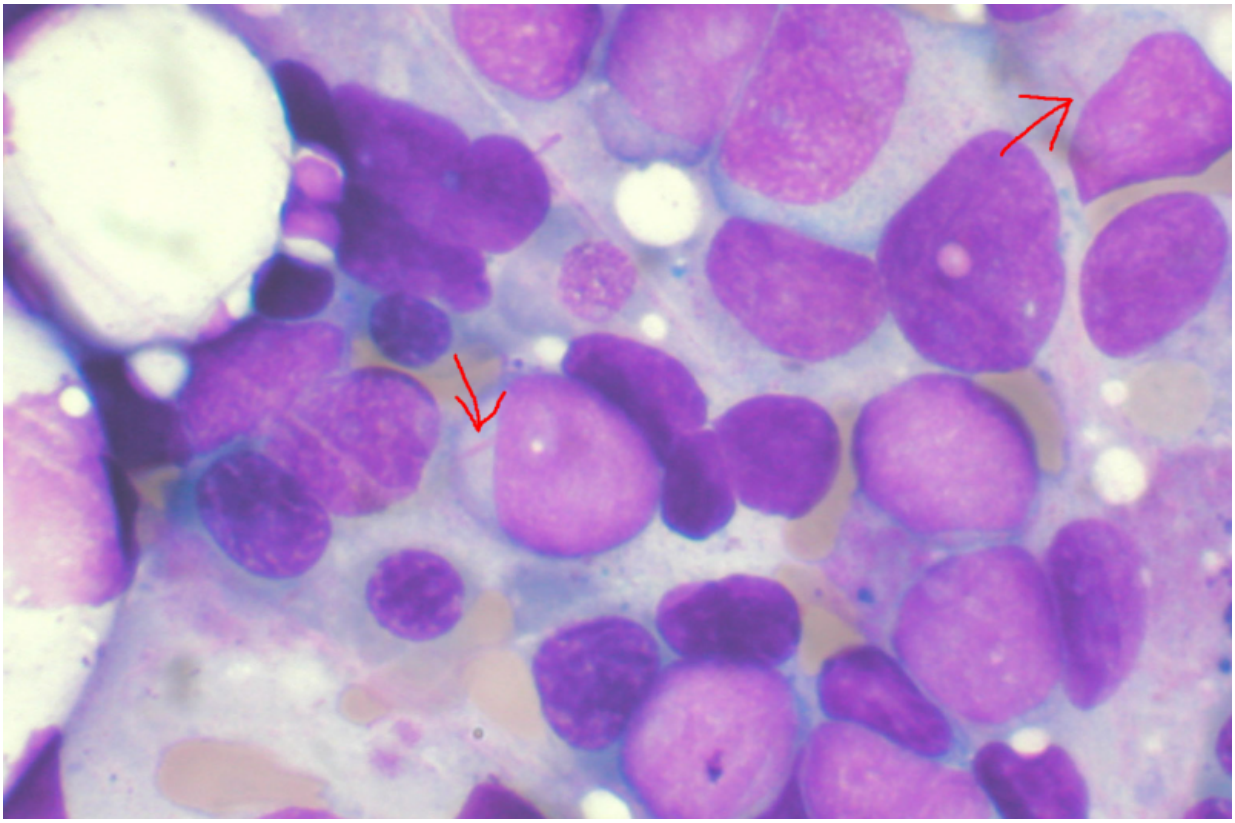
New metabolic profile in patients with acute myeloid leukemia

July 13 2022



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

An article published in the journal *Nature Communications* describes a specific metabolic adaptation in some patients with acute myeloid

leukemia affected by tandem mutations in the FLT3 gene. The findings, which could shed light on future specific-type combined therapies for these patients, is the result of the collaboration between the teams led by Professor Marta Cascante, from the Faculty of Biology, the Institute of Biomedicine of the University of Barcelona (IBUB) and the Liver and Digestive Diseases Networking Biomedical Research Centre (CIBEREHD), and Professor Jan Jacob Schuringa, from the University of Groningen (the Netherlands).

The study includes the participation of lecturer Silvia Marín (UB-IBUB) and its first author is the researcher Ayşegül Erdem, who finished her doctoral studies under the supervision of Cascante and Schuringa as part of the European project "Deciphering the metabolism of hematological cancers" (HaemMetabolome).

The great genetic and metabolic variability of acute myeloid leukemia

Acute myeloid leukemia (AML) is a pathology with a high genetic, clinical and metabolic heterogeneity which hinders the success of the currently available therapeutic treatments. Specifically, the FTL3 internal gene duplications (FLT3-ITD$^+$) represent the most prevalent mutations in AML patients and are associated with high relapse rates in those affected.

The new study defines a new specific metabolic profile related to the patients with the FLT3-ITD$^+$ phenotype. To get the results, the team applied innovative techniques of metabolomics, proteomics and stable isotope-resolved metabolomics (SIRM). The team found that leukemic cells in patients with these mutations present high levels of the succinate-CoA Ligases enzymes and a high activity of the chain of mitochondrial electron transport complex II which provides energy to the cell

metabolism.

Moreover, "the study shows for the first time that this subtype of leukemic cells uses the lactate as a substrate for mitochondrial respiration. Therefore, this profile of cancer cells could be sensitive to the simultaneous pharmacological inhibition of complex II of the respiratory chain and lactate transporter," notes Professor Marta Cascante, from the Department of Biochemistry and Molecular Biomedicine of the UB.

In all cells, the main substrates of the mitochondrial respiration chain are pyruvate (from glucose) and other carbohydrates and amino acids that lead to pyruvate, apart from ketone bodies, glutamine and fatty acids. "However, in general, lactate had not been described to date as a substrate of mitochondrial respiration in tumor cells," adds Marta Cascante, also ICREA Academic researcher.

Customized medicine depending on the identified mutations

As stated in the study, the chain of mitochondrial respiration in these leukemic cells could be inhibited pharmacologically if we combine synergistically the complex II inhibitors (specifically, TTFA and 3-NPA compounds) with those from the MCT1 lactate transporter (CHC and AZD3965).

This better knowledge of the metabolic profile of a patient's leukemic cells could lead to new and potential possibilities in the design of specific-type combined therapies according to the mutations identified at the genetic level. "Customized medicine, which aims to establish specific therapies for each patient according to the phenotype of their tumor, implies having the best knowledge of each patient's tumor in

order to be able to offer them the best therapeutic option for their specific tumor," concludes researcher Marta Cascante.

More information: Ayşegül Erdem et al, Inhibition of the succinyl dehydrogenase complex in acute myeloid leukemia leads to a lactate-fuelled respiratory metabolic vulnerability, *Nature Communications* (2022). DOI: 10.1038/s41467-022-29639-0

Provided by University of Barcelona

Citation: New metabolic profile in patients with acute myeloid leukemia (2022, July 13) retrieved 23 June 2024 from https://medicalxpress.com/news/2022-07-metabolic-profile-patients-acute-myeloid.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.