Scientists create powerful, most-accurate tools to research deadliest blood cancer, study says

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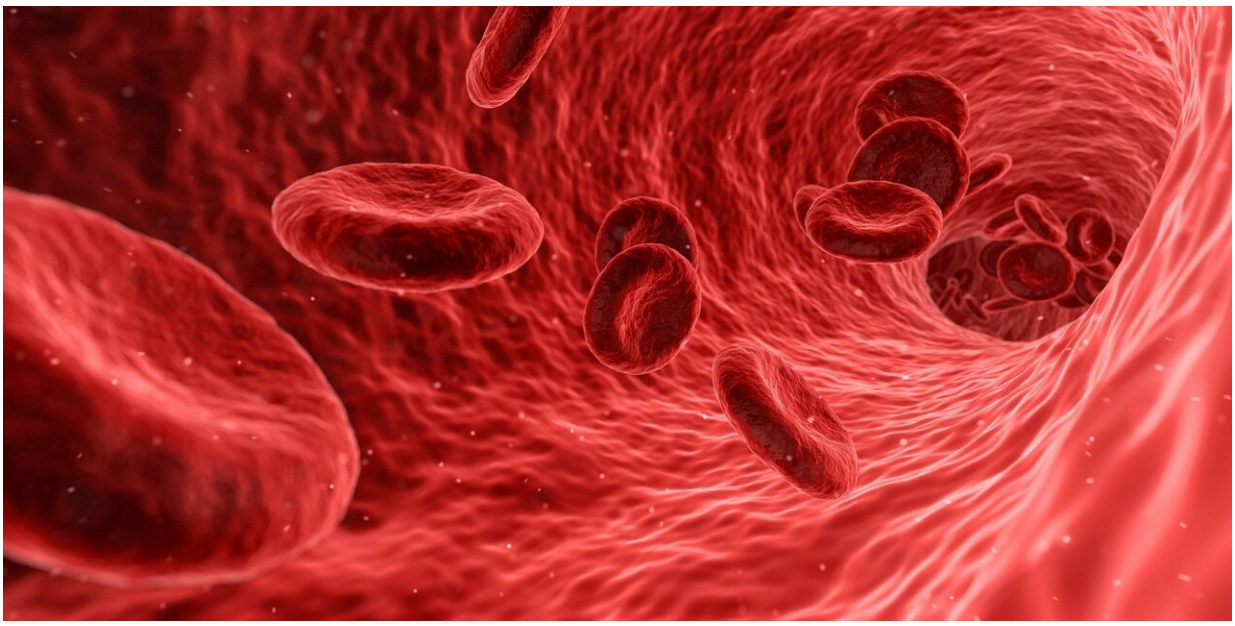

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Tisch Cancer Center scientists have developed unique models of the deadliest blood cancer, acute myeloid leukemia (AML), creating a transformative resource to study this cancer and eventually its drug response and drug resistance. The models were described in a late-breaking abstract at the annual meeting of the American Association of Cancer Research and simultaneously published in *Blood Cancer*

Discovery, a journal of the American Association for Cancer Research.

These are the first powerful models that are nearly identical to AML found in patients. The researchers said these models represent the disease accurately in genetic composition and in disease characteristics found in laboratory cell cultures, animal models, and patients.

AML is a fast-growing cancer with only a 29% survival rate. It has often already spread widely in the bone marrow and blood by the time it's first discovered in a patient, so being able to study the cancer, its progression, and its response to drugs in accurate and viable cell lines is crucial.

"We show that these models are nearly identical to the leukemias of the patients that they came from and thus are faithful models for acute myeloid leukemia," said senior author Eirini Papapetrou, MD, Ph.D., Professor of Oncological Sciences, and Medicine (Hematology and Medical Oncology), at The Tisch Cancer Institute, part of the Tisch Cancer Center, and Director of the Center for Advancement of Blood Cancer Therapies (CABCT) at the Institute for Regenerative Medicine at the Icahn School of Medicine at Mount Sinai. "Animal models do not provide accurate genetic models of AML, AML cells from the bone marrow or blood survive poorly outside of the body, and AML cell lines carry many additional genetic and karyotypic abnormalities that make them distinct from primary tumors. Our new models are groundbreaking tools that can uniquely empower leukemia research."

To create these models, researchers used genetic reprogramming technology to convert blood or bone marrow cells from 15 patients representing all major genetic groups of AML to a particular type of stem cells (called induced pluripotent stem cells) that can mimic different stages of disease progression, from a healthy state to pre-malignancy and finally full-blown leukemia. Importantly, the leukemia cells derived from these lines can be transplanted into animal models and

create a disease remarkably similar to that seen in the patients.

Many of these lines have been distributed to other researchers, who, along with Dr. Papapetrou and her colleagues, will pursue a number of new studies into leukemia pathogenesis and drug responses. A commentary on the significance of Dr. Papapetrou's journal article in *Blood Cancer Discovery* explains how the study advances the field, both practically and conceptually.

"The large panel of genetically defined iPSC clones ... are versatile disease models and important resources for the community," the commentary, written by Sergei Doulatov, Ph.D., Associate Professor of Hematology at the University of Washington, says. "This study dispels the notion that leukemias are difficult or impossible to reprogram."

More information: Andriana G. Kotini et al, Patient-Derived iPSCs Faithfully Represent the Genetic Diversity and Cellular Architecture of Human Acute Myeloid Leukemia, *Blood Cancer Discovery* (2023). DOI: 10.1158/2643-3230.BCD-22-0167

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