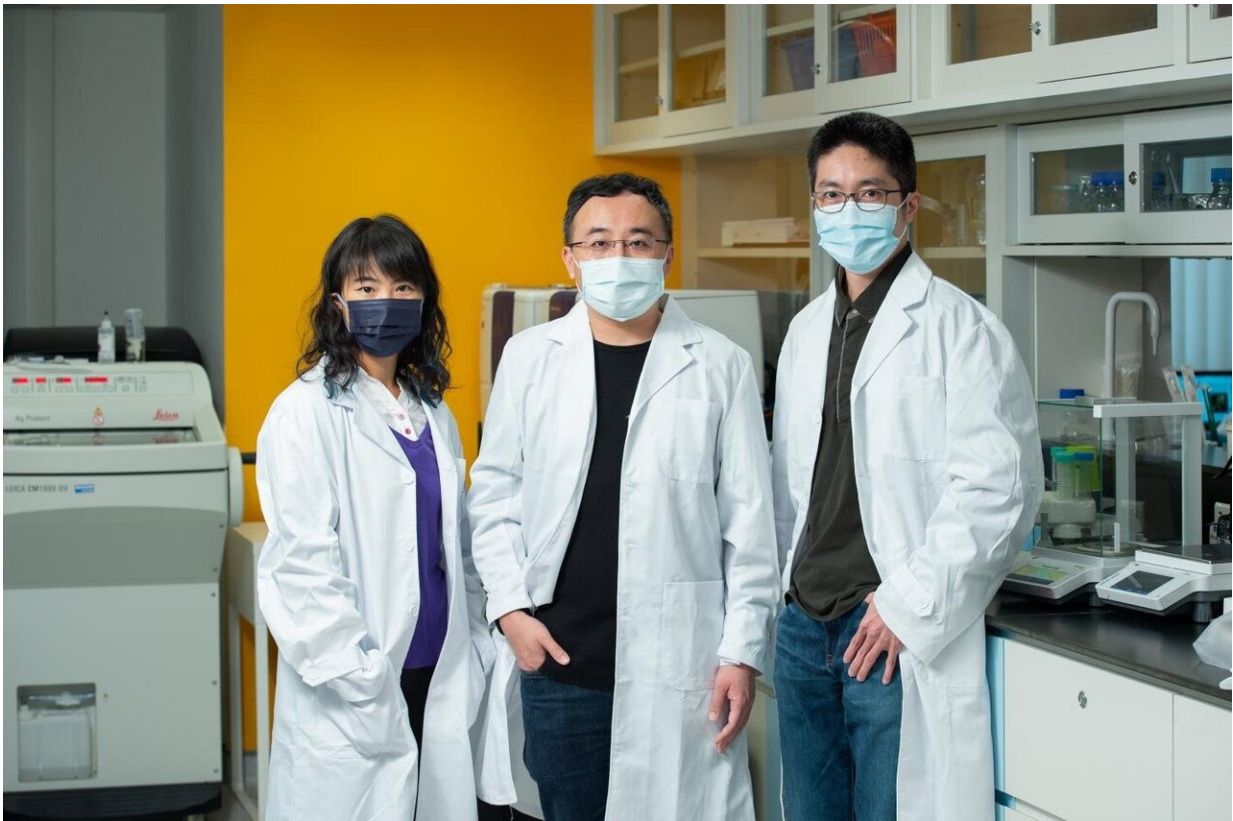


Researchers develop dual-targeting drug for EBV-related cancers

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A research team led by Professor Gary Wong Ka-Leung (center), Dr Lung Hong Lok (right) and Dr Law Ga-lai develop a novel dual-targeting drug for treating cancers associated with EBV. Credit: Hong Kong Baptist University

A Hong Kong Baptist University-led (HKBU) research team has developed a novel drug which has the potential to become a next-

generation treatment for cancers associated with Epstein-Barr virus (EBV).

The peptide-linked [drug](#), which is responsive to the acidic environment found in tumors, is the first known agent to have successfully targeted two [viral proteins](#) that are simultaneously produced by EBV. It also offers a new strategy by increasing the uptake of anti-cancer drugs in tumor [cells](#), thus allowing the application of lower drug dosages which helps reduce treatment side effects and health risks.

The research results were published in the international academic journal *Advanced Science*.

New drug targets two EBV-specific viral proteins

EBV is one of the most common viruses in humans, having infected more than 90% of the human population worldwide. It is widely known that the virus plays a key role in several cancers such as nasopharyngeal carcinoma (NPC), which is highly prevalent in Hong Kong and southern China.

Led by Professor Gary Wong Ka-Leung, Professor and Head of the Department of Chemistry at HKBU, Dr. Lung Hong Lok, Assistant Professor of the Department of Chemistry at HKBU, and Dr. Law Galai, Associate Professor of the Department of Applied Biology and Chemical Technology at The Hong Kong Polytechnic University, the research team constructed a novel drug with a peptide, i.e., a component of the building blocks of various proteins, that can target two EBV-specific viral proteins—Latent membrane [protein](#) 1 (LMP1) and Epstein-Barr nuclear antigen 1 (EBNA1). They are the viral proteins which are expressed in all EBV-infected tumor cells, and both play a vital role in the development and progression of EBV-associated tumors.

Leveraging the success of the first-generation drugs developed by the research team in recent years, this novel dual-targeting drug employs the treatment mechanisms of: (1) targeting and binding to EBNA1, making it no longer functional, and (2) inhibiting LMP1 and serving as an imaging agent. Since LMP1 is more accessible to drug targeting due to its presence on the surface of cells, the ability of the new drug to selectively identify EBV-infected cancer cells is largely enhanced.

pH-sensitivity improves drug targeting

In addition, the researchers engineered the drug so that it has excellent sensitivity to an acidic environment. When the drug binds to a tumor cell, its peptide will cleave and be released in response to the acidic tumor microenvironment. It then enters the nucleus of the tumor cell and hinders the function of EBNA1. Since normal cells have a neutral environment, and cancer cells usually prevail in an acidic environment, the new drug's excellent sensitivity to acidic environments can minimize its off-target rate. As a result, unintended damage to normal cells can be reduced.

The synergistic combination of pH sensitivity (in an [acidic environment](#)) and the specific targeting of an accessible surface protein (LMP1) will dramatically raise the new drug's efficacy. The resulting increase in drug uptake rates will allow the application of a lower drug dosage and it will also minimize the side effects and health risks whilst maintaining the drug's functions.

The study also showed that the drug can emit unique responsive fluorescent signals once it has bound to the viral proteins, illustrating its potential role in tumor cell imaging.

Animal model demonstrates drug efficacy and safety

The [novel drug](#) was tested in an animal model by injecting it into mice with EBV-positive NPC tumors. The results showed that a low drug dosage of 12.5 mg per kg of body weight could reduce the NPC tumor size by half. In addition, the average body weight of the mice increased slightly during the experimental period, indicating an improvement in their health condition.

"The experimental results are good indicators that prove the drug's efficacy and safety. Since this is the first example of simultaneous imaging and inhibition of two EBV viral proteins, it can serve as a blueprint for a next-generation drug for the safe monitoring and treatment of a specific cancer," said Professor Wong.

More information: Shuai Zha et al. Dual-Targeting Peptide-Guided Approach for Precision Delivery and Cancer Monitoring by Using a Safe Upconversion Nanoplatfrom, *Advanced Science* (2021). [DOI: 10.1002/advs.202002919](#)

Provided by Hong Kong Baptist University

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