Study finds potential therapeutic target for pediatric acute myeloid leukemia

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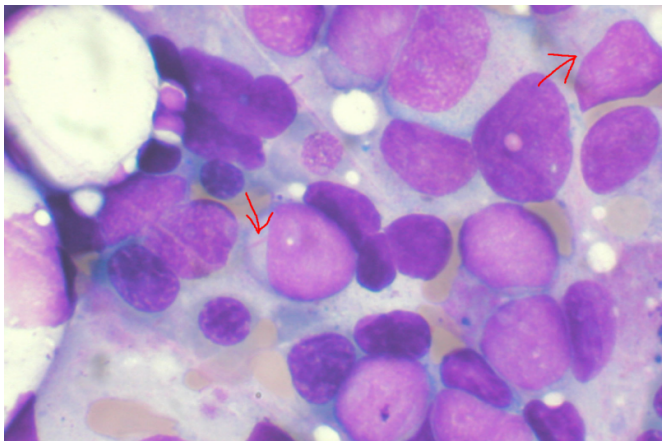

Bone marrow aspirate showing acute myeloid leukemia. Several blasts have Auer rods. Credit: Wikipedia

Researchers have identified a gene expressed in children with acute myeloid leukemia (AML) that could serve as a new immunotherapy treatment target, according to a new study published today in *Blood Advances*, a journal of the American Society of Hematology. The study, co-authored by researchers with Nemours Children's Health System, outlines the process and potential path for new immunotherapy drugs that improve survival and reduce treatment-related toxicity in children with AML.

Leukemia is the most common cancer in children and teens, and AML accounts for nearly one-fourth of those cases. AML is a fast-growing cancer that typically starts in immature bone marrow cells.

"Using genomic sequencing data, we identified novel targets for children's cancer and worked with collaborators to engineer new therapies for children with AML, rather than repurpose drugs from the adult cancer realm that don't work well in children," said E. Anders Kolb, MD, director of Nemours' Center for Childhood Cancer Research and a senior author of the study.

The researchers obtained genomic data from more than 2,000 pediatric patients with leukemia, to identify associated gene variants. Through genomic sequencing, they found that the gene mesothelin (MSLN) is abnormally expressed in more than one-third of childhood and young adult AML cases but was absent in normal bone marrow cells.

After this discovery, the researchers chose new immunotherapy drugs that would target MSLN to test in cell lines and animal models, to gauge pre-clinical effectiveness of leukemia therapies. Two experimental immunotherapy drugs were tested: anetumab ravtansine (Bayer), which is being tested in adult cancers, and a new compound, anti-MSLN-DGN462 (ImmunoGen). Each drug, in lab testing and in mouse models, produced potent destruction of leukemia cells. These drugs belong to a new class of cancer treatments known as anti-body drug conjugates (ADCs), which combine an antibody with a cancer-killing toxin. The antibody targets specific types of cancer cells and delivers the toxin directly to them, minimizing damage to healthy cells.

"We are working to show a proof of principle that we can create custom therapies for pediatric malignancies and turn the drugs we're testing in the lab into clinical trials," said Sonali P. Barwe, Ph.D., the study's co-lead author and head of the Preclinical Leukemia Testing Laboratory in Nemours' Center for Childhood Cancer Research.

The rapid evolution of genomic sequencing funded by the National Institutes of Health has led to the identification of new gene targets that are relevant for a significant number of patients. In addition, local organizations, such as the Leukemia Research Foundation of Delaware, have funded efforts like this study by Nemours to find new treatments.

More information: Allison J. Kaeding et al, Mesothelin is a novel cell surface disease marker and potential therapeutic target in acute myeloid leukemia, *Blood Advances* (2021). DOI: 10.1182/bloodadvances.2021004424

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