A heart failure drug to treat leukemia: A promising new therapeutic approach

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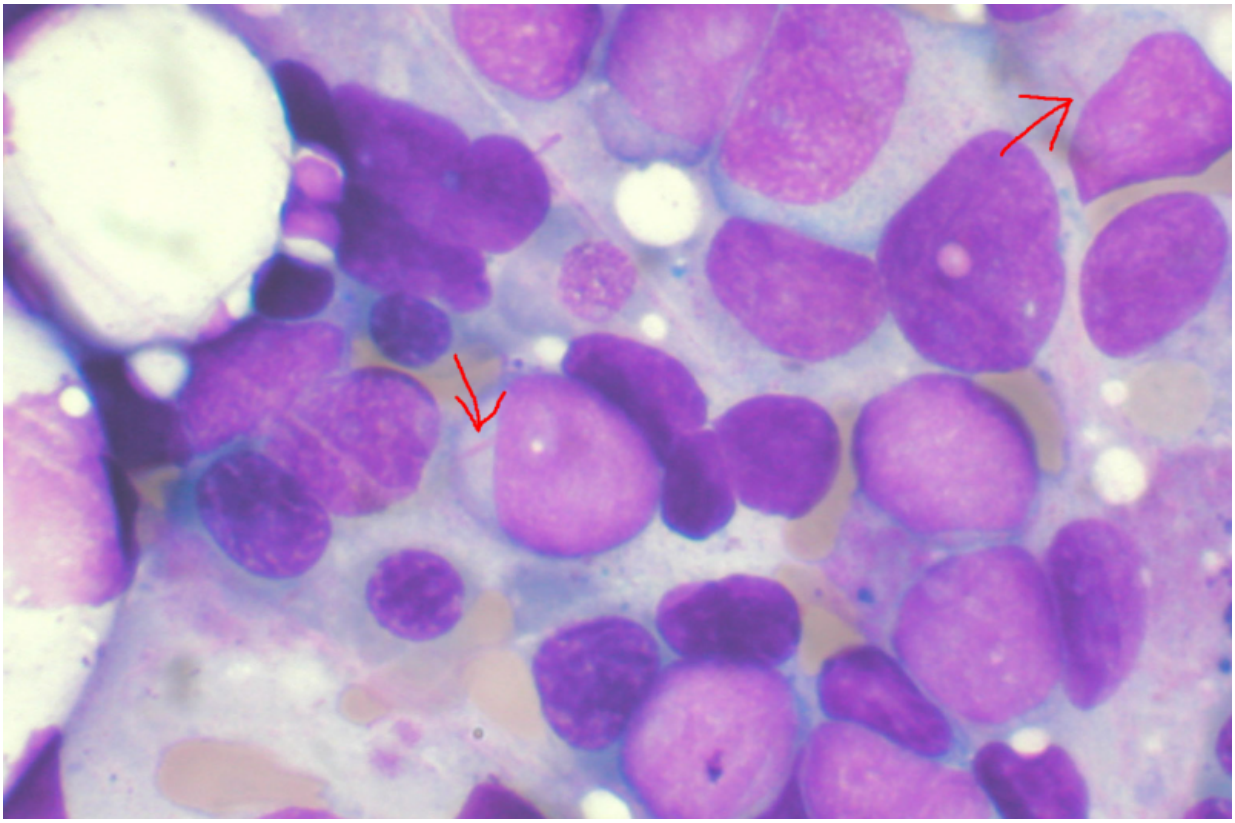

Bone marrow aspirate showing acute myeloid leukemia. Several blasts have Auer rods. Credit: Wikipedia

Canadian researchers followed their intuition that a drug initially intended for heart failure could be effective in treating cancer. Those

efforts have borne fruit, as demonstrated by their work published in the *Journal of Experimental and Clinical Cancer Research*.

"Some drugs designed for certain therapeutic indications can be used for other diseases; this is called drug repositioning. Since these drugs have already passed the critical approval stages in toxicology, preclinical safety, pharmacokinetics, etc., they represent a real advantage in initiating new clinical trials more quickly," says Elodie M. Da Costa, a doctoral student at Université de Montréal and first author of the study.

"Here, we observed for the very first time the anticancer and epigenetic properties of proscillaridin A—a cardiotonic used to treat heart failure or cardiac arrhythmia—in leukemias in children expressing the MYC gene. When subjected to mutations or overexpression, this gene induces uncontrolled cell proliferation, thus promoting the development of cancer," explains Elodie M. Da Costa.

Currently, no effective treatment is approved to target this type of alteration in leukemias. This approach therefore represents a promising avenue for developing strategies to inhibit the MYC gene and its oncogenic partners.

To achieve these results, the research team used various advanced techniques in molecular biology, next-generation sequencing and pharmacology to evaluate the efficacy and mechanism of action of this drug in the treatment of leukemias. The team observed that the molecule preferentially attacks leukemic stem cells, which drive the spread of the disease.

"Each cancer is unique, and to increase the chances of survival, precision medicine is a promising way forward by developing patient-specific therapeutic strategies," says Noël J.M. Raynal, researcher at CHU Sainte-Justine and professor at Université de Montréal. "It is therefore essential

to analyze the different characteristics of each cancer in genomic, epigenetic and proteomic terms in order to identify optimal therapies. Research on drug repositioning opens a new path toward innovative therapeutic options in the treatment of cancer. "

Leukemia, a relentless battle

Over the past few decades, the survival rate of patients with pediatric leukemias has improved significantly. However, some patients remain resistant to current therapies and two-thirds of patients have significant long-term side effects related to the toxicity of treatments (metabolic and neurological disorders, and sometimes secondary cancers).

"In the medium term, we hope to complete the preclinical characterization of this drug to eventually initiate clinical trials. Our ultimate goal is to identify more specific and less toxic therapeutic strategies for children with leukemia characterized by the MYC gene in order to improve survival rates and quality of life," notes Elodie M. Da Costa. "CHU Sainte-Justine is a leader in North America in cancer care and research and we are proud to contribute to the advancement of knowledge in this field," adds Noël J.M. Raynal.

According to Canadian Cancer Society statistics, leukemias are the most commonly diagnosed cancers in children aged 0 to 14 years and account for about 32% of childhood cancers in Canada. Leukemia is the second leading cause of childhood cancer death in Canada. The proto-oncogene MYC is deregulated in nearly 80% of leukemias.

Provided by University of Montreal

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