MedicalXpress

Antibodies Against Abnormal Glycoproteins Identified as Possible Biomarkers for Cancer Detection

February 2 2010

(PhysOrg.com) -- Scientists have found that cancer patients produce antibodies that target abnormal glycoproteins (proteins with sugar molecules attached) made by their tumors. The result of this work suggests that antitumor antibodies in the blood may provide a fruitful source of sensitive biomarkers for cancer detection. The study, supported in part by the National Cancer Institute (NCI), part of the National Institutes of Health, appears in the Feb. 15, 2010 issue of the journal *Cancer Research*.

"Thanks to emerging technologies such as the one used in this study, scientists have identified biomarkers based on the carbohydrate (sugar) portion of a glycoprotein that may be novel targets for early detection and diagnosis of certain cancers," said Sudhir Srivastava, Ph.D., M.P.H., chief of the Cancer Biomarkers Research Group in NCI's Division of Cancer Prevention.

An antibody is a type of protein that the body's immune system produces when it detects harmful substances called antigens. Antigens include microorganisms such as bacteria, fungi, parasites, and viruses. Antibodies are also produced when the immune system mistakenly considers healthy tissue a harmful substance. These antibodies, called autoantibodies, target a person's own molecules and tissues. Research has shown that cancer patients sometimes make autoantibodies against their own malignant cells and tissues, as part of an immune response against

their cancers. It is unclear why some cancer cells evade immune defenses. Scientists hope that such antibodies may ultimately have the potential to help doctors detect cancer by a simple blood test.

The glycoproteins that were the focus of this study are called mucins. Mucins comprise a family of glycoproteins, called O-glycoproteins, which are on the outer surface of cells and play an important role in cell-to-cell interactions. Tumors have been found to produce different types and amounts of mucins compared with normal cells and to produce mucins that have altered sugar groups.

Scientists led by Hans H. Wandall, M.D., Ph.D. and Ola Blixt, Ph.D., Center for Glycomics, Copenhagen University in Denmark, hypothesized that the abnormal molecular structures of the O-glycoproteins manufactured by cancer cells might cause patients to develop autoantibodies to them. To test this theory, the scientists had to overcome a number of challenges to develop a tool that could successfully identify autoantibodies to abnormal O-glycoproteins. The team used this approach to screen blood specimens from breast, ovarian and prostate cancer patients.

They found distinct abnormal mucin-type O-glycopeptide epitopes (parts of molecules that antibodies will recognize and bind to) that were targeted by autoantibodies in cancer patients — but such antibodies were absent in healthy controls.

Although larger sets of specimens will have to be analyzed to fully appreciate the clinical value of this technology, the preliminary results are very promising.

The study was an international collaboration that was funded in part by NCI through the trans-NIH Alliance of Glycobiologists for Detection of Cancer and Cancer Risk. The alliance is a consortium of NCI-supported

tumor glycomics laboratories that are working to reveal the cancer-related dynamics of complex carbohydrates and develop biomarkers for early cancer detection and risk assessment.

Provided by National Institutes of Health