Study could improve treatments for prostate cancer

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Van Andel Research Institute (VARI) scientists have determined how two proteins required for the initiation and development of prostate cancer interact at the molecular level, which could lead to improved treatments for the disease.

One of the proteins, androgen receptor, is already an important drug target for prostate cancer. The other, steroid receptor coactivator-3 (SRC3), was originally identified for its role in the development of breast cancer. SCR3 has also been characterized as a key factor in the development of prostate cancer, but, until now, the exact relationship between androgen receptor and SCR3 has been unclear.

Understanding the relationship between these two proteins, and targeting this interaction, could lead to new, more effective treatments for prostate cancer, the most common form of cancer in men, with more than 192,000 new cases and more than 27,000 deaths reported in the United States in 2009 (Source: National Cancer Institute).

"Anti-androgen therapies become less effective over time," said VARI Distinguished Scientific Investigator H. Eric Xu, Ph.D., whose laboratory published the findings recently in the Journal of Biological Chemistry, where it was named Paper of the Week by the journal. "To develop the next generation of prostate cancer treatments, we need to find ways to disrupt the interaction between androgen receptor and the molecules it depends on to work, such as SRC3."

Androgen receptor activity is required for the initiation and development of prostate cancer. When activated by hormones, androgen receptor binds to DNA in the cell nucleus and regulates gene expression with the help of molecules called coactivators, including SRC3. As a result, genes create more or less of specific proteins in the cell, which can affect cell behavior. Although androgen receptor needs coactivators such as SRC3 to have an effect, little has been known about precisely how androgen receptor interacts with its coactivators.

VARI researchers used peptide profiling and other techniques of molecular biology to discover that SRC3 is a preferred coactivator for androgen receptor. They went on to determine the crystal structures that reveal how androgen receptor and SRC3 interact at the molecular level. This detailed information could be used to develop new, more effective treatments that disrupt interaction between the two proteins.

Provided by Van Andel Research Institute