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Study identifies new target to fight prostate, lung cancer

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A newly identified molecular chain of events in a mouse model of prostate cancer highlights novel targets to treat it and other cancers. A team led by Marcelo Kazanietz, PhD, a professor of Systems Pharmacology and Translational Therapeutics, published in *Cell Reports* that the overexpression of a protein called PKCε with the loss of the tumor suppressor Pten causes the progression of prostate cancer.

This deadly combination produces an uptick in the levels of the cancer-promoting molecule CXCL13. When the team purposely disrupted CXCL13, or CXCR5, the cell-surface receptor it attaches to, the metastatic and tumor-forming characteristics of the mouse prostate cancer cells were impaired.

"In addition to providing evidence for a vicious cancer cycle driven by PKCε, our studies identified a compelling rationale for blocking the CXCL13-CXCR5 molecules as a new cancer treatment," Kazanietz said. He and colleagues plan to identify compounds to block CXCR5 or CXCL13 with potential to be developed as anti-cancer agents. The researchers also suggested that CXCL13 levels in blood could be used as a biomarker to measure the precise state of prostate cancer progression in a patient.

The team's next step will be to interfere with CXCR5/CXCL13 signals not only from the cancer cells but also from other cells in the tumor microenvironment that contribute to cancer growth.

Pulmonologists and oncologists have also observed that PKCε is overexpressed in lung cancer patients, but they do not fully understand its exact molecular consequences. In general, a high level of PKCε is associated with a poor prognosis.

"We are in the midst of extending these findings to lung cancer," said Kazanietz, who is collaborating with Penn Medicine researchers David Feldser, PhD, an assistant professor of Cancer Biology, Steven M. Albelda, MD, a professor of Pulmonary, Allergy and Critical Care, and Evgeniy Eruslanov, PhD, a research assistant professor of Thoracic Surgery.

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