MedicalXpress

Hormone refractory prostate cancers more likely to spread to other organs

February 20 2008

Prostate cancers that are resistant to androgen deprivation therapy are more invasive and more likely to spread to other organs than androgen dependent prostate cancers, UCLA cancer researchers have found.

Virtually all prostate cancers are androgen dependent at first, but they progress and become resistant over time. These hormone refractory or castration resistant cancers can grow despite surgical or medical therapies that deplete testosterone. The UCLA study is the first to link that progression with the cancer's tendency to spread to other organs. The findings could change the way some prostate cancers are treated, spurring earlier use of hormone therapy to prevent the cancer's spread, said Dr. Robert Reiter, a professor of urology, a researcher at UCLA's Jonsson Cancer Center and senior author of the study.

Published in the Feb. 15 issue of the journal *Cancer Research*, the study makes the connection between androgen receptor and the spread of prostate cancer as well as the progression to androgen independence. Previous studies have shown that the androgen receptor is responsible for the growth of hormone refractory prostate cancer. However, no one has associated the spread of prostate cancer to the androgen receptor, Reiter said.

"We started noticing that the castration resistant prostate cancer models in the lab seemed to express genes that are typically associated with the spread of cancer," Reiter said. "We began to ask what cell signaling pathways might be responsible. We looked at the androgen receptor and

were surprised to find that it was not only overexpressed in castration resistant cancers but also in invasive cancers that still relied on androgen to grow."

The study found that overexpression of the androgen receptor was critical to the cancer becoming more invasive. If a therapy could be found that blocked overexpression of the receptor, it might prevent the spread of certain prostate cancers.

Traditionally, doctors don't like to use hormone treatment – which stops the production of testosterone - early on in the treatment of prostate cancer because of the harsh side effects, which can include hot flashes, osteoporosis and sexual dysfunction. In the past, doctors have waited until the cancer spread to prescribe hormone therapy, Reiter said.

"This study may provide additional scientific rationale to support the recent trend that giving hormone treatment early on is better than waiting," Reiter said. "Early hormone treatment in this group of men might allow them to live longer. High levels of androgen receptor in the primary tumor might also predict which cancers are more likely to spread despite initial surgery or radiation."

This strategy could be particularly effective in high risk men, those with large primary tumors, high Gleason scores and those that have lymph node involvement at diagnosis.

Prostate cancer is the most common cancer in men in the United States. This year alone, more than 218,000 men will be diagnosed with prostate cancer. About 27,000 men will die from the disease.

Reiter and his team will next seek to understand the mechanism by which androgen receptor overexpression is causing the cancer to spread. If they can uncover the mechanism, they might find new and better

targets for drug therapy in addition to targeting the androgen receptor.

Source: University of California - Los Angeles