

New drug combination shows promise for resistant leukaemia

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A Wright's stained bone marrow aspirate smear of patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

Patients with acute myeloid leukaemia (AML) can look forward to the development of new therapies following the discovery by Walter and Eliza Hall Institute researchers of a new way to kill cells that are dangerously multiplying.

A process known as apoptosis (programmed [cell death](#))—which is a natural and necessary response to keep the proliferation of human [cells](#) in check—is interrupted in cancers, including AML, leading to unchecked cell growth.

Institute researcher Dr Gabriela Brumatti and her PhD student Chunyan Ma are part of a team, led by Professor John Silke from the Institute and Professor Paul Ekert from the Murdoch Childrens Research Institute in Melbourne, investigating ways to target particular types of AML, hoping to increase the chance of a cure for the patient while limiting damage to healthy cells.

Dr Brumatti said traditional chemotherapies, which induce apoptosis, had a high relapse rate. For example, within five years of completing treatment 50 per cent of AML patients suffer a relapse of their cancer. Of those who relapse, only 50 per cent survive.

Her team tried a 'blue sky' approach to their research and inhibited apoptosis of AML cells in order to unleash an alternative form of cell death called necroptosis. They found this necroptosis cell death pathway was more effective at killing AML than apoptosis. These findings have just been published in the research journal, *Science Translational Medicine*.

In preclinical trials they used a combination of drugs—birinapant, a new anti-cancer drug, and emricasan, a US Food and Drug Administration (FDA) approved inhibitor of apoptosis—to kill AML.

"It has been speculated that inducing necroptosis might be an effective way to kill cancer cells", said Professor Silke. "Our work now demonstrates clearly it is a clinically feasible and safe approach."

Dr Brumatti said since [cancer cells](#) often acquire resistance to traditional

chemotherapy-induced apoptosis, this novel type of chemotherapy had the potential to be used to treat otherwise impossible to treat leukaemias.

More information: "The caspase-8 inhibitor emricasan combines with the SMAC mimetic birinapant to induce necroptosis and treat acute myeloid leukemia," *Science Translational Medicine*, [DOI: 10.1126/scitranslmed.aad3099](https://doi.org/10.1126/scitranslmed.aad3099)

Provided by Walter and Eliza Hall Institute

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