Increased alternative splicing of the KLF6 tumour suppressor gene correlates with prognosis and tumour grade in patients with pancreatic cancer.

The aim of this study was to correlate the status of the KLF6 tumour suppressor gene including loss of heterozygosity (LOH), mutation and alternative splicing in human pancreatic cancer with tumour grade and survival. Whereas neither KLF6 loss nor mutation was identified, expression of the KLF6 alternative splice forms was significantly increased in pancreatic tumour samples and cell lines. These cancers demonstrated marked cytoplasmic KLF6 expression, consistent with over-expression and accumulation of KLF6 splice form(s), which lack a nuclear localisation signal. In addition, KLF6 splicing correlated significantly with tumour stage and survival. In summary, pancreatic cancer displays a novel pattern of KLF6 dysregulation through selectively increased expression of KLF6 splice variants. Therefore, determination of KLF6 mRNA splicing levels may represent a novel biomarker predicting prognosis.