

Two-pronged attack increases potency of new anti-cancer drugs

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Walter and Eliza Hall Institute researchers have discovered that the treatment of the most deadly form of blood cancer may be improved by combining two recently developed drugs.

The combination of birinapant and p38 inhibitors showed promise in preclinical studies as a new treatment for [acute myeloid leukaemia](#) (AML). Both drugs have been studied alone in clinical trials for treating cancer, offering hope that the combination could be safely given to people with AML who have few other treatment options.

Dr Najoua Lalaoui, Professor John Silke and colleagues from the Walter and Eliza Hall Institute made the discovery when searching for ways to enhance birinapant's anti-cancer effects. Their findings were published in the latest edition of the journal *Cancer Cell*.

Dr Lalaoui said the team was excited to discover that the combination of p38 inhibitors and birinapant had a much stronger anti-cancer effect than either agent alone. "Both p38 inhibitors and birinapant have been safely used in humans in clinical trials," she said. "We are hopeful that the combination of these agents could be an effective anti-cancer treatment."

AML causes around 850 deaths in Australia each year, more than any other type of [blood cancer](#). Many people with AML respond poorly to treatment, with fewer than one-third surviving for five years after their diagnosis.

Dr Lalaoui said that high-dose chemotherapy, the current treatment for people with AML, had many toxic side effects. "Our findings have made us hopeful that a combination of birinapant and a p38 inhibitor may be more effective in treating AML than current therapies, and also have less toxicity for patients," she said. "We tested forms of AML that are highly resistant to chemotherapy and found that birinapant and p38 inhibitors could even

kill these cancer cells, which is great news."

Professor Silke said the discovery was underpinned by two decades of research at the institute, mostly funded by the Australian National Health and Medical Research Council, into proteins called IAPs, which are targeted by birinapant.

"We have had a long term interest in how IAPs function in healthy and diseased cells," he said. "Our research into how IAPs work made an important contribution to the initial development of birinapant as a specific IAP inhibitor.

"Birinapant has been used in [clinical trials](#) for several types of cancers. Our latest research is part of an exciting next step, fine tuning how birinapant can be used in the clinic to enhance its anti-cancer effects," Professor Silke said. Birinapant is being developed by TetraLogic Pharmaceuticals Corporation based in Malvern, US.

The research team worked closely with Pam, a community representative, through the Walter and Eliza Hall Institute's consumer-researcher buddy system. "The involvement of Pam in this project provided us with invaluable feedback and review, and opportunities to discuss our ideas with someone who has a personal experience of [cancer](#)," Dr Lalaoui said.

Provided by Walter and Eliza Hall Institute

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