

Newly discovered epidermal growth factor receptor active in human pancreatic cancers

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Finally some promising news about pancreatic cancer, one of the most fatal cancers, due to the difficulties of early detection and the lack of effective therapies: Johns Hopkins University pathologist Akhilesh Pandey has identified an epidermal growth factor receptor aberrantly active in approximately a third of the 250 human pancreatic cancers studied.

In a presentation April 18, at [Experimental Biology](#) 2009 in New Orleans, Dr. Pandey explained why this finding and related work in his Hopkins laboratory is promising in terms of both a new treatment for a large subset of pancreatic cancers and a potential blood or urine screening tool that might eventually do for [pancreatic cancer](#) detection what biomarkers like prostate-specific antigen levels have done for prostate cancer. His presentation was part of the scientific program of the American Society for Investigative Pathology.

Personalized treatment. Phosphorylated epidermal growth factor receptor (pEGFR), the receptor identified by Dr. Pandey, is closely related to HER-2, a growth factor receptor found and used as a drug target in a subset of breast cancers. After he found and profiled the pEGFR activated in the pancreatic cancers, Dr. Pandey realized the same receptor had been found by other researchers to be activated in a subset of lung cancers. And, most promising, an EGFR inhibitor named erlotinib already has been through the long and complex [Food and Drug Administration](#) approval process and is in use for treatment of these specific lung cancers.

But would the drug work in pancreatic cancers? Dr. Pandey's group moved from studies of human cell lines to studies in mice in which human pancreatic tumor cells with activated EGFR had been placed. The tumors began growing. But when treated with erlotinib, they began to shrink. Other tumors without activated pEGFR showed no response.

The promise - and the challenge - of using pEGFR is that of personalized medicine, says Dr. Pandey. Obviously a growth factor receptor that is activated only in a subset of all pancreatic cancers cannot be a one-size-fits-all target for treatment. Earlier studies in other laboratories and clinical trials already had tried EGF inhibitors as a treatment for pancreatic cancer and concluded that they did not work. When Dr. Pandey's collaborators allowed them to re-examine their samples, they found that the only case in 12 cases that had responded to the EGF inhibitor was the only case with an activated EGF receptor. Dr. Pandey would like to see other researchers go back and re-analyze their data, separating patients with and without the activated receptor, and then determining the success rate. He believes it would tell a different, more hopeful story.

Screening for pancreatic cancer. Dr. Pandey's other goal in his research is to use mass spectrometry to find additional markers of pancreatic cancer in the tumors themselves but also in blood and urine, which would avoid the problems of invasive biopsies. As a first step, his team has gone through the scientific literature to create a compendium of several hundred proteins and genes reported to be overexpressed in pancreatic cancers, making them excellent candidates for further study. The compendium already is being used by a consortium of investigators who are developing antibodies against the 60 most promising targets.

Source: Federation of American Societies for Experimental Biology
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