Custom-built molecule shows promise as anti-cancer therapy

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Credit: AI-generated image (disclaimer)

Scientists at the University of Bath funded by Cancer Research UK have custom-built a molecule which stops breast cancer cells from multiplying in laboratory trials, and hope it will eventually lead to a treatment for the disease.

But perhaps even more importantly the method they used to create the molecule has potential to be applied to develop new treatments for a wide range of cancers and other diseases.

The team, from the Department of Biology & Biochemistry, working with colleagues at the University of Queensland in Australia and the University of Bristol, modified a protein which can interfere with cell multiplication in many cancers, including breast cancer, by binding with another protein and rendering it inactive.

They took a small piece of the protein, called a peptide, that is known to be important in binding, and modified it to retain the structure otherwise lost when cut out. The modification has the additional advantage of protecting the peptide from being broken down within cells. The resulting molecule still binds to its target protein and inhibits cancer cell multiplication, but crucially can travel across cell membranes to get at it. The full-sized proteins, which the peptides are taken from, are usually too large to protect from breakdown or to cross protective cell membranes so this removes a literal barrier to developing treatments.

The study is published in the journal *ACS Chemical Biology*.

Dr Jody Mason, one of the lead researchers on the project, said: "Peptides have the potential to be incredibly potent drugs which are exquisitely specific for their target. However they are easily broken down in the body, much like when we eat a steak. We have modified the peptides so that they retain the structure they have within the full-size protein and can therefore bind to the target "

Professor David Fairlie, from the University of Queensland added "This is a particularly challenging cancer target involving intertwined proteins and large surfaces that must be blocked. International collaborations like this one have the potential to combine resources and scientific skills

from multiple disciplines to conquer difficult problems in targeting human disease."

Dr Justine Alford, Cancer Research UK's senior science information officer, said: "This early study may have laid the groundwork for a potential new treatment for certain cancers by creating a sophisticated designer molecule that can effectively block a cancer-fuelling target in cells.

"Cancer survival is improving, but people still die from their disease, so we need to develop innovative ways such as this that could help more people survive in the future."

The team now intend to continue to work on the molecule to improve its stability, with a long-term view to it eventually becoming a cancer drug, although this is still years away.

They are also interested in finding other candidate peptides for similar trials.

The researchers believe that other small peptides are a promising avenue of research to create new treatments for different types of cancer, and potentially other diseases such as Alzheimer's disease.

More information: Daniel Baxter et al. Downsizing Proto-oncogene cFos to Short Helix-Constrained Peptides That Bind Jun, *ACS Chemical Biology* (2017). DOI: 10.1021/acschembio.7b00303

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