New targeted therapy finds and eliminates deadly leukemia stem cells

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New research describes a molecular tool that shows great promise as a therapeutic for human acute myeloid leukemia (AML), a notoriously treatment-resistant blood cancer. The study, published by Cell Press in the July 2nd issue of the journal *Cell Stem Cell,* describes exciting preclinical studies in which a new therapeutic approach selectively attacks human cancer cells grown in the lab and in animal models of leukemia.

AML is a cancer of the white blood cells that has an extremely poor prognosis and does not respond well to conventional chemotherapy. "The cellular and molecular basis for this dismal picture is unclear," offers senior study author Associate Professor Richard Lock from the Children's Cancer Institute Australia and the University of New South Wales. "However, previous research has suggested that leukemia stem cells (LSCs) may lie at the heart of post-treatment relapse and chemoresistance." LSCs are cells that can initiate AML and are critical for its long-term growth.

Associate Professor Lock and colleagues exploited the fact that the molecule CD123 is expressed at very high levels on LSCs but not on normal blood cells. CD123 is part of the interleukin-3 receptor, a protein that interacts with a growth factor (called a cytokine) that influences cell survival and proliferation. The researchers created a therapeutic antibody that recognized and bound to CD123 with the hope that this antibody would selectively interfere with AML-LSC survival.

When AML-LSCs from human patients were transplanted into mice treated with the antibody, called 7G3, cytokine signaling in the tumor cells was blocked. Further, 7G3 impaired migration of the AML-LSCs to bone marrow and activated the innate immune system of the host mouse to destroy the AML-LSCs. Overall, treatment with 7G3 substantially improved mouse survival when compared with control groups. The researchers go on to report that a CD123-targeting antibody is currently being used in phase 1 clinical trials of advanced AML and that there are no signs of treatment-related toxicity.

These results hold substantial promise for future cancer therapeutics. "The recent characterization of defined populations of cancer stem cells in a range of human malignancies, as well as their relative resistance to conventional chemotherapy and radiotherapy, supports the broad applicability of our approach and provides rationale for the progression of AML-LSC-targeted therapeutics from preclinical evaluation to clinical trials," concludes Associate Professor Lock.

Source: Cell Press (news : web)