Research Grants Council 研究資助局

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Project Details

Funding Scheme :	General Research Fund
Project Number :	462109
Project Title(English) :	Regulation of S100P expression by IL-6 in pancreatic ductal adenocarcinoma
Project Title(Chinese) :	胰腺癌中白细胞介素-6 对 S100P 基因表达的调控
Principal Investigator(English) :	Prof Chen, Yangchao
Principal Investigator(Chinese) :	
Department :	School of Biomedical Sciences
Institution :	The Chinese University of Hong Kong
Co - Investigator(s) :	Prof Kung, Hsiang-fu
Panel :	Biology & Medicine
Subject Area :	Medicine, Dentistry & Health
Exercise Year :	2009 / 10
Fund Approved :	850,230
Project Status :	Completed
Completion Date :	31-12-2012
Abstract as per original application (English/Chinese):	The aim of this study is to investigate the regulation of S100P expression by interleukin 6 (IL-6) in pancreatic ductal adenocarcinoma (PDAC) and the signal transduction pathways involved. S100P is a member of the S100 protein family involved in calcium signaling. Expression of S100P has been associated with immortalized, malignant, hormone-independent and chemoresistant phenotype. S100P is expressed in more than 90% of pancreatic tumors and is associated with tumor growth and invasion. S100P expression

	shows a steady increase from pancreatic intraepithelial neoplasia (PanIN) precursor lesions to PDAC, suggesting a critical role in disease progression. Despite increasing evidence showing biological significance of S100P and its relationship to cancer, the regulation of S100P expression remains elusive. Our preliminary data have shown that IL-6, a cytokine well implicated in pancreatic cancer growth, shows a similar expression pattern as S100P in pancreatic cancer cell lines. Exogenous IL-6 increases S100P mRNA level and transactivates S100P promoter in human pancreatic cancer cells. It is dose-dependent and possibly organ-specific, since IL-6 exerts no effect on S100P expression and promoter activity in human embryonic kidney 293 cells. IL-6 activation of S100P transcription is STAT3-dependent, since siRNAs targeting STAT3 significantly abolish IL-6-induced up-regulation of S100P mRNA. These results give us strong evidence to believe that S100P expression is regulated by IL-6. To test this hypothesis, we will investigate the regulation of S100P transcription by both endogenous and exogenous IL-6 in pancreatic cancer cells and the signal transduction pathways involved. We will characterize the role of STAT3 in IL-6 regulation of S100P. We will also examine the expression patterns of S100P and IL-6 in our collected PDAC specimens. Finally, we will employ our established lentiviral vectior to target S100P (Lenti-shS100P). The potential anti-cancer action of Lenti-shS100P and its effect on gemcitabine chemosensitivity will be tested in preclinical animal models. Knowledge gained from this project will improve our understanding of the regulation of S100P expression and lay the foundations for the development of more effective therapeutics for pancreatic cancer.