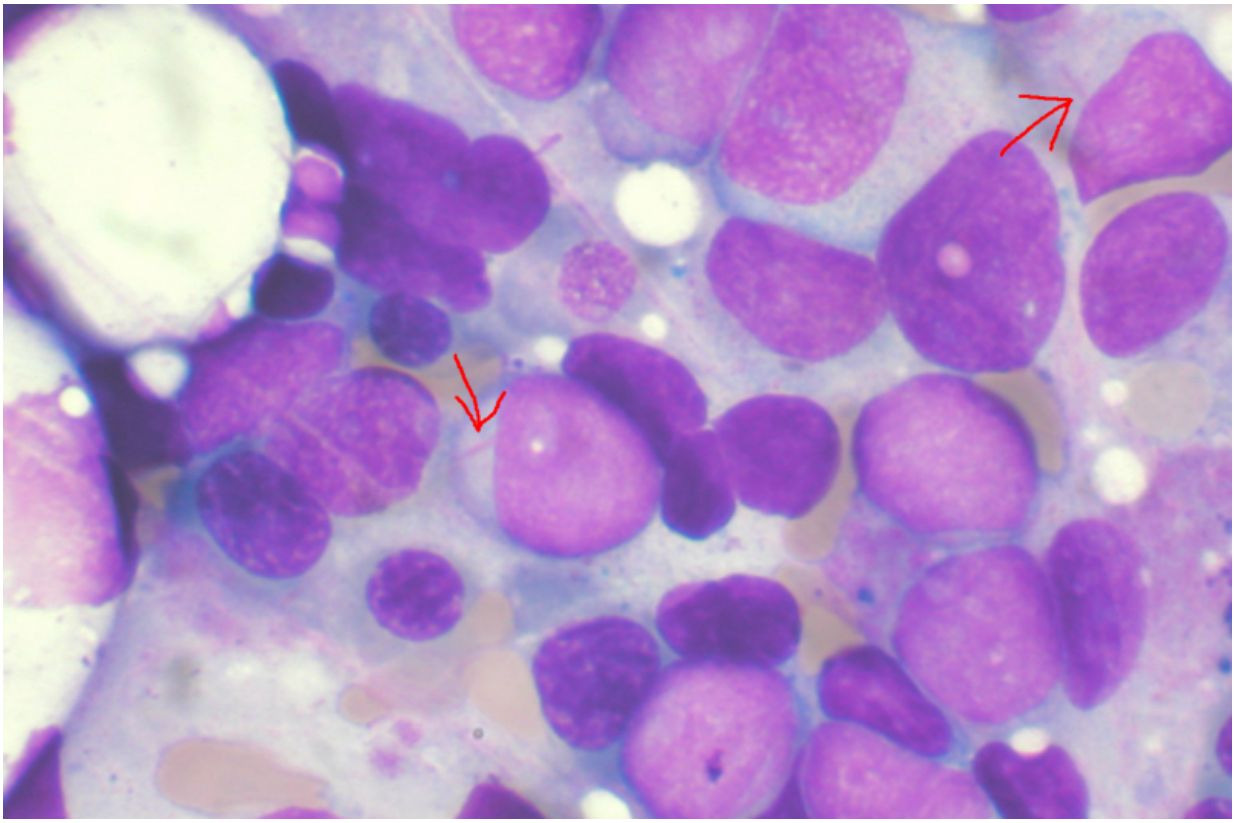
Scientists show that a novel therapy could be effective against pediatric leukemia

September 29 2021



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

Mount Sinai researchers have developed a therapy that shows promise against a deadly pediatric leukemia. The small-molecule therapy was

highly effective in fighting a type of acute myeloid leukemia in both *in vitro* and *in vivo* experiments, according to research published in *Science Translational Medicine* in September.

The therapy, named MS67, causes the degradation of the WDR5 protein, which drives the proliferation of acute myeloid leukemia with a specific genetic makeup called mixed lineage leukemia rearrangement. This type of leukemia is more common in children, has very poor response to standard treatments and a dismal prognosis, and until now has confounded researchers.

WDR5 also plays an important role in driving the proliferation of other cancers such as pancreatic cancer, so researchers believe that it is likely that WDR5 small-molecule degraders such as MS67 could also be effective in treating those cancers.

"This study is the first to demonstrate that pharmacological degradation of WDR5, which selectively eliminates the proten, is an effective and superior therapeutic strategy than pharmacological inhibition, or blocking, of WDR5 for the treatment of WDR5-dependent cancers including acute myeloid leukemia with mixed lineage leukemia rearrangement," said Jian Jin, Ph.D., the Mount Sinai Professor in Therapeutics Discovery and Director of the Mount Sinai Center for Therapeutics Discovery at the Icahn School of Medicine at Mount Sinai. "In addition, MS67 is the first WDR5 small-molecule degrader that exhibits robust anti-tumor activities *in vivo*."

The research team led by Dr. Jin; Greg Wang, Ph.D., of the University of North Carolina at Chapel Hill; and Aneel Aggarwal, Ph.D., Professor of Pharmacological Sciences, and Oncological Sciences, at The Tisch Cancer Institute at Mount Sinai, discovered MS67, a novel, highly potent and selective small-molecule degrader of WDR5, which effectively suppressed the growth of this type of acute myeloid leukemia cells

derived from patients both *in vitro* and *in vivo*, using patient cancer cells in mouse models. Using a battery of biochemical, biophysical, structural, cellular, genomic, and *in vivo* studies, the research team demonstrated that MS67 is a much superior therapeutic agent than other therapies that inhibit instead of degrade WDR5.

More information: A selective WDR5 degrader inhibits acute myeloid leukemia in patient-derived mouse models, *Science Translational Medicine* (2021). DOI: 10.1126/scitranslmed.abd5016

Provided by The Mount Sinai Hospital