Researchers develop first 'theranostic' treatment for acute lymphoblastic leukemia (ALL)

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A team of researchers at Case Western Reserve University School of Medicine has developed the first "theranostic" agent for the treatment of acute lymphoblastic leukemia (ALL). ALL is the most common type of childhood cancer diagnosed in approximately 5,000 new cases each year in the United States. The findings provide insight into pediatric oncology that specifically focuses on the development of "theranostic" agents-- a treatment platform that combines a selective diagnostic test with targeted therapy based on the test results.

Discovery of this new class of drugs is the first step towards new diagnostic markers and therapeutic approaches in treatments with anti-cancer agents of numerous other cancers in addition to ALL.

"This discovery takes a chemical biology approach to target ALL. Our nucleosides represent a new class of theranostic agents that provide an original approach to achieving personalized treatments against pediatric leukemia," says Anthony J. Berdis, PhD, assistant professor of pharmacology at Case Western Reserve School of Medicine.

"We've developed a non-natural nucleoside that specifically targets this form of childhood leukemia. The combination of therapeutic and diagnostic activities will provide more selective and more expedient ways to treat patients by optimizing the dosages needed to kill the cancer cells without affecting normal cells. This selectivity should minimize the

development of adverse side effects typically associated with conventional anti-cancer nucleosides," says Dr. Berdis.

Using an enzyme implicated in the disease, terminal deoxynucleotidyl transferase (TdT) which serves as a biomarker and is overexpressed in 90 percent of ALL patients, Dr. Berdis and his team designed a new selective anti-cancer agent against ALL. By evaluating the anti-leukemia activities of two non-natural nucleotides designated 5-NITP and 3-Eth-5-NITP, the investigators strategically placed novel functional groups on these agents so that they could be tagged with fluorogenic dyes. These taggable nucleotides improve the accuracy of dosing regiments and could accelerate clinical decisions regarding therapeutic intervention. The next steps will be validation in animal studies and toxicology testing, leading to clinical trials.

This study appears online this week in *ACS* Chemical Biology. In addition to Dr. Berdis, co-authors on the paper include Edward A. Motea and Dr. Irene Lee, in the Department of Chemistry and Department of Pharmacology at Case Western Reserve.

Acute lymphoblastic leukemia (ALL) is a form of leukemia, or cancer of the white blood cells characterized by excess lymphoblasts. Acute refers to the relatively short time course of the disease (being fatal in as little as a few weeks if left untreated). This disease is caused when malignant, immature white blood cells continuously multiply and are overproduced in the bone marrow. ALL causes damage and death by crowding out normal cells in the bone marrow and by spreading to other organs. Although ALL is most common in childhood with a peak incidence at 2-5 years of age, this type of leukemia is also prevalent in people over the age of 60.

Provided by Case Western Reserve University