Cell receptor may lead to new 'biomarker' for pancreatic cancer

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A research team led by University of Cincinnati (UC) scientists has identified a potential biological target for pancreatic cancer, a finding they say could help scientists better understand -- and eventually treat -- the disease that kills more than 33,000 people each year.

In laboratory studies led by Andrew Lowy, MD, and Susan Waltz, PhD, the Cincinnati researchers found that a specific cell receptor -- known as the RON receptor tyrosine kinase -- was “overexpressed,” or increased, in pancreatic cancer cells. This, says Waltz, suggests the receptor may also contribute to the disease’s development.

The RON receptor has been found to be active in several cancers -- including breast cancer -- but its role in pancreatic cancer was unknown. This is one of the first studies, published in the July 1, 2007, issue of the journal *Cancer Research*, to report a link between the RON receptor and pancreatic cancer.

Receptor tyrosine kinases are proteins on the cell surface used to activate specific body functions -- for example cell growth and migration.

“A normal pancreas has very low levels of RON, but our study showed that as tumors progress, so does the level of RON expression in the pancreas cells -- and those overexpressed levels were maintained in ‘metastases,’ the areas that the tumors spread to,” explains Waltz, associate professor and director of the oncology research program in UC’s surgery department.

The team found that the RON receptor was active in 93 percent of what is known as pancreatic intraepithelial neoplasia, an early form of pancreatic duct cancer. In addition, the receptor was present in 79 percent of primary pancreatic cancers and 83 percent of metastatic cancers.

UC researchers believe the RON receptor's signaling pathways could be a key factor contributing to pancreatic cancer progression. Waltz says if the receptor could be blocked, it would give drug developers a new target for RON-directed therapies that are more effective in treating this deadly disease.

"When cells became invasive," Waltz said, "we saw higher levels of RON expression that correlated with the aggressive nature of this disease and cancer metastasis. Clearly, this signaling pathway is associated with pancreatic cancer and merits further investigation."

A relatively rare but difficult disease to treat, pancreatic cancer will affect about 37,000 Americans in 2007. According to the National Cancer Institute, overall survival for the disease is only about 4 percent -- often because the disease spreads before it can be clinically detected.

In the December 2006 issue of Cancer Research, Waltz reported that the RON receptor can also be involved in breast cancer. Based on those earlier findings, she and Lowy wanted to know if the receptor was also expressed in pancreatic cancer -- an aggressive, highly metastatic cancer -- and whether it played a role in disease development.

For the UC study, researchers used the protein HGFL (hepatocyte growth factor-like) to activate the RON receptor. Although stimulating the RON receptor had no effect on pancreatic cell growth, blocking it with targeted antibodies killed more cancer cells than did the standard treatment drug gemcitabine (gem-SITE-uh-bean) alone.

“Our findings suggest that combining antibodies that block the RON receptor and the standard chemotherapy drugs might stop progression of pancreatic cancer more effectively,” says Waltz. “RON could be a promising molecular target for future cancer drug development.”

Waltz stresses, however, that additional preclinical research is needed before RON receptor blockers become available for human testing.

Source: University of Cincinnati