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Experimental agent blocks prostate cancer in animal study

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An experimental drug has blocked the progression of prostate cancer in an animal model with an aggressive form of the disease, new research shows. The agent, OSU-HDAC42, belongs to a new class of drugs called histone deacetylase (HDAC) inhibitors, compounds designed to reactivate genes that normally protect against cancer but are turned off by the cancer process.

The study, conducted by the Ohio State University Comprehensive Cancer Center researchers who also developed the drug, showed that the agent kept mice with a precancerous condition from developing advanced prostate cancer.

Instead, the animals either remained at the precancerous stage, called prostatic intraepithelial neoplasia (PIN), or they developed benign enlargements of the prostate called adenomas. The main side effect of the treatment was a reversible shrinkage of the testicles.

Of the animals not given the drug, 74 percent developed advanced prostate cancer.

The findings are reported in the May 15 issue of the journal *Cancer Research*. Human testing of the compound is expected to begin early next year.

“This study shows that an agent with a specific molecular target can dramatically inhibit prostate cancer development in an aggressive model

of the disease," says coauthor Dr. Steven Clinton, director of the prostate and genitourinary oncology clinic at Ohio State's James Cancer Hospital and Solove Research Institute. "We hope to see this agent in clinical trials soon and ultimately used for prostate-cancer prevention or therapy."

Furthermore, when the drug treatment was stopped after 24 weeks, two of the animals were followed for an additional 18 weeks. The animals developed adenomas but were alive after 42 weeks, well beyond their normal 32-week life span.

"The drug not only kept the animals cancer free, but also prolonged their life span," says Ching-Shih Chen, who led the drug's development and the new study at the Comprehensive Cancer Center. Chen is also professor of pharmacy and of internal medicine.

A veterinary pathologist on the study, first author Aaron Sargeant, graduate research associate in veterinary biosciences, was intrigued that adenomas occurred in the treated animals. "Adenomas are not commonly found to be part of prostate-cancer development in this system," he says. "This drug appears to shift tumor progression from its usual aggressive course to a more benign direction."

For this study, Chen, Sargeant, Clinton and their colleagues used a strain of transgenic mice that develops PIN at about six weeks of age, then progresses to advanced prostate cancer by 24 to 32 weeks.

The researchers added the drug to the diet of 23 of the cancer-prone mice beginning at six weeks of age, when the animals develop the precancerous condition, and continued the treatment for 18 weeks.

They then examined the animals. Of the treated mice, one showed signs of early stage cancer, but 12 still had only the precancerous condition

and 10 had adenomas.

In contrast, 17 of 23 control animals developed advanced prostate cancer, two had early stage cancer, three had the precancerous condition and one an adenoma.

Experiments using a nontransgenic strain of the same mouse – they do not develop prostate cancer – showed that the degeneration of the testicles that accompanied the drug treatment was reversible when the drug treatment stops.

Chen noted that 186,320 cases of prostate cancer are expected this year, with 28,660 deaths from the disease. “Our findings are very exciting, considering that an agent capable of reducing prostate-cancer risk by only 10 percent could prevent 18,600 cases of the disease in the United States each year,” Chen says.

Source: Ohio State University