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# Study implicates protein as a trigger of advanced prostate cancer recurrence

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Scientists with the Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill have for the first time implicated a growth-promoting cellular protein as one trigger of the inevitable recurrence of advanced prostate cancer in men who are undergoing drug treatment to shut down their sex hormones, or androgens.

The new research may help solve a mystery: why does prostate cancer recur in men treated to get rid of circulating androgens such as testosterone"

Moreover, because chemotherapy after recurrence extends life by only a few months, the new research, "raises the exciting possibility that we can develop a specific drug against this," said senior study co-author Dr. Young Whang, associate professor of medicine at UNC-Chapel Hill.

The study appeared online May 7, 2007, in the *Proceedings of the National Academy of Sciences*. It is slated for print publication in the journal on May 15.

The protein, named Ack1, is a member of the tyrosine kinase gene family. Ack1 exerts its effect on the reemergence of the cancer by biochemically altering the now inactive androgen receptor in the nucleus of prostate of cells, according to a series of experiments conducted by lead author Dr. Nupam P. Mahajan, assistant professor of pharmacology, and other Lineberger scientists. The kinase activates the receptor via

phosphorylation – by adding a phosphate group to this protein molecule.

"This biochemical action converts a prostate cell that would need an androgen signal for its growth to one that is independent of the androgen signal," said senior study co-author Dr. Shelton Earp, director of the cancer center, Lineberger professor of cancer research and professor of pharmacology and medicine.

Earp noted that until now scientists haven't completely understood what that conversion means. "Our experiments show that this heretofore understudied protein Ack1 may be crucial in at least a portion of these tumor recurrences. Nupam's study nails down the mechanism by which that conversion happens."

Among the experiments were those that involved mice that were unable to produce androgen. The animals were implanted with human prostate tumor cells containing an activated form of Ack1. "We found that when prostate tumor cells express activated Ack1, cancer grew aggressively in these mice," Mahajan said. "This mimics what happens in patients undergoing hormone therapy."

The researchers noted that approximately one-third of androgen-independent human prostate tumors contain an activated Ack1 molecule. "The study is telling us this is a target for therapy and perhaps a very important target for therapy," Earp said.

Source: University of North Carolina