Circulating Mesothelin Serves as a Marker of Pancreatic Cancer

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(PhysOrg.com) -- Researchers have expanded on previous studies, and there may be a new weapon in the arsenal for immune-based strategies in treating pancreatic cancer - mesothelin protein. Findings also showed that circulating mesothelin is a marker of pancreatic disease.

According to research published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, the vast majority (99 percent) of patients with pancreatic adenocarcinoma have readily detectable circulating levels of the adenocarcinoma-associated protein mesothelin compared with barely detectable levels in normal healthy donor samples analyzed.

Peter Goedegebuure, Ph.D., and colleagues at the Washington University School of Medicine in St. Louis, evaluated the presence of mesothelin in the serum of patients and examined the correlation of the mesothelin levels with the presence of pancreatic disease. Furthermore, they assessed if patients with pancreatic adenocarcinoma have increased anti-mesothelin immunity.

The researchers used immunohistochemistry (n=10 patients) and ELISA (n=81 patients) to evaluate levels of tumor cell-bound and soluble mesothelin, respectively in patients with pancreatic cancer.

Significantly elevated levels of circulating mesothelin protein were detected in 73 of the 74 patients with pancreatic adenocarcinoma, and in all five patients with benign pancreatic disease, but not in the healthy

controls. This suggests that mesothelin is a marker of pancreatic disease, according to Goedegebuure. Furthermore, patients with pancreatic adenocarcinoma had a higher proportion of mesothelin-specific CD4 and CD8 T-cells compared to age-matched healthy controls (50 percent of patients vs. 20 percent of healthy controls).

“Mesothelin is an attractive target from a diagnostic and therapeutic perspective in patients with pancreatic cancer,” said Goedegebuure, who is a research associate professor in the Department of Surgery. “Our findings call for additional studies to evaluate the usefulness of circulating mesothelin as a marker of pancreatic disease.”

Previous studies have suggested the potential usefulness of mesothelin as a target of immunotherapy in malignancies: researchers at the National Institutes of Health reported that mesothelin may be a therapeutic target for ovarian cancer, and researchers from Johns Hopkins correlated a cytolytic T-cell response to mesothelin with some clinical benefit in pancreatic carcinoma patients who received a cell-based tumor vaccine. This study corroborates these findings in pancreatic cancer.

“Given the lethality of this malignancy and its usual late presentation, any clinical tool that could be used for widespread screening and early detection of pancreatic cancer would be a monumental advance in the management of this insidious disease,” said Colonel George E. Peoples, M.D., F.A.C.S., who is not affiliated with this study. He is director of the Cancer Vaccine Development Program, deputy director of the United States Military Cancer Institute and chief of surgical oncology at the Brooke Army Medical Center in Fort Sam Houston.

The study results may be tempered somewhat by the additional findings that the levels of mesothelin could not differentiate between malignant and benign pancreatic neoplasms, nor predict the burden of disease, according to Peoples. Additional studies of levels and/or timing of

assessments may better define the potential clinical utility of circulating mesothelin levels in pancreatic cancer.

“However, these are very encouraging results, and if validated in larger studies including more healthy controls, then a screening tool for pancreatic disease, including cancer, may be within sight,” Peoples concluded.

Provided by American Association for Cancer Research (news : web)