Cancer-killing pill that annihilates tumours hailed as ‘holy grail’ breakthrough

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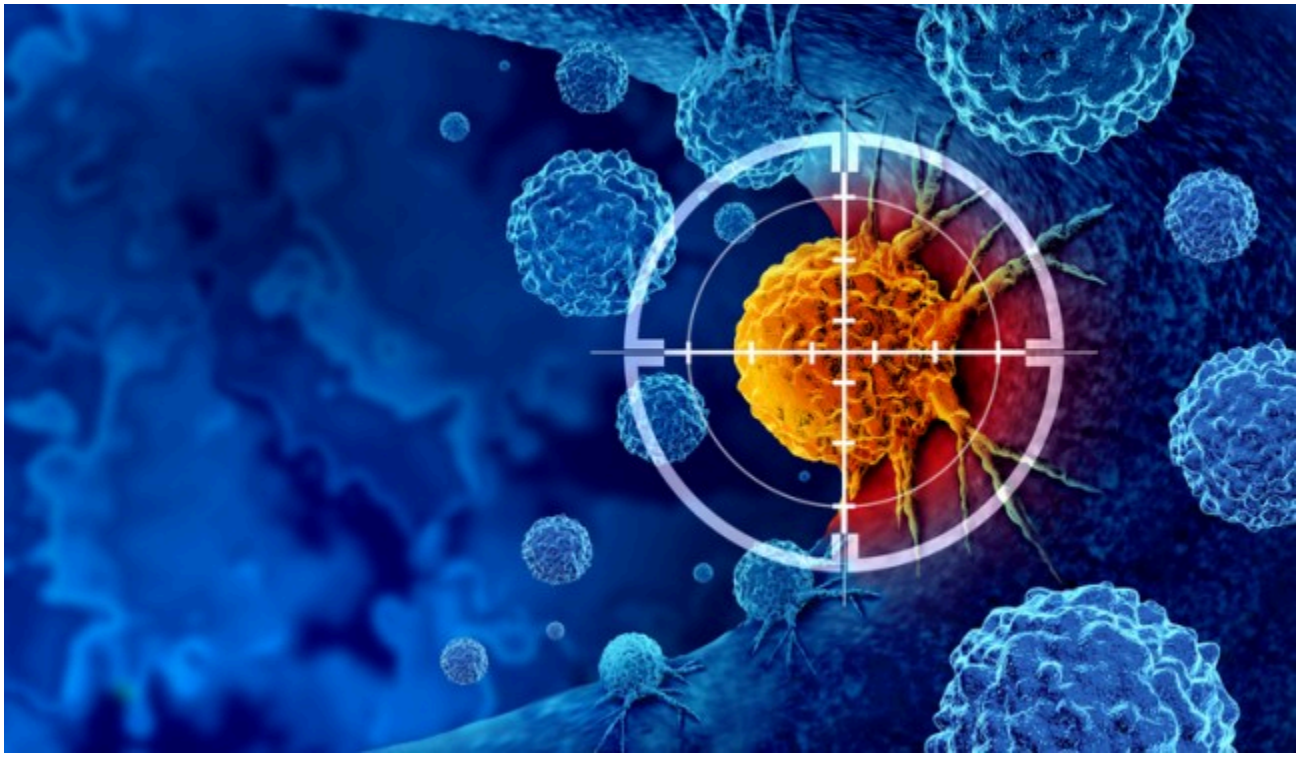


A breakthrough treatment could target cancer cells without damaging other tissues (Picture: Getty/iStockphoto)

Scientists have developed a ‘holy grail’ molecule that kills all solid cancer tumours, leaving healthy cells unaffected.

The team at the City of Hope, one of the largest cancer research and treatment organisations in the US, made the breakthrough against the proliferating cell nuclear antigen (PCNA) protein.

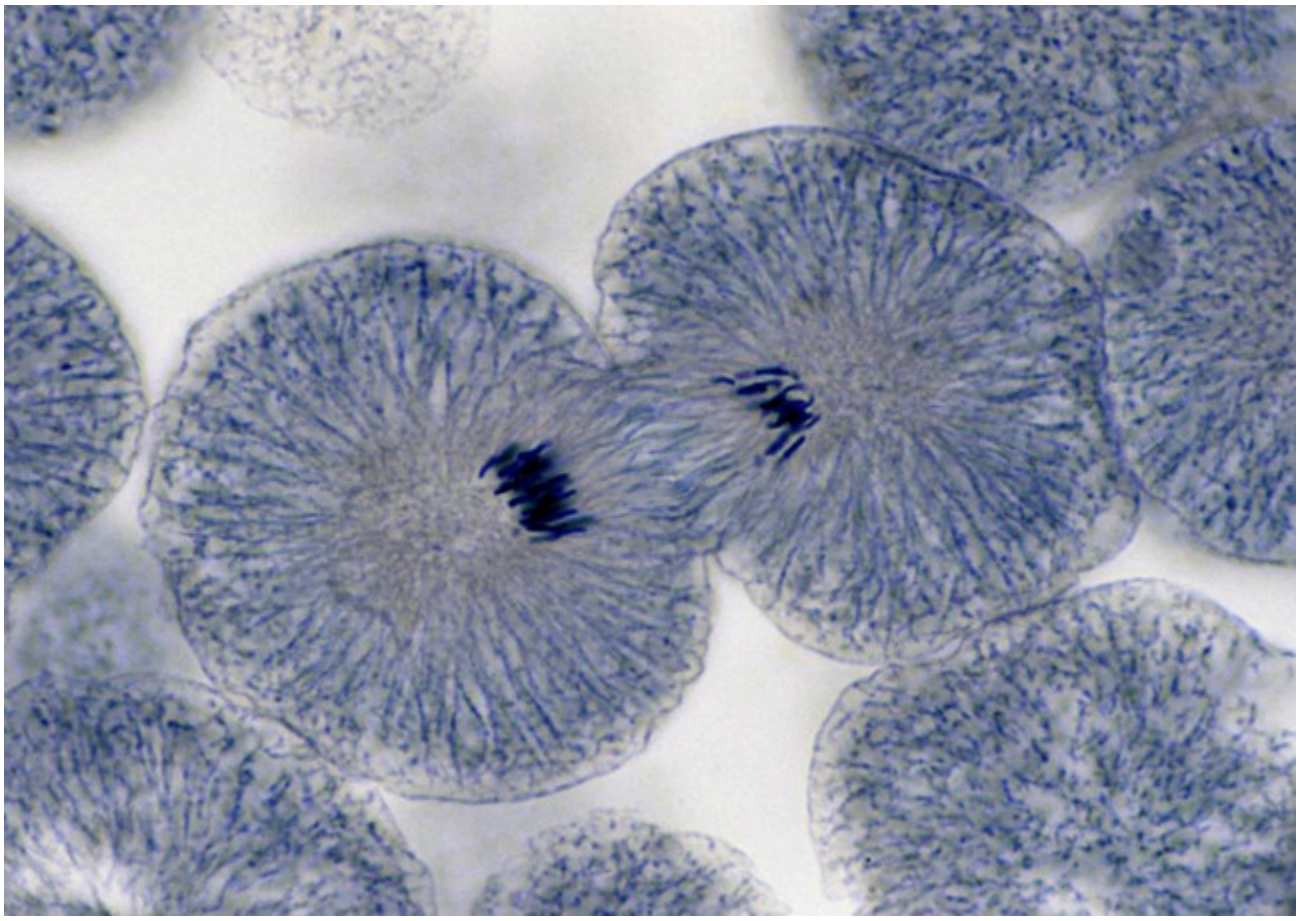
In a mutated form PCNA is critical in DNA replication and repair of all expanding tumours, but a molecule developed by the team, AOH1996, targets and kills the mutated PCNA.

Previously PCNA was thought too challenging to be a target for therapy, but preclinical research shows AOH1996 seems to annihilate all solid tumours – without effects on other body cells.

The team is continuing to investigate the mechanisms that make this cancer-stopping pill work in animal models, while a Phase 1 clinical trial test is also ongoing in humans.

However, it is not yet known if the drug will continue to be taken in pill form once fully developed and approved for use.

The new therapy is the result of 20 years of research and development – and is named after Anna Olivia Healey (AOH), a young girl born in 1996 who unfortunately was not able to beat cancer.



PCNA is essential for cell division – but in a mutated form helps cancer tumours grow (Picture: Getty)

‘Most targeted therapies focus on a single pathway, which enables wily cancer to mutate and eventually become resistant,’ said team leader Dr Linda Malkas, a professor in City of Hope’s department of molecular diagnostics and experimental therapeutics.

‘PCNA is like a major airline terminal hub containing multiple plane gates.

‘Data suggests PCNA is uniquely altered in cancer cells, and this fact allowed us to design a drug that targeted only the form of PCNA in cancer cells.

‘Our cancer-killing pill is like a snowstorm that closes a key airline hub, shutting down all flights in and out only in planes carrying cancer cells.’

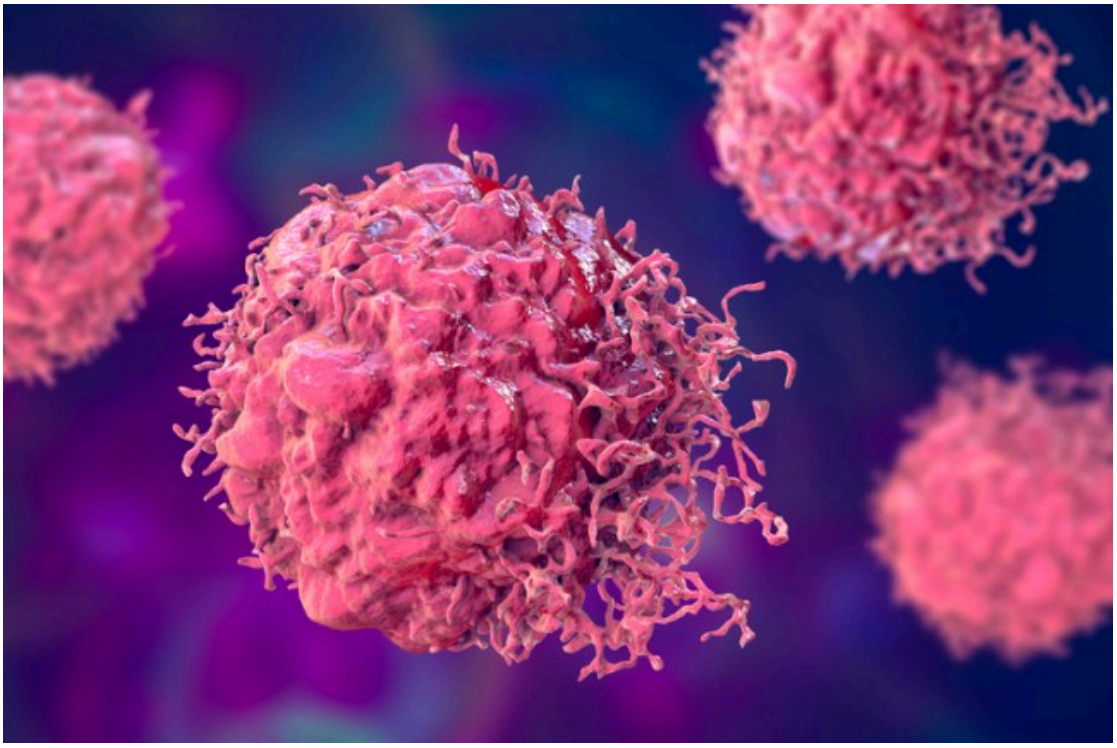
The study, published in the journal Cell Chemical Biology, claims AOH1996 has been effective in preclinical research treating cells derived from breast, prostate, brain, ovarian, cervical, skin and lung cancers.

‘Results have been promising,’ said Dr Malkas. ‘AOH1996 can suppress tumor growth as a monotherapy or combination treatment in cell and animal models without resulting in toxicity.

‘The investigational chemotherapeutic is currently in a Phase 1 clinical trial in humans at City of Hope.

The researchers have tested AOH1996 in more than 70 cancer cell lines and several normal control cells. They found the molecule selectively kills cancer cells by disrupting the normal cell reproductive cycle.

In their research, the team has found AOH1996 prevented cells with damaged DNA from dividing and from making a copy of faulty DNA, causing cancer cell death – known as apoptosis – but it did not interrupt healthy stem cells.



AOH1996 has been found to be effective against many different types of cancer (Picture: Getty/iStockphoto)

Study co-author and associate research professor Dr Long Gu said: 'No one has ever targeted PCNA as a therapeutic because it was viewed as 'undruggable', but City of Hope was able to develop an investigational medicine for a challenging protein target.

'We discovered that PCNA is one of the potential causes of increased nucleic acid replication errors in cancer cells.

'Now that we know the problem area and can inhibit it, we will dig deeper to understand the process to develop more personalised, targeted cancer medicines.'

Experiments showed that the investigational pill made cancer cells more susceptible to chemical agents that cause DNA or chromosome damage, hinting that AOH1996 could become a useful tool in combination therapies and new chemotherapeutics.

Professor Daniel Von Hoff, co-author, added: 'City of Hope has world leaders in cancer research. They also have the infrastructure to drive translational drug discovery from the laboratory into the clinic for patients in need.'

The Phase 1 clinical trial began in October.

As a next step, the researchers will look to better understand the mechanism of action to further improve the ongoing clinical trial in humans.