News
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******Researchers use new type of blood test to detect cancer.

DALLAS--A blood test for cancer may sound far-fetched.

But a group of researchers at The University of Texas Health Science Center at Dallas are already using a new kind of blood test to monitor the progress of certain types of cancer in the lymph nodes (lymphoid cancers). The procedure may eventually allow doctors to detect the presence of these cancers long before traditional methods of detection could give a warning.

That's the long-range goal of the Cancer Center group, a mixture of basic scientists and physicians involved in the research, diagnosis and treatment of lymphoid tumors. Headed by clinical hematologist Dr. Eugene Frenkel, the group also includes Dr. Graham Smith, a tumor specialist (oncologist); Drs. Jonathan Uhr and Ellen S. Vitetta, molecular immunologists; and Drs. Jack Kettman, James Forman and Frances Ligler, cellular immunologists.

"We've found that in many cases we can almost predict the remission or recurrence of lymphoid tumors when we test the blood samples from patients with known lymphoid cancers," says Vitetta. "It's sort of a barometer of the patient's condition. When the physician sees that the patient is doing well, we're seeing a parallel to that in the blood samples. When the patient is doing poorly, that's reflected in the blood samples."

Precise monitoring of the disease is vital to treatment, says Vitetta. "The earlier you treat the malignancy, the better chances of killing the tumor. But you want to avoid overtreatment with toxic drugs that kill not only the malignant cells but the normal, healthy cells as well. You want to have the treatment parallel the disease."

Conventional methods of examining blood cells usually can't distinguish between malignant and normal cells. A reappearing lump is in many cases the first sign that the cancer has returned. But the research group has developed a method of detecting a small tumor cell population (less than one percent) in a blood sample containing otherwise normal cells. To do this, they're using a sophisticated new research tool developed at Stanford University, the fluorescence activated cell sorter (FACS), and specialized computer programs for analyzing the FACS data developed here by Dr. Kettman.

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The FACS employs a laser beam that causes the surfaces of certain cells to "glow" when these cells are treated with a "fluorescent" antibody specific for that type of cell. These glowing cells can then be analyzed and sorted according to the intensity of brightness, telling the scientists which cells are tumor cells and which are normal cells.

Researchers here are looking specifically at the detection of B cell lymphoid cancers. Normal B cells are a part of the body's immune system and produce antibodies against viruses and bacteria. They are a type of lymphoid cell having only one of two types of immunoglobulins or antibodies on their surface and are monoclonal, meaning that all the malignant cells come from a single malignant parental cell and are identical to it.

Studies at the Cancer Center have shown that in every normal human about half of the B cells have one type of surface light chain marker, the "Kappa" type, and the other half of the B cells have the "Lambda" type--an approximate one-to-one ratio of the two cell variations. But monoclonal B cells, in contrast, will be of only one type--all Lambda or all Kappa. Some of these malignant cells will "leak" into the blood stream from the tumor, altering the one-to-one ratio of Kappa to Lambda cells. It's this altered ratio that the FACS can detect at a level of one percent or less.

"It's as if you had a half dozen oranges and a half dozen apples and then added another orange. You could see the change in the ratio of oranges to apples. That's what the FACS does--it detects the change in the ratio of Kappa to Lambda B cells," explains Vitetta.

Currently, the group uses the FACS technique to screen various forms of B cell lymphoid cancers, in particular the solid tumor forms. In the early stage of research, blood samples from lymphoid cancer patients and patients with a variety of other infectious and non-malignant diseases have been tested to answer some basic questions. Vitetta explains: "Patients who are sick have antibody responses going on, which means they have activated B cells. We wanted to make sure that these other diseases didn't trigger the type of B cell reaction we were studying in lymphoid tumors. We also had to determine if the number of tumor cells in the blood sample was a barometer of the state of the disease. That is, do patients who are very sick with the disease have more of these cells, and do patients who have undergone treatment and are doing well have fewer of these cells in the blood?"

Preliminary findings indicate that the changes in Kappa versus Lambda bearing B cells are peculiar to lymphoid cancers and that these "clonal excesses" that alter the ratio of B cell types in the blood are indeed a barometer of the disease stage.

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The next step is to determine at what stage in the disease this blood test can diagnose the presence of these cancer cells. Must the cancer be in a well-developed stage before the tumor cells begin to leak into the blood, or can the disease be detected in its earliest stages? Only testing on a vast scale can answer this question.

Early diagnosis of cancer is just part of the research going on at the Cancer Center. Working with the group from Stanford University, the team has developed a mouse tumor "model" which is very similar to the CLL found in humans. It's an important milestone in the diagnosis and treatment of this type of cancer because for the first time, researchers have an animal model to study how the tumor grows, why it grows and how it can be treated.

By duplicating a human tumor cell system in a mouse model, the researchers were able to develop a specific antibody for any B cell tumor. Like a key fits a lock, only one specific antibody will "fit" the B cell tumor it was designed for. It identifies one particular clone of B cells out of all the millions of other clones of B cells. Since the tumor comes from one specific clone, this antibody will identify all these tumor cells, but not normal cells.

"We've used this antibody to look at the growth of the tumor in the mouse, and we are now attempting to couple it to drugs to kill the tumor in the mouse--a sort of 'guided missile' for the tumor cells that will leave normal cells unaffected by the treatment," says Vitetta.

Part of the study includes shipping the tumor-laden mice to Israel, where researchers at the Hebrew University of Jerusalem treat the mice with a new irradiation-transplantation procedure to "shrink" the tumor. The mice are shipped back to Dallas for "mopping up" treatment on the tumor, using the experimental antibody-coupled drug.

It's too early to tell how successful these studies will be cautions Vitetta. "But with these mouse models, we can't help but find something out. All the things you can't do in humans, we can do in mice."

Other members of the Cancer Center research team include postdoctoral fellows Drs. Sally Anderson, Peter Isakson, Keith Krolick and Michael Muirhead. Research assistant Joyce Himes is responsible for the development and use of the FACS.

This new method of detecting lymphoma cells in the blood was reported in the September issue of the JOURNAL OF IMMUNOLOGY and the Nov. 1979 issue of the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

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