Osteoporosis drug may be effective against pancreatic cancer

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Bazedoxifene, a therapeutic approved by the U.S. Food and Drug Administration (FDA) for the prevention of osteoporosis, suppressed the growth of pancreatic tumors by inhibiting the IL-6/STAT3 signaling pathway that the cancer cells use to survive and multiply, according to preclinical data presented here at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held Nov. 5–9.

"Almost 50,000 people are expected to be diagnosed with pancreatic cancer in the United States in 2015, and, unfortunately, no more than 5 percent of these patients are expected to survive more than five years. Moreover, pancreatic cancer is intrinsically resistant to cytotoxic therapies. This barrier to treatment and the low survival rate are significant, and indicate the urgent need for new therapeutic strategies for this disease," said Jiayuh Lin, PhD, an associate professor of pediatrics in the College of Medicine, Translational Therapeutics Research Program at The Ohio State University Comprehensive Cancer Center.

Lin explained that IL-6 is a cytokine, a type of small protein, which plays an important role in cancer development, and high serum IL-6 levels are a poor prognostic factor for overall survival in pancreatic cancer; therefore, IL-6 is considered a viable target for pancreatic cancer therapy.

Bazedoxifene is a third-generation selective estrogen receptor modulator,

which received FDA approval in 2013 as part of a combination drug for the prevention of postmenopausal osteoporosis in women, Lin said.

In a previous study, Lin; Chenglong Li, PhD, associate professor of medicinal chemistry at The Ohio State University; and colleagues had identified bazedoxifene as a novel inhibitor of IL-6 using computational and medicinal methods and cell-based assays. In the current study, the researchers further explored the utility of this drug in inhibiting pancreatic cancer growth stimulated by the IL-6 cell-signaling pathway.

"Repositioning a drug such as bazedoxifene already approved for safety by the FDA as a novel inhibitor of IL-6 signaling should provide an easier path to clinical trials and have a high potential to improve the outcome of pancreatic cancer," Lin said. Drug repositioning refers to repurposing existing FDA-approved drugs to new indications, Lin explained.

In the current study, the researchers found that human pancreatic cancer cell lines expressing IL-6 were sensitive to bazedoxifene inhibition, which induced cell death by inhibiting the IL-6/STAT3 signaling pathway including the downstream signaling molecule, AKT. The drug was also found to suppress tumor growth in mice carrying human pancreatic cancer cells, which persistently activate IL-6/STAT3 pathway for their growth.

"We are planning to apply for grant funding from the NIH for obtaining additional research data on the use of bazedoxifene for pancreatic cancer," Lin said.

The researchers noted that some of the limitations of the study include that bazedoxifene may need to be modified chemically to be more efficacious as single agent, and/or it may need to be combined with other drugs such as nab-paclitaxel.