amount of p53 isoform proteins in some cell lines and normal human tissues. We investigated regulation of p53 internal promoter and p53 protein isoforms degradation. We established that p53 isoform expressions are regulated at the mRNA and protein levels. We show that p53 protein isoforms are ubiquitinated and degraded in a MDM2 independent manner, demonstrating that p53 protein isoforms and full-length p53 are differentially regulated. Moreover, other known p53 specific E3 ligases, COP1 and ARF-BP, can discriminate between p53 isoforms, each degrading specifically different p53 isoforms.

By chromatin immunoprecipitation, we established that p53 isoforms bind preferentially to some promoters. We determined by luciferase assay that p53 β p53 γ and Δ 133p53 can modulate differentially p53 transcriptional activity. In light of these results, we will discuss the fact that p53 isoforms are frequently abnormally expressed in 106 breast tumours analysed.