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**Basic Transcription Factor 3 (BTF3) Regulates Transcription of Tumor-Associated Genes in Pancreatic Cancer Cells**

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In the present study the role of BTF3 in pancreatic adenocarcinoma has been investigated. Our results show that there are 1.3-fold ($p<0.001$) increased median total BTF3 mRNA levels in PDAC compared to the normal pancreas, with median BTF3a mRNA expression levels 4.6-fold ($p<0.0001$) higher in PDAC compared to normal pancreatic tissues. However, total BTF3 mRNA was much more abundant than the BTF3a isoform suggesting that BTF3b is the prominent isoform, despite a higher ratio of BTF3a/total BTF3 in cancer versus normal pancreatic tissues. These findings imply the specific involvement of BTF3a in the pathogenesis of PDAC. These data were in accordance with the localization of BTF3. It was strongly localized in the cytoplasm and nuclei of tubular complexes both in chronic pancreatitis and PDAC tissues as well as in the nuclei of cancer cells.

Silencing of BTF3 using specific siRNA molecules did not result in significant changes in the sensitivity or resistance of Aspc-1 or Capan-1 cells to chemotherapeutic agents or radiotherapy, indicating that BTF3 does not directly influence cell apoptosis and/or cycle arrest in PDAC. It is also possible that its anti-apoptotic effect is cell/tissue type-dependent.

Deriving from the DNA microarray analysis following BTF3 silencing by siRNA, we have identified transcriptional targets of BTF3 in pancreatic cancer cells.
BTF3 silencing led to decreased expression of a number of genes. Most notably is ephrin receptor B2 (EPHB2). Further assays of EPHB2 have proven that there is a significant up-regulation (2.7-fold, $p<0.005$) in the median mRNA expression levels of both EPHB2 and BTF3a, but not total BTF3, as well as co-localization of both BTF3 and EPHB2 in the cytoplasm of pancreatic cancer cells and tubular complexes of PDAC cases. These findings point to the importance of BTF3 in regulating the expression of signaling molecules that may be involved in the progression of PDAC.
Other noteworthy examples are V-ABL ablation murine leukemia viral oncogene homolog 2 (ABL2); heparanase 2 (HPSE2), which plays an important role in regulating extracellular matrix degradation; and ataxia-telangectasia mutated gene (ATM), which is essential in the regulation of cell cycle/apoptosis.

Silencing of BTF3 led to the induction of k-ras oncogene-associated gene (KRAG), related ras viral oncogene homolog (RRAS2), murine retrovirus integration site 1 (MRVI1), mucosal vascular addressin cell adhesion molecule 1 (MADCAM1) and nuclear factor kappa-B (NFκ-B). These five genes are frequently associated with tumorigenesis.

Overall it can be deduced that BTF3 is over-expressed in PDAC, where it acts as a transcriptional regulator rather than a direct modulator of apoptosis.