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Editorial

Insulin-Like Growth Factor Receptor as a Target of Molecular Therapy

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EDITORIAL

Insulin-like growth factor (IGF) -1, and 2 (IGFs) are involved in growth and development. Once IGFs bind, their receptors (IGF-1 receptor, IGF-1R) are phosphorylated and the signal is transmitted mainly by phosphatidyl inositol - 3 (PI3) kinase pathway and mitogen activated protein (MAP) kinase. IGFs are secreted in fetus, but the secretion of the factors decrease and are almost no detectable after birth. It is expected that inhibition of IGFs have no effects on adults.

Several line of evidence suggests that IGFs act as growth factors in pancreatic cancer and hepatocellular carcinoma. Insulin-like growth factor (IGF) -I is up-regulated in human pancreatic cancer tissues while not expressed in surrounding non-cancerous ones [1]. Serum level of IGF-I is elevated in pancreatic cancer patients [2]. Histological analysis shows that IGF-IR is positive in membrane of cells of pancreatic cancer tissues while not expressed in surrounding non-tumourous tissues [3]. These facts imply that IGF-I act as a growth factor for pancreatic cancer. Serum-free media is a model of surrounding non-cancerous tissues that are consisted of collagen fiber. Interestingly, IGF-1R is phosphorylated even in serum-free media [4]. This phenomenon paves a way to a new concept of a molecular therapy to pancreatic cancer cells that are invading to surrounding non-cancerous tissues [5]. IGF-1R specific inhibitor, picorpodophyllin (PPP), successfully suppresses proliferation of pancreatic cancer cells in serum-free media. PPP also suppresses cell proliferation of hepatocellular carcinoma cell lines [6]. Inhibitors of IGF-1R have a potential of a novel molecular therapy to cancers.

Currently, one clinical trial with a combination of monoclonal antibody to IGF-1R, cetuximab and irinotecan has been reported on colorectal cancer [7]. Leukopenia and dermatitis are main adverse effects. The combination of three agents is tolerable. Future basic research will develop more sophisticated approach to cancers with IGF-1R inhibitors.

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