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Researchers identify novel approach for suppressing prostate cancer development

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Researchers at the University of Southern California (USC) have found that inactivating a specific biomarker for aggressive prostate cancer blocks the development of prostate cancer in animal models.

Researchers say the upcoming study in the *Proceedings of the National Academy of Sciences*—now available online—may lead to a novel cancer therapy for humans.

"This research has far-reaching implications in a wide range for human cancers," says Amy Lee, Ph.D., the study's principal investigator and the associate director for basic research and holder of the Freeman Cosmetics Chair at the USC/Norris Comprehensive Cancer Center, and professor of biochemistry and molecular biology at the Keck School of Medicine of USC. "It is a breakthrough study."

Prostate cancer is the most common cancer in men and develops through successive stages. The glucose-regulated protein GRP78 has been identified as a crucial entity in the development of prostate cancer by promoting cancer cell proliferation, mediating oncogenic signaling and protecting cancer cells against cell death resulting from the stress of tumor development, Lee explains. By suppressing GRP78 expression or activity, the USC researchers found that they could block prostate cancer activation and development resulting from the loss of PTEN, a powerful tumor suppressor gene for a number of human cancers.

Researchers spent more than three years monitoring prostate cancer

development in animal models that had been genetically engineered to have both the GRP78 and PTEN tumor suppressor genes inactivated. The research was conducted by Yong Fu, a Ph.D. candidate at the Keck School of Medicine of USC and the first author on the study, in collaboration with Ph.D candidates Shiuan Wey, Miao Wang, Risheng Ye and Chun-Peng Liao and Pradip Roy-Burman, M.D., professor of pathology, biochemistry and molecular biology at the Keck School.

Future research should test the role of GRP78 in other types of cancer and isolate drugs that inhibit GRP78, Lee says. "To our knowledge, this is the first demonstration that inactivation of a specific molecular chaperone from the mouse prostate epithelial cells can potently block prostate cancer development and suppress the activation of AKT, which is a protein kinase that promotes cell proliferation and survival and is a major factor in many types of cancer," Lee says. "With the recent advances in identifying agents that suppress GRP78 expression, anti-GRP78 therapy may open up an entirely new approach to stop human cancer."

Citation: Yong Fu, Shiuan Wey, Miao Wang, Risheng Ye, Chun-Peng Liao, Pradip Roy-Burman, and Amy S. Lee. "Pten null prostate tumorigenesis and AKT activation are blocked by targeted knockout of ER chaperone GRP78/BiP in prostate epithelium." *Proceedings of National Academy of Sciences.* Nov. 2008.
www.pnas.org/content/early/recent

Source: University of Southern California