Self-assembling anti-cancer molecules created in minutes

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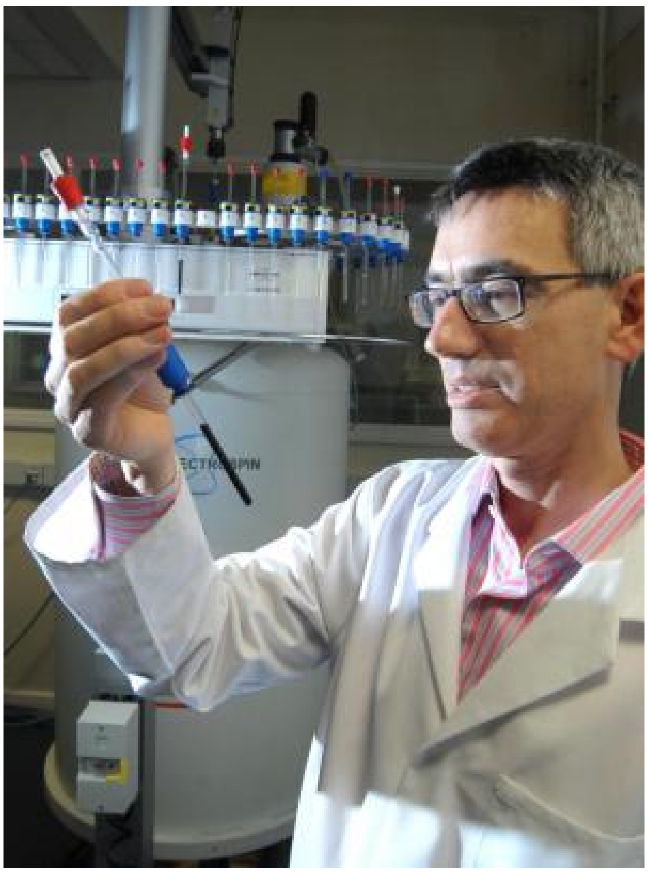

Professor Peter Scott of the University of Warwick. Credit: University of Warwick

Researchers have developed a simple and versatile method for making artificial anti-cancer molecules that mimic the properties of one of the body's natural defence systems.

The chemists, led by Professor Peter Scott at the University of Warwick, UK, have been able to produce molecules that have a similar structure to peptides which are naturally produced in the body to fight cancer and infection.

Published in *Nature Chemistry*, the molecules produced in the research have proved effective against colon cancer cells in laboratory tests, in collaboration with Roger Phillips at the Institute for Cancer Therapeutics, Bradford, UK.

Artificial peptides had previously been difficult and prohibitively expensive to manufacture in large quantities, but the new process takes only minutes and does not require costly equipment. Also, traditional peptides that are administered as drugs are quickly neutralised by the body's biochemical defences before they can do their job.

A form of complex chemical self-assembly, the new method developed at Warwick addresses these problems by being both practical and producing very stable molecules. The new peptide mimics, called triplexes, have a similar 3D helix form to natural peptides.

"The chemistry involved is like throwing Lego blocks into a bag, giving them a shake, and finding that you made a model of the Death Star" says Professor Scott. "The design to achieve that takes some thought and computing power, but once you've worked it out the method can be used to make a lot of complicated molecular objects."

Describing the self-assembly process behind the artificial peptides Professor Scott says: "When the organic chemicals involved, an amino alcohol derivative and a picoline, are mixed with iron chloride in a solvent, such as water or methanol, they form strong bonds and are designed to naturally fold together in minutes to form a helix. It's all thermodynamically downhill. The assembly instructions are encoded in the chemicals themselves."

"Once the solvent has been removed we are left with the peptide mimics in the form of crystals", says Professor Scott. "There are no complicated separations to do, and unlike a Lego model kit there are no mysterious bits left over. In practical terms, the chemistry is pretty conventional. The beauty is that these big molecules assemble themselves. Nature uses this kind of self-assembly to make complex asymmetric molecules like proteins all the time, but doing it artificially is a major challenge."

Whilst the peptide mimics created by the process have been successful in laboratory tests on colon cancer cells they will require further research before they can be used in clinical trials on patients. Nevertheless they are made of simple building blocks and in early tests the team have shown that they have very low toxicity to bacteria. "This is very unusual and promising selectivity," says Professor Scott.

More information: Asymmetric triplex metallohelices with high and selective activity against cancer cells, *Nature Chemistry*, DOI: 10.1038/nchem.2024

Provided by University of Warwick