

Gene test could pinpoint patients sensitive to new type of cancer drug

22 December 2016



Credit: National Cancer Institute

Testing for a gene commonly mutated in ovarian cancers could pick out patients who will respond well to a promising new class of cancer drugs, a major new study reveals.

Scientists found that defects in a gene called ARID1A caused sensitivity to [new drugs](#) targeting the DNA repair process within tumour cells.

The new drugs – called ATR inhibitors – are already being tested in early clinical trials, and the new research could help identify those patients who will benefit most.

Scientists at The Institute of Cancer Research, London, used molecular screening techniques to find that cancers with mutations in ARID1A were particularly sensitive to ATR inhibitors.

ARID1A is mutated in a wide range of hard-to-treat tumour types, including ovarian [cancer](#) and stomach cancer, but until now there has been no way of targeting treatment at tumours with this genetic defect.

The research, which is published in the journal *Nature Communications*, was funded by Cancer Research UK and Breast Cancer Now.

Scientists at The Institute of Cancer Research (ICR) found that ATR inhibitors stopped cancer cells with ARID1A mutations from growing, both in culture dishes and in mice.

They also found that switching off the ARID1A gene in breast and bowel cancer cells greatly increased their sensitivity to ATR inhibitors.

The researchers found the treatment killed cancer cells with ARID1A mutations through a process called 'synthetic lethality'.

Cancer cells with ARID1A mutations become particularly reliant on the DNA safeguarding activity of the ATR protein to survive – so they are especially sensitive to drugs that block its effects.

Patients on clinical trials of ATR inhibitors could now start to be tested for ARID1A mutations in their tumours – in order to assess whether those with the genetic defects are particularly likely to benefit.

Dr Chris Lord, Leader of the Gene Function Team at The Institute of Cancer Research, London, said: "Our research has opened up a potential way of personalising treatment for cancer by targeting drugs to those patients who will benefit most.

"We found in cell cultures and in mice that cancers with defective versions of the ARID1A gene are particularly sensitive to a new class of drug called ATR inhibitors."

"Our research could lead to patients with ARID1A mutant tumours being assessed for whether they respond particularly well to this new class of cancer treatment."

Dr Justine Alford, Cancer Research UK's senior

science information officer, said: "By identifying a potential way to exploit a specific genetic vulnerability in cancer this research could point the way to tailoring treatments to each patient, helping to make them kinder and more effective. The next steps will be to better understand the effects of targeting this weakness, and to find out whether this promising strategy will work in people."

Katie Goates, Senior Research Communications Officer at Breast Cancer Now, said: "This early finding could bring us a step closer to more 'personalised' medicine, targeting treatment to exploit weaknesses in patients' tumours and hopefully improve their chances of survival.

"It's particularly exciting to see an idea that was initially tested in breast [cancer cells](#) be translated into potential benefit for a number of other cancers. We hope these findings now lay the groundwork for [clinical trials](#) to investigate the potential of ATR inhibitors as a targeted cancer treatment in the near future."

More information: Chris T. Williamson et al. ATR inhibitors as a synthetic lethal therapy for tumours deficient in ARID1A, *Nature Communications* (2016). [DOI: 10.1038/ncomms13837](https://doi.org/10.1038/ncomms13837)

Provided by Institute of Cancer Research

APA citation: Gene test could pinpoint patients sensitive to new type of cancer drug (2016, December 22) retrieved 12 June 2022 from <https://medicalxpress.com/news/2016-12-gene-patients-sensitive-cancer-drug.html>

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