New compound discovered that rapidly kills liver cancer

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Scientists have identified a new compound that rapidly kills hepatocellular carcinoma (HCC) cells, the most common form of liver cancer and fifth most common cancer worldwide, while sparing healthy tissue. The compound, Factor Qunolinone Inhibitor 1 (FQI1), works by inhibiting an oncogene originally discovered by a team of researchers led by Devanand Sarkar, M.B.B.S., Ph.D., Harrison Scholar at Virginia Commonwealth University (VCU) Massey Cancer Center, Blick Scholar and assistant professor in the Department of Human and Molecular Genetics and member of the VCU Institute of Molecular Medicine at the VCU School of Medicine.

Recently published in the journal P*roceedings of the National Academy of Sciences*, the study demonstrates that HCC cells have what is known as an "oncogene addiction" to the transcription factor Late SV40 Factor (LSF). Oncogene addiction is a term used when a cancer cell is found to be dependent on a single gene to survive. Using the compound Factor Quinolinone Inhibitor 1 (FQI1), the scientists prevented LSF from binding to HCC DNA during the transcription process, which is the first step in a series of actions that lead to cell division and duplication. This action caused rapid HCC cell death in laboratory experiments and a dramatic reduction in tumor growth in mouse models with no observable toxicity to normal liver cells.

"We may be on the verge of developing a new, effective drug for liver cancer," said Sarkar. "In the last 2 to 3 years, we demonstrated the role of LSF in liver cancer and have been screening over 110,000 compounds to identify the ones that inhibit LSF function. We identified FQI1 as one of a class of effective compounds, but we never anticipated it would work this well."

Sarkar discovered LSF's role in liver cancer in 2010 when he demonstrated significantly higher LSF levels in HCC patients in comparison to healthy individuals, and showed that inhibition of LSF reduced the progression of HCC in laboratory experiments. This finding led to the collaboration between VCU and Boston University that resulted in the discovery of FQI1.

Now that FQI1 has been identified, pharmacokinetic studies are being conducted to determine how the drug behaves in the human body. Once the scientists have determined how the drug is absorbed, distributed, metabolized and eliminated from the body, they will work with clinicians to translate their findings into phase I clinical trials in patients with liver cancer.

"We have proven this compound is effective and nontoxic in living animals," said Sarkar. "While we won't know how FQI1 reacts in humans until the first clinical trial, we are very excited by our findings and hope they lead to a new drug for a disease that is currently very difficult to treat."

More information:
www.pnas.org/content/early/201 …
601109.full.pdf+html

Provided by Virginia Commonwealth University

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