J. Transl. Med. Res 2016;21(1):32-37

MAP4K4 Expression is Selectively Upregulated and Increases Cell Invasion in Pancreatic Ductal Adenocarcinoma

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ABSTRACT

The objective of this study was to determine whether the mitogen-activated protein kinase kinase kinase kinase 4 (MAP4K4) expression can differentiate pancreatic ductal adenocarcinoma (PDA) from chronic pancreatitis (CP) and to analyze its biological and clinical significance in PDA. We have previously found by gene array analysis that MAP4K4 is overexpressed in PDA tissues. Here, we measured MAP4K4 gene and protein expression in 58 PDA and 9 CP surgical specimens using RT-PCR and immunohistochemistry, and analyzed their association with clinical outcomes. MAP4K4 mRNA expression was significantly higher in PDA versus CP tissues (Mann Whitney test, $p<0.003$), and correlated with TNM stage (Kruskal-Wallis test, $p\leq0.026$). MAP4K4 protein expression was significantly correlated with tumor grade (Spearman's Rho = 0.449, $p\leq 0.01$), and tended to associate with shorter overall survival ($p\leq0.076$, log-rank test). In conclusion, our data indicate that the level of MAP4K4 expression directly correlates with PDA progression. Thus these data suggest that MAP4K4 may be a biomarker and potentially a target for therapy in PDA.

Key words: mitogen-activated protein kinase kinase kinase kinase 4 (MAP4K4), pancreatic cancer