DNA-repairing protein may be key to preventing recurrence of some cancers

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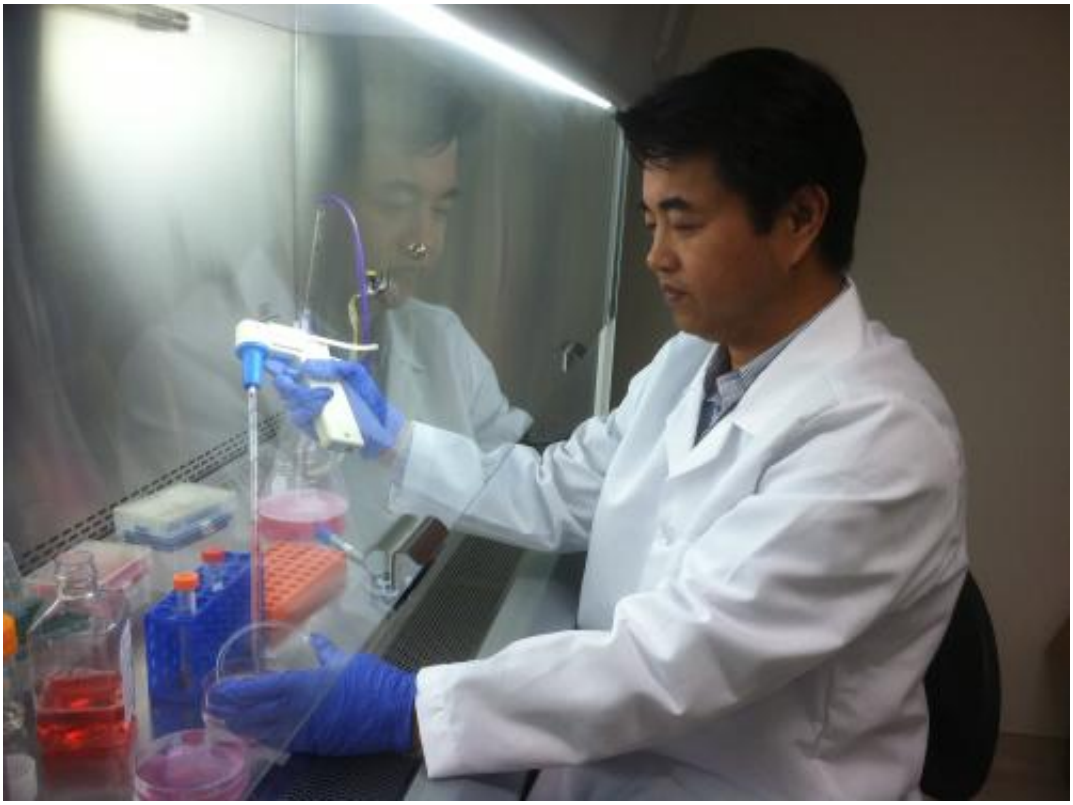

Dr. Zhao works in his lab at the Burnett School of Biomedical Sciences at the UCF College of Medicine. Credit: University of Central Florida

Just as the body can become resistant to antibiotics, certain methods of killing cancer tumors can end up creating resistant tumor cells. But a University of Central Florida professor has found a protein present in several types of cancer, including breast and ovarian cancer, which could

be helpful in preventing tumors from coming back.

The protein, KLF8, appears to protect tumor cells from drugs aimed at killing them and even aid the tumor cells' ability to regenerate.

"All cells have a DNA-repair mechanism," explained Jihe Zhao, a medical doctor and researcher who in the past few months has published several articles related to the protein in the Journal of Biological Chemistry and *Oncogene*, among others. "That's why we survive constant DNA damage threats. But KLF8 is overexpressed in specific cancers, such as breast cancer and ovarian cancer. The thought is that if we can stop it from switching on, we may be able to stop the tumors from coming back as part of therapy. We still need to do a lot more research, but it is plausible."

There are between 2.5 million and 2.7 million women who have breast cancer in the United States and 10 to 20 percent will experience a recurrence, according to the American Cancer Society. Current treatment options, depending on the stage of cancer, include surgical removal followed by chemotherapy using a combination of cancer killing drugs. Each year about 22,200 women are also diagnosed with ovarian cancer.

DNA damage-based chemotherapies depend on failure of cancer cells to repair the DNA damage and subsequent cell death, according to the journal article. Aberrant high levels of DNA repair function in the cells likely increase not only the resistance of the cells to such therapies but also the malignancy of the cells due to improper DNA repair-mediated genomic and chromosomal instability.

In the study, Zhao's team tested one specific cancer-fighting drug used in the treatment of breast cancer to determine the role of the protein.

"Indeed, our results have clearly linked the KLF8-promoted DNA repair to the cell resistance to doxorubicin-induced cell death," Zhao said. "It remains to be determined whether KLF8 plays a similar role in repairing DNA damage caused by other types of genotoxic agents such as DNA alkylating agents and ionizing radiation."

Even so, the results suggest that in addition to enhancing the drug resistance of the cancer cells, KLF8 could play a role in disturbing genomic integrity through its aberrant DNA repair function and subsequently contribute to aggressive progression of cancer.

More information: http://www.jbc.org/content/287/52/43720 and http://www.nature.com/onc/journal/vaop/ncurrent/full/onc2012545a.html

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