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Cancer drug mystery solved

BY STAFF WRITER
MICHAEL WENTZEL

University of Rochester scientists have discovered why a treatment for men with prostate cancer loses its effectiveness against the disease.

A drug that blocks the hormone that feeds the cancer eventually activates a protein that causes cancer cells to grow.

"The drug does good work at first but then, instead of suppressing, it stimulates prostate cancer growth," said Chawnschang Chang, director of the George Whipple Laboratory for Cancer Research at the University of Rochester Medical Center.

The findings, published this month in the journal *Cancer Research*, could provide a target for new drugs.

"No one had recognized that this process could even occur," said Dr. Edward Messing, chairman of UR's Department of Urology.

"This is another trick the



Chawnschang Chang is director of cancer research lab at UR Medical Center.



Yi-Fen Lee helped to track prostate cancer drug's double nature.

cells have. If we could understand the mechanism, we could work on drugs that would stop the trigger."

The university has applied for a patent on the concept and molecular pathways described in the research by Chang, Yi-Fen Lee, a UR assistant professor of urology, Wen-Jye Lin, a graduate student, and others.

Prostate cancer cells usually depend on the hormone testosterone for survival. To treat the disease when it has spread out of the prostate to other parts of the body, doctors use surgery and radiation to knock out the supply of the hormone.

In many cases, treatment also includes a drug known as an anti-androgen, which

blocks the molecule through which testosterone works, the androgen receptor.

"Somehow during the course of this treatment, the disease reoccurs," Messing said.

"This is true in almost every case. When it reoccurs, we stop anti-androgen and paradoxically the patients get better, but only for a period of time."

Chang and Lee studied a drug called hydroxyflutamide. Lee initially compared cancer cells from four men early in their disease with cells after hormonal therapy became ineffective. The team found a molecule known as MAP kinase at much higher levels in the cells that had survived hormone therapy.

This kinase promotes tumor cell growth and is known to play a role in several cancers. In cell studies in the lab, Lee and the team found hydroxyflutamide turned on MAP kinase in prostate cancer cells.

Surprisingly, the drug acted on cells independent of the androgen receptor, routinely believed to be its primary path.

In spite of the research findings, the scientists said hormonal therapy still is the best treatment for patients whose prostate cancer has spread.

"These drugs are necessary for patients who otherwise have few options," Lee said.

"Perhaps these findings will help lead to a new drug target so that men with this disease can be treated more effectively."

The work by the UR scientists earned an award for outstanding research recently from the American Urological Association. □

E-mail address: mwentzel@DemocratandChronicle.com