Experimental 'stapled peptide' drug blocks key cancer molecule

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(Medical Xpress)—US scientists have developed an artificial molecule called a 'stapled peptide' that can shut down the cancer-fuelling effects of a molecule called Wnt.

The peptide has so far only been tested in mice, but "may serve as a prototype therapeutic agent" for patients, according to the researchers from Harvard Medical School.

Wnt is part of a molecular signalling network that controls several normal cell processes. But this system of regulating the cell can go awry and lead to cancer.

Faults in Wnt signalling are found in many cancers, particularly bowel cancer.

The new peptide mimics the structure of a naturally occurring molecule called BCL9, which is necessary to transmit signals sent by Wnt in cancer cells, but not in healthy cells.

Because of its similarity to BCL9, the synthetic peptide stops signals being sent, shutting off the cancer-driving signals inside cancer cells.

Commenting on the US team's findings, Dr Mariann Bienz, a Cancer Research UK scientist from the MRC Laboratory of Molecular Biology in Cambridge, said that scientists have been trying to find ways to block Wnt or the molecules it interacts with for several years.

She said: "One of the biggest challenges in cancer research is finding ways to disarm the molecules that fuel the disease, and blocking the interaction between proteins inside cells is notoriously difficult. This work builds on ours and other groups, and shows that it's possible to block the cancer-promoting interaction between BCL9 and beta-catenin, two key proteins in the Wnt signalling pathway.

"The technology they've used – called stapled peptides – is very interesting, and could be used against other molecules that are currently considered 'undruggable'."

She also said that significant challenges remain. Scientists do not yet know whether stapled peptides-based treatments can effectively reach their targets inside cells, nor how they are processed by the body.

"But this is a very active area of research, and it will be exciting to see where it leads," she added.

More information: Takada, K. et al. (2012). Targeted Disruption of the BCL9/ -Catenin Complex Inhibits Oncogenic Wnt Signaling, *Science Translational Medicine*, 4 (148) 148ra117. DOI: 10.1126/scitranslmed.3003808