Team finds new target for treatment of advanced prostate cancer

July 6 2010

(PhysOrg.com) -- In its early stages, prostate cancer requires androgens (hormones that promote the development and maintenance of male sex characteristics) for growth, and current first-line therapies target the receptor for these hormones to slow cancer's development and spread.

However, advanced prostate cancers are often androgen-independent, meaning that androgen-blocking therapies are ineffective.

Scientists aren't sure how this shift occurs as prostate cancer advances.

One idea is that prostate cancer cells acquire the ability to make their own androgen. Another says that the androgen receptor that is known to stimulate tumor growth can still be active even when the hormone is not present. Most likely, both are important.

A recent study by UNC researchers, published in the Journal of Biological Chemistry, provides evidence for the second theory, demonstrating that expression of one of a group of genes found only in humans and non-human primates can promote androgen receptor activity in concert with other proteins called coregulators.

One of a group of MAGE genes, so named because they were originally identified in melanoma, called MAGE-11 interacts with another protein, called p300, to provide the cancer cells with a way to enhance androgen receptor signaling and promote tumor growth, even when patients are undergoing androgen deprivation therapy.

According to team leader Elizabeth M. Wilson, PhD, professor of pediatrics and biochemistry and biophysics at UNC-Chapel Hill, "We found that a small portion of the androgen receptor interacts with the MAGE-11 molecule which serves as a bridge to p300, a strong histone modifying enzyme that increases androgen receptor activity. This is exciting because it shows how the cancer cells have developed a way to boost androgen receptor activity, even in the absence or at low levels of the hormone that binds the androgen receptor."

Wilson, who is also a UNC Lineberger member, goes on to explain that understanding this mechanism opens the door to additional targets for new therapies and broader clinical applications of new drugs.

"The MAGE-11 molecule is a promising target for shutting down androgen receptor activity that promotes the growth of cancer cells," she adds.

Provided by University of North Carolina School of Medicine