Research reveals molecular pathway behind invasive prostate cancers

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University of Cincinnati (UC) cancer and cell biologists have identified a new molecular pathway key to the development of invasive prostate cancers.

In a preclinical study led by Maria Diaz-Meco, PhD, the UC team found that simultaneous inactivation of two particular genes—known as PTEN and Par-4—caused the rapid development of invasive prostate cancer tumors in mice.

"We knew that independent mutations in either of these genes could result in benign tumors, but when those changes occur simultaneously it appears to have a synergistic effect that causes prostate cancer," explains Diaz-Meco, an associate professor of cancer and cell biology at UC and corresponding author of the paper. "This switch affects the cell's ability to both grow and survive, leading to more aggressive and invasive tumors."

"This is an important discovery because—until now—those signaling pathways were not clearly defined. Without a clear molecular target, it's impossible to develop effective drugs to treat this disease without causing harm to the patient," she adds.

Diaz-Meco and her team report their findings online ahead of print in *Proceedings of National Academy of Sciences* (PNAS) the week of May 18.

PTEN is a well-defined gene shown to be suppressed in prostate cancer tumors, as well as in other types of cancer. Its mutation has been shown to result in the formation of benign tumors. Par-4 gene is also mutated in prostate cancer, but this study is the first to report its relationship with PTEN mutations and aggressive prostate cancer tumor development.

The UC study was done in a laboratory mouse model over the course of two years. Data from the mouse model was correlated and compared to human prostate cancer tissue samples to determine if their findings were applicable in humans as well.

"Theoretically, this new knowledge could be used to better categorize a tumor's aggressiveness by measuring the levels of PTEN and Par-4 expressed in a tissue biopsy," adds Diaz-Meco. "That would help clinicians make tough decisions about how aggressively to treat a patient's prostate cancer and minimize unnecessary treatment."

Cancer and cell biologists are working on identifying the molecular targets involved in cancer progression to develop a better understand the mechanisms of action that lead to prostate cancer so that pharmaceutical companies and clinicians can develop better methods of diagnosing and treating the disease.

Source: University of Cincinnati Academic Health Center