News
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** Researchers look for leukemia predictor in children.

DALLAS -- A $100,000 grant from the Children's Cancer Fund of Dallas will allow researchers at The University of Texas Health Science Center at Dallas to continue work on predicting the recurrence of a certain type of leukemia.

Acute lymphoblastic leukemia (ALL) is the most common kind of childhood leukemia, says Dr. George Buchanan, associate professor of Pediatrics and director of Hematology-Oncology at Children's Medical Center. Currently first remission is achieved in about 95 percent of the children who suffer from ALL, but recurrences are common.

"Although about 95 percent of the patients with ALL go into remission with chemotherapy within a month, we know there are still malignant cells in the body even though we can't see them with a microscope," says Buchanan. "And while around 40 percent of the children have no relapse, about 60 percent of them do--often suddenly and without warning. There has been no way of predicting these relapses. What we need is a marker to indicate the presence of a tiny amount of tumor."

About three years ago Buchanan and his associate Dr. Graham Smith began looking at terminal deoxynucleotidyl transferase (TdT) as a "marker." This substance is an enzyme present in the cells of the thymus and bone marrow of normal people and in the leukemic cells of nearly all ALL patients.

The pediatric oncologist and Smith, a hematologist and associate professor of Internal Medicine, looked for TdT in the blood of children with leukemia who were in remission. Bone marrow tests, usually given to check for the presence of cancer cells, are not appropriate for a TdT test because of the presence of the enzyme in the bone marrow of normal people. Blood tests have other advantages, too. They are less traumatic to the patient, easier to do and less expensive.

The test may allow physicians to discover the recurrence of the disease before the patient shows any signs or symptoms. Thus, treatment could be started earlier, giving the patient a better chance in the battle against ALL. In addition, says Buchanan, a sensitive test to monitor extremely small numbers of leukemia cells would be a help in indicating the dose size for individual patients on chemotherapy. Then those who are

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predicted for relapse could be given large doses, and those doing well would not be overmedicated.

The gift, says Buchanan, will allow the research team to refine the TdT test, as well as to search for other markers to indicate this minimal residual disease. It will also allow the studies to be expanded so the research activities can be carried out "more regularly and rigorously" and with a larger number of patients. A full-time medical research technician has already been hired, and a cell sorter to count the flourescent cells carrying the enzyme markers is now available.

Since their first publication on TdT, the researchers have studied 23 patients with nine suffering relapses. The TdT test picked up seven of the nine relapses before there were any other indications of the disease.

Buchanan recently returned from a meeting in Rotterdam on identifying residual diseases. He is optimistic about his project: "There wasn't anyone else at the meeting having better results."

Another exciting project Buchanan and Smith have been involved with recently is work with the case of an 11-year-old girl that supports the theory linking cancers to broken chromosomes. This work was published in the September New England Journal of Medicine.

Although broken chromosomes have long been associated with birth defects, some researchers in recent years have been looking at their role in cancer. This young patient was diagnosed by health science center physicians as having chronic lymphocytic leukemia, a type of cancer usually found in middle-aged and elderly adults. In chronic lymphocytic leukemia the patients have an abnormal number of B lymphocytes that look normal but do not function normally in their role to help protect the person from infection.

"Children just don't have this disease," says Buchanan. "There are only three cases (of children with chronic lymphocytic leukemia) in the literature, and they are not certain. The question is, 'What happened in this case?'"

Laboratory tests showed that the girl had a translocation, or exchange, of chromosomes #2 and #14 in her cancer cells. This translocation of chromosomes that are broken off is suspicious, says Buchanan, because a different translocation involving chromosome #14 has been found in the tumor cells of patients who have Burkitt's lymphoma, a different type of B cell malignancy. Researchers who work with this disease think that perhaps the fragments of the broken chromosomes somehow "turn on" oncogenes (cancer-activating genes) when they are attached to the second chromosome.

"There are a number of genes present in normal people that seem to induce malignancy if altered." he said. "Oncogenes seem to be present where the break is. The question is whether the breaking off of the chromosomes caused the activation of the oncogenes."

Buchanan and Smith are also working with Dr. Philip Tucker, associate professor of Microbiology, and graduate student Perry Fell in analyzing the child's DNA.

"We want to precisely map the break points in the chromosomes," he said. "This kind of information may lead us closer to the answers."

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