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Oxidative stress response in pancreatic adenocarcinoma BxPC-3 cells and identification of diagnostic biomarkers

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Abstract

Pancreatic cancer is one of the most aggressive human malignancies and ninth leading cause of cancer death in the world. Most patients diagnosed with pancreatic cancer die within 6 months, and only 4% survive 5 years after diagnosis. Early diagnosis and better treatments are desperately needed to improve the survival rate of pancreatic cancer patients. Pancreatic ductal adenocarcinomas, the majority of the exocrine pancreatic tumors, are thought to develop in a multistep process, involving a series of specific genetic mutations in each step. The comprehensive genetic analysis of 24 pancreatic cancers has shown 63 genetic alterations, and majority of which are point mutations. Interestingly, these alterations have been shown to affect 12 signaling pathways leading to pancreatic tumorigenesis. Because of nonspecific biomarkers for PDAC which lack specificity and sensitivity, high numbers of PDAC cases are diagnosed too late in the disease process for surgical resection to be an effective option. Even among the 10–20% of PDAC cases where surgical resection is an option, most patients ultimately die of recurrent or metastatic disease. In current investigation we were able to identify 41 proteins involved in oxidative stress response in pancreatic cancer and among them the presence of SOD2- mitochondrial, peroxiredoxin 2 and 4 and glutathione peroxidase was quite prominent, whereas these proteins were absent in control, suggesting aberrant regulation of redox homeostasis and stress adaptation in cancer cells. Mounting evidence suggests that, compared with their normal counterparts, many types of cancer cell have increased level of reactive oxygen species. Under persistent oxidative stress, many cancer cells become well-adapted to such stress and develop an enhanced, endogenous antioxidant capacity, which makes the malignant cells resistant to exogenous stress. As a consequence cancer cells that survive intrinsic oxidative stress may have activated adaptive mechanisms, which switch on ROS-scavenging systems to cope with the stress. Recent evidence suggests that such adaptation contributes to malignant transformation, metastasis and resistance to anticancer drugs. This approach might be a promising option to develop diagnostic biomarker and therapy for pancreatic cancer.

Biography

Hem D Shukla has recently joined as Research Scientist in Department of Pharmaceutical Sciences at University of Maryland. He has also worked as Research Faculty in Department of Biology at Johns Hopkins University. Dr Shukla has worked on proteomic analysis of oxidative stress response in BxPC-3 cell lines and identification of biomarkers for pancreatic cancer. He has worked on integrin pathway analysis in BxPC-3 cell lines and has shown that aberrant modification in alpha and beta integrin triggers the downstream signaling process which might be responsible for transcription of oncogene and onset of pancreatic cancer. The quantitative proteomic analysis has suggested a potential role of Annexin-2 and Caveolin-1 as a therapeutic agent for Pancreatic Ductal Adenocarcinoma.