Researchers to publish paper in Molecular Cancer journal

December 7 2011

(Medical Xpress) -- Erxi Wu, assistant professor of pharmaceutical sciences, and Fengfei Wang, research associate in pharmaceutical sciences, co-wrote the article, "β2-adrenoceptor blockage induces G1/S phase arrest and apoptosis in pancreatic cancer cells via Ras/Akt/NFkB pathway," which will be published by *Molecular Cancer*.

According to the authors, pancreatic cancer risk factors, smoking and stress, stimulate nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and catecholamines production respectively. Nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and catecholamine bind the β-adrenoceptors and induce pancreatic cancer cell proliferation; and they have previously indicated that β-adrenergic antagonists may suppress proliferation and invasion and stimulate apoptosis in pancreatic cancer. To clarify the mechanism of apoptosis induced by β2-adrenergic antagonist, they hypothesize that blockage of the β2-adrenoceptor could induce G1/S phase arrest and apoptosis and Ras may be a key player in pancreatic cancer cells.

Their results showed that the β1 and β2-adrenoceptor proteins were detected on the cell surface of pancreatic cancer cells from pancreatic carcinoma specimen samples by Immunohistochemistry. The β2-adrenergic antagonist ICI118,551 significantly induced G1/S phase arrest and apoptosis compared with the β1-adrenergic antagonist metoprolol, which was determined by the flow cytometry assay. β2-adrenergic antagonist therapy significantly suppressed the expression

of extracellular signal-regulated kinase, Akt, Bcl-2, cyclin D1 and cyclin E and induced the activation of caspase-3, caspase-9 and Bax by Western blotting. Additionally, the β2-adrenergic antagonist reduced the activation of NFkB in vitro cultured pancreatic cancer cells.

“The blockage of β2-adrenoceptor markedly induced pancreatic cancer cells to arrest at G1/S phase and consequently resulted in cell death, which is possibly due to that the blockage of β2-adrenoceptor inhibited NFkB, extracellular signal-regulated kinase and Akt pathways. Therefore, their upstream molecule Ras may be a key factor in the β2-adrenoceptor antagonist induced G1/S phase arrest and apoptosis in pancreatic cancer cells. The new pathway discovered in this study may provide an effective therapeutic strategy for pancreatic cancer,” Wu said. Collaborator for this paper is Ma lab at Xi’an Jiaotong University, China. “We have established a productive collaboration with the Ma lab in finding cancer therapeutics and elucidating the mechanisms of the targeted therapy for pancreatic cancer, one of the most lethal malignancies,” Wu said.

More information: www.molecular-cancer.com

Provided by North Dakota State University