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Mass spectrometry based proteomic analysis of oxidatively stressed pancreatic adenocarcinoma BxPC-3 cells: Identification of caveolin-1 as potential prognostic biomarker

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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 six months, and only 4% survive even five years after diagnosis. Approximately one-fifth of patients with presumably 'curable' pancreatic ductal adenocarcinoma (PDA) experience impending relapse and death, making surgical removal almost futile. Early diagnostic, prognostic and predictive biomarkers and better therapeutic options which could help personalize treatment regimens are desperately needed to improve the survival rate of pancreatic cancer patients. By employing BxPC-3 cell line model, high throughput comparative, quantitative and system proteomic analysis, we have been able to identify caveolin-1, K-RAS, integrin-α6β4 proteins which were significantly up-regulated in oxidatively stressed BxPC-3 pancreatic cancer cells. The present investigations have shown the presence of quite robust oxidative response in BxPC-3 cells as compared to HPDE control. The high throughput proteomic and bioinformatics analysis have shown the aberrantly regulated Cav-1-Fyn-SOS-cRAF-ERK (where Cav-1 is caveolin-1) signaling pathway, reveals that oxidative stress might activate Cav-1 protein in the membrane which in turn aberrantly activate the downstream proto-oncogene K-RAS and MAPK/ERK pathways. The data suggest that the above stated proteins could be used as diagnostic and prognostic biomarkers and using Cav-1-Fyn-SOS-cRAF-ERK pathway better therapeutic options could be explored.

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