Lung cancer may be treatable with use of SapC-DOPS technology, research shows

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Lung cancer is the most common and the deadliest type of cancer worldwide, with about 221,000 new cases and an estimated 158,000 deaths in 2015 in the U.S., according to the American Cancer Society.

Cigarette smoking is the leading cause of lung cancer, followed by environmental and occupational exposure to pollutants.

A University of Cincinnati (UC) study, published in the advance online edition of the journal *Molecular Cancer Therapeutics*, provides hope that the therapeutic agent SapC-DOPS could be used for treatment of this cancer.

Xiaoyang Qi, PhD, associate director and associate professor in the Division of Hematology Oncology at the UC College of Medicine and a member of the Cincinnati Cancer Center, the UC Cancer and Neuroscience Institutes and the Brain Tumor Center, says these findings indicate that SapC-DOPS shows promise for treatment of one of the deadliest cancers globally. The findings also provide stronger evidence that this agent could be a key treatment for a variety of cancers.

"I partnered with scientists at Nanjing Medical University in China for this research, as lung cancer in China is a major health issue," Qi says. "As reported by the International Agency for Research on Cancer, more than half of lung cancer deaths caused by air pollutants worldwide occurred in China and other East Asian countries.

"Standard treatment options for lung cancer, including chemotherapy, radiation and surgery, have undesirable side effects that impact the quality of life of the cancer patient, which is why the targeted use of SapC-DOPS could be so beneficial."

SapC-DOPS consists of a lysosomal protein, saposin C (SapC), and a phospholipid named dioleoylphosphatidylserine (DOPS), which are combined and assembled into tiny cavities, or nanovesicles, to target and kill various forms of cancer cells.

Lysosomes are membrane-enclosed organelles that contain enzymes capable of breaking down all types of biological components; phospholipids are major components of all cell membranes and form lipid bilayers—or cell membranes.

Qi and collaborators have previously found that the combination of these two natural cellular components, called SapC-DOPS, caused cell death in many cancer cell types including brain, skin, prostate, blood, breast and pancreatic cancer, while sparing normal cells and tissues.

"Liposomal formulations as vehicles for drug delivery are the subject of intense research," he continues. "Compared with non-encapsulated, free drugs, they provide improved biocompatibility and targeted delivery. Despite promising results in preclinical models of lung cancer and many other cancer types, only a few non-targeted liposomal formulations have been approved for cancer treatment by regulatory agencies. Clinical trials are under way to evaluate some of these in lung cancer patients. However, so far, these liposomes have been shown to be less effective when compared with free drug administration, which is why the SapC-DOPS research is promising as a targeted treatment for lung cancer."

In this study, researchers used SapC-DOPS to selectively target the cell membrane of lung tumors in animal models and in human cell cultures.

Qi says a distinguishing feature of SapC-DOPS is its ability to bind to phosphatidylseriine (PS), a lipid, which is found on the membrane surfaces of all tumor cells.

"To evaluate the role of external cell PS, we evaluated PS exposure in human tumor and non-tumor cells in culture," he says. "We also introduced these cells into animal models and then injected the SapC-DOPS vesicles intravenously to see if we could halt tumor growth."

"Using a double-tracking method in live models, we showed that the nanovesicles were specifically targeted to the tumors. These data suggest that the acidic phospholipid PS is a biomarker for lung cancer, as it has been found to be for pancreatic and brain tumors in previous studies, and can be effectively targeted for therapy using cancer-selective SapC-DOPS nanovesicles."

"We observed that the nanovesicles selectively killed human lung cancer cells, and the noncancerous, or untransformed cells, remained unaffected," Qi continues. "This toxic effect correlated to the surface exposure level of PS on the tumor cells."

Importantly, animals treated with SapC-DOPS showed clear survival benefits and their tumors shrank or disappeared.

"Our results show that SapC-DOPS could be a promising treatment option for lung cancer worthy of further clinical study."

Provided by University of Cincinnati Academic Health Center