Scientists bioengineer a protein to fight leukemia

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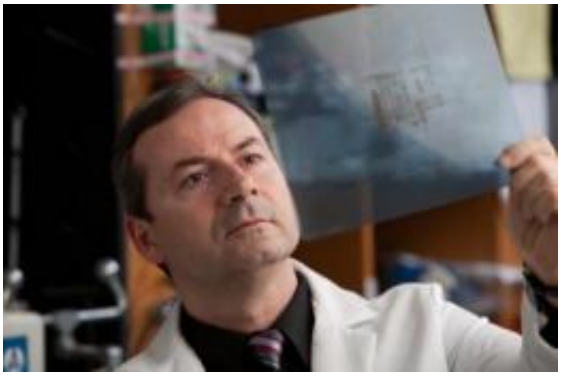

This is Fatih Uckun, M.D., Ph.D., of the Saban Research Institute of Children's Hospital Los Angeles. Credit: Photo courtesy of Children's Hospital Los Angeles

Scientists at the Children's Center for Cancer and Blood Diseases and The Saban Research Institute of Children's Hospital Los Angeles today announced a breakthrough discovery in understanding how the body fights leukemia. They have identified a protein called CD19-ligand (CD19-L) located on the surface of certain white blood cells that facilitates the recognition and destruction of leukemia cells by the immune system. This work represents the first report of a bioengineered version of CD19-L, a recombinant human biotherapeutic agent, targeting CD19-positive leukemic stem cells.

B-lineage acute lymphoblastic leukemia (ALL) is the most common cancer occurring in children and adolescents. Despite having received

intensive chemotherapy, some patients have recurring disease. For these individuals, the prospect of long-term survival is poor.

"We need new anti-leukemia therapies capable of killing chemotherapy-resistant leukemia cells in patients with relapsed ALL. These are the cells that are the most difficult to treat. The challenge is to kill these cells while leaving healthy cells intact," said Fatih Uckun, MD, PhD, first author on the paper that has been published in the *British Journal of Haematology*. Dr. Uckun is also a professor of Pediatrics at the University of Southern California Keck School of Medicine and a member of the Developmental Therapeutics Program at the Norris Comprehensive Cancer Center.

Lymphocytes are a type of white blood cell involved in immune function and are categorized as either B-cells or T-cells. This newly discovered element, CD19-L, is expressed on the surface of T-lymphocytes and allows them to selectively bind to the CD19 receptor on the surface of B-lineage leukemia cells, and most importantly on leukemic stem cells responsible for the survival and expansion of the leukemia cell population. Once the CD19-L binds to leukemia cells, cell death occurs. Although CD19 is abundantly expressed on leukemia cells from B-lineage ALL patients, it is absent on red cells, T-cells, and normal bone marrow stem cells, making it specific, and therefore, a good therapeutic target.

Dr. Uckun and colleagues have bioengineered and prepared a highly purified liquid formulation of the human CD19-L protein. This recombinant protein not only shows selective binding to leukemia cells but also causes their rapid destruction within 24 hours. Perhaps most importantly, CD19-L killed even those leukemia cells that were highly resistant to both standard chemotherapy drugs as well as radiation.

CD19-L is the first CD19-specific recombinant human protein with

potent anti-leukemic activity against B-lineage ALL, the most common form of childhood cancer and the second most common form of acute leukemia in adults. The identification of CD19-L may lead to therapeutic innovation for childhood leukemia by allowing a selective destruction of leukemic stem cells. According to Dr. Uckun, the next step will be to carefully evaluate this new agent for clinical potential against leukemia and to confirm in preclinical studies that leukemic cell destruction can be achieved at non-toxic dose levels.

"The CD19-ligand offers a previously unrecognized defense system against leukemia and opens a new range of therapeutic opportunities for the treatment of leukemia," said Stuart Siegel, MD, director of the Center for Cancer and Blood Diseases at Childrens' Hospital Los Angeles.

More information: Recombinant human CD19-ligand protein as a potent anti-leukaemic agent. Uckun FM, Sun L, Qazi S, Ma H, Ozer Z. Br J Haematol. 2011. doi:10.1111/j.1365-2141.2011.08583.x. [Epub ahead of print]

Provided by Children's Hospital Los Angeles

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