# Protein found to block benefits of vitamin A cancer therapy

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Devanand Sarkar, M.B.B.S., Ph.D., led a team of scientists who demonstrated that a protein known as AEG-1 blocks the effects of retinoic acid in leukemia and liver cancer. Credit: VCU Massey Cancer Center

Retinoic acid is a form of vitamin A that is used to treat and help prevent the recurrence of a variety of cancers, but for some patients the

drug is not effective. The reason for this resistance was unclear until this week when researchers from Virginia Commonwealth University (VCU) Massey Cancer Center demonstrated that a protein known as AEG-1 blocks the effects of retinoic acid in leukemia and liver cancer. Because AEG-1 is overexpressed in nearly every cancer, these findings could impact the care of countless cancer patients.

Details of the study were published this week in the online edition of the journal *Cancer Research*, a journal of the American Association for Cancer Research. The team of scientists led by Devanand Sarkar, M.B.B.S., Ph.D., demonstrated that the protein AEG-1 binds to retinoid X receptors (RXR), which help regulate cell growth and development. RXR is typically activated by retinoic acid, but the overexpressed AEG-1 proteins found in cancer cells block these signals and help promote tumor growth. Using complex animal models, the researchers showed that blocking the production of AEG-1 allowed retinoic acid to profoundly kill liver cancer cells.

"Our findings are the first to show that AEG-1 interacts with the retinoid X receptor," says Sarkar, Harrison Scholar at VCU Massey Cancer Center, Blick Scholar and associate professor in the Department of Human and Molecular Genetics and member of the VCU Institute of Molecular Medicine (VIMM) at VCU School of Medicine. "This research has immediate clinical relevance such that physicians could begin screening cancer patients for AEG-1 expression levels in order to determine whether retinoic acid should be prescribed."

Sarkar and his colleagues have been studying AEG-1 for years. They were the first to create a mouse model demonstrating the role of AEG-1 in liver cancer, and they have been actively working to develop targeted therapies that block AEG-1 production. The present study expanded their knowledge of the molecular interactions of AEG-1.

"We are continuing to test combination therapies involving AEG-1 inhibition and retinoic acid in animal models, and the initial results are promising," says Sarkar. "If we continue to see these results in more complex experiments, we hope to eventually propose a phase 1 clinical trial in patients with liver cancer."

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