Microbubble-delivered combination therapy eradicates prostate cancer in vivo

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Cancer researchers are a step closer to finding a cure for advanced prostate cancer after effectively combining an anti-cancer drug with a viral gene therapy in vivo using novel ultrasound-targeted microbubble-destruction (UTMD) technology. The research was conducted by scientists at Virginia Commonwealth University Massey Cancer Center, VCU Institute of Molecular Medicine and School of Medicine, in collaboration with colleagues from Washington University School of Medicine and Sanford-Burnham Medical Research Institute.

In their study, published in the journal Proceedings of the National Academy of Sciences, prostate cancer growth in mice with functioning immune systems was inhibited by sensitizing the cancer cells with the drug Sabutoclax (BI-97C1) and using UTMD technology to deliver a viral gene therapy that expresses the gene mda-7/IL-24. This powerful new approach to treating prostate cancer builds upon prior studies by principle investigator Paul B. Fisher, M.Ph., Ph.D., Thelma Newmeyer Corman Endowed Chair at VCU Massey, professor and chair of the Department of Human and Molecular Genetics in the VCU School of Medicine and director of the VCU Institute of Molecular Medicine.

Sabutoclax works by inhibiting the protein Mcl-1, which is known to promote cell survival by preventing a form of cell suicide known as apoptosis. Fisher's laboratory studies previously showed that the gene mda-7/IL-24 increases apoptosis in tumor cells, prevents tumor growth and blood vessel formation, synergizes with other cancer treatments and also regulates cellular immune responses while having no ill effects on

normal, healthy cells. By showing the combined effectiveness of these agents, the researchers have discovered a novel treatment approach for prostate cancer.

"Successful execution of viral gene therapy is typically limited by the body's natural defenses, such as trapping the virus in the liver and attacking the virus with its natural immune system response," says Fisher. "This study not only identifies a potential new therapy for prostate cancer, it also provides a new way of using therapeutic viruses that could transform the way we deliver viral gene therapy."

UTMD uses microscopic, gas-filled bubbles that provide great contrast against soft tissue when viewed using ultrasound equipment. The microbubbles can also be paired with complexes made to bind to specific areas of the body, allowing them to be targeted. In this study, a weakened adenovirus (a virus that is typically associated with respiratory infections) engineered to deliver the tumor-suppressing gene mda-7/IL-24 was joined to the microbubbles and delivered through the blood stream directly into the prostate. UTMD's ability to systematically target a disease site could revolutionize gene therapy.

"Although our studies focused on prostate cancer, in principle, they could be applied to many other cancers," says Fisher. "Additionally, ultrasound-targeted microbubble destruction could deliver directly to cancers other viruses, therapeutic genes not contained in a virus and potentially other therapeutic proteins."

UTMD technology is currently utilized in Phase III clinical trials to treat heart disease. Because the technology is already being applied in the clinic, the researchers plan to partner with clinicians to develop a Phase I clinical trial to evaluate the safety of viral gene therapy using UTMD in patients with prostate cancer.