BTG1 Low Expression in Pancreatic Ductal Adenocarcinoma is Associated with a Poorer Prognosis

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Abstract

Objective: BTG1 is a member of the TOB/BTG protein family, which is a transducer of ErbB-2 and TOB2. BTG1 is known to inhibit tumor genesis, but the role of it in pancreatic ductal adenocarcinoma is still unknown. The purpose of this study is to investigate the expression of BTG1 protein in pancreatic ductal adenocarcinoma (PDAC) and to determine its prognostic significance.

Methods: Immunohistochemistry is used to determine the protein expression level of *BTG1* gene in 79 surgically resected pancreatic ductal adenocarcinoma. Association of BTG1 expression with all the patients' clinicopathologic parameters was analyzed using statistical software SPSS22.0. The correlations between BTG1 expression and clinicopathological features were evaluated by Pearson's chi-square (χ^2) test, Fisher's exact test, and Spearman's rank. Univariate and multivariate Cox regression analyses were used to identify correlations between the immunohistochemical data for BTG1 expression and the clinicopathologic characteristics in pancreatic ductal adenocarcinoma. Kaplan-Meier analysis was used to demonstrate the correlation between overall survival and the expression of BTG1.

Results: BTG1 positive expression was observed in 27.8% (22/79) of the PDAC tissues, which was significantly lower than the 58.2% (46/79) of corresponding normal adjacent non-cancerous tissues by immunohistochemical

*PR: Positive Rate

Table 1: BTG1 expression in pancreatic cancer tissue and in normal tissue.

Figure 1: Immunohistochemical labeling for BTG1 protein.

Variables	**n**	**BTG1 expression in cancer tissues** **positive (%)** **negative(%)**		**P***
Sex				P=0.290
Male	54	17 (31.5%)	37 (68.5%)	
Female	25	5 (20.0%)	20 (80.0%)	
Age				P=0.247
<57	37	8 (21.6 %)	29 (78.4%)	
≥ 57	42	14 (33.3%)	28 (66.7%)	
Tumor site				P=0.943
Head	57	16 (28.1%)	41 (71.9%)	
Non-head	22	6 (27.3%)	16 (72.7%)	
Tumor size				P=0.183
≤ 2 cm	52	17 (32.7%)	35 (67.3%)	
>2 cm	27	5 (18.5%)	22 (81.5%)	
Histological differentiation				P=0.738
Poor	30	9 (30%)	21 (70.0%)	
Well-Moderate	49	13 (26.5%)	36 (74.5%)	
PNI				P=0.002

Present	44	6 (13.6%)	38 (86.4%)	
Absent	35	16 (45.7%)	19 (54.3%)	
Surgical margin				P=0.126
R0	76	20 (26.3%)	56 (73.7%)	
R1	3	2 (66.7%)	1 (33.3%)	
T stage				P=0.000
T1-2	32	17 (53.1%)	15 (46.9%)	
T3-4	47	5 (10.6%)	42 (89.4%)	
N stage				P=0.018
N0	37	15 (40.5%)	22 (59.5%)	
N1	42	7 (16.7%)	35 (83.3%)	
TNM Stage				P=0.000
I-II	30	19 (63.3%)	11 (36.7%)	
III-IV	49	3 (6.1%)	46 (93.9%)	

progression, increase cell apoptosis, reduce vascular endothelial growth factor expression in tumors [19].

According to previous studies, we can draw some useful conclusions about BTG1. BTG1 overexpression was considered as a marker for favorable prognosis in breast, non-small cell lung cancer, gastric cancer, ovarian carcinoma, hepatocellular carcinoma, nasopharyngeal cancer, esophageal squamous cancer and thyroid cancer [9-13,20]. Zheng HC et al. indicated that BTG1 expression is associated with the worse prognosis in gastric cancer patients by inhibiting proliferation, enhancing autophagy and apoptosis [11]. Zheng HC et al. also