

Scientists discover secret to promising new cancer drug

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Dr Brandon Aubrey of the Walter and Eliza Hall Institute of Medical Research.
Credit: The Walter and Eliza Hall Institute of Medical Research

Australian researchers have resolved a mystery about how a promising new class of anti-cancer drugs, called nutlins, work - paving the way for improving the future of cancer treatment.

Nutlins, which are in early clinical trials for treating blood cancers, sparked interest worldwide for their ability to stop [cancer](#) growth by activating the body's natural cancer-suppressing mechanism - a gene called P53 - while at the same time avoiding some of the damaging effects of chemotherapy. However, until now, it was unknown whether nutlins were killing the cancerous cells, or just suppressing them temporarily.

Dr Liz Valente, Dr Brandon Aubrey, Professor Andreas Strasser and colleagues from the Walter and Eliza Hall Institute have found the answer to the long-standing question of how nutlins work by discovering that nutlins cause cancer cells to self-destruct and not just go to 'sleep'.

The research, published in the journal *Cell Reports*, revealed that nutlins activated P53 to trigger programmed cell death (apoptosis) of blood cancer cells. This was identified through the presence of a protein called PUMA.

Dr Aubrey, who is also a clinical haematologist at The Royal Melbourne Hospital, said the discovery not only reinforced that nutlins were a promising new treatment for blood cancer, but also that it provided invaluable information for a more tailored approach to patient care.

"Our findings will help identify which patients are most likely to benefit from nutlins and which types of cancers are most likely to respond to nutlins as a treatment," Dr Aubrey said.

"Understanding in detail how the drugs work will help in the design of better clinical trials and bring the world closer to more precise and personalised medical treatments for cancer."

Professor Strasser said previous research around P53 showed the gene was like a natural 'guardian' of healthy cells in the body and was a major barrier to developing cancer.

"When functioning properly, P53 is activated in response to early cancerous changes in the cell," Professor Strasser said. "P53 acts by either halting the cell while repairs are made or by forcing the cell to die if it cannot be repaired.

"Without the 'help' of P53, a damaged cell can be allowed to multiply, leading to cancer development. P53 lies dormant in many types of cancer - that do not have mutations in P53 - and the nutlins work through re-awakening its activity."

Professor Strasser said knowing more information about what nutlins were capable of by identifying how nutlins were activating P53 to trigger cell death in cancers was a critical step towards developing more sophisticated treatments for cancer.

"By understanding how nutlins are killing [cancer cells](#), we can begin to formulate their best possible use, including choosing the best partner drugs to combine the nutlins with," Professor Strasser said.

Dr Aubrey is a PhD student at the Walter and Eliza Hall Institute enrolled through The University of Melbourne's Department of Medical

Biology. Professor Strasser is a joint division head in the Molecular Genetics of Cancer division at the Walter and Eliza Hall Institute.

The research was supported by the National Health and Medical Research Council, the Leukemia and Lymphoma Society, Cancer Council Victoria, the Leukaemia Foundation of Australia, the Victorian Cancer Agency and the Victorian Government Operational Infrastructure Support Scheme.

The Walter and Eliza Hall Institute is the research powerhouse of the Victorian Comprehensive Cancer Centre, an alliance of leading Victorian hospitals and research centres committed to controlling cancer.

More information: Therapeutic Response to Non-genotoxic Activation of p53 by Nutlin3a Is Driven by PUMA-Mediated Apoptosis in Lymphoma Cells, *Cell Reports*, DOI: dx.doi.org/10.1016/j.celrep.2016.01.059 , [www.cell.com/cell-reports/full...2211-1247\(16\)30037-7](http://www.cell.com/cell-reports/full...2211-1247(16)30037-7)

Provided by Walter and Eliza Hall Institute

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