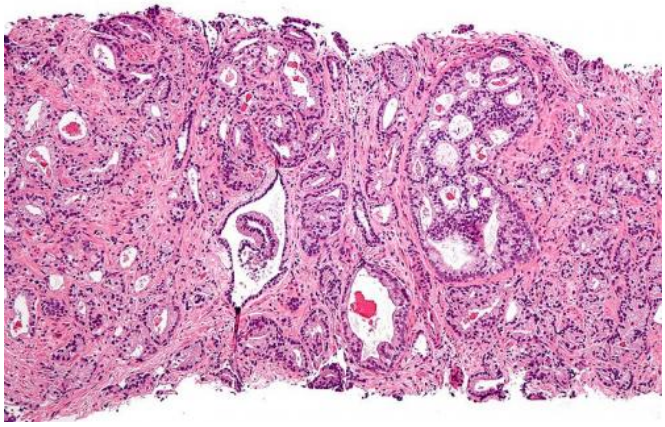
Researcher finds mechanism triggering spread of prostate cancer to bones

13 March 2017



Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia

A Washington State University researcher has found a way that prostate cancer cells hijack the body's bone maintenance, facilitating the spread of bone cancers present in some 90 percent of prostate-cancer fatalities.Working with colleagues at the Cedars-Sinai Medical Center and elsewhere, Jason Wu found that the process appears to respond to the same drugs found in certain antidepressants. The findings appear in the journal *Cancer Cell*.

"Our findings provide a rationale to pursue the new use of these 'old' antidepressant drugs to benefit late-stage prostate cancer patients with signs and symptoms of metastasis," said Wu, an assistant professor of pharmacy at WSU Spokane.

Enzyme activates bone degradation

Introducing human prostate cancer cell lines into mice, Wu and his colleagues saw a particular enzyme called MAOA activate a cascade of signals that made it easier for tumor cells to invade and grow in bone. Ordinarily, bone is built up by cells called osteoblasts and reabsorbed during growth and healing by cells called osteoclasts. But the MAOA enzyme triggers three proteins that enhance the function of the destructive osteoclasts.

"The cancer cells can specifically activate the osteoclasts for bone degradation," Wu said. "The experimental phenomenon we've observed is actually a lot more bone destruction than new bone formation."

The researchers used several human cancer lines in the mice with consistent results, he said.

"When we reduced this enzyme expression in prostate cancer cells, we found a lower prostate cancer bone metastasis," he said. "On the other hand, if we overexpress this enzyme in prostate cancer cells, we found increased bone metastasis in mice."

Antidepressant drug inhibits enzyme

The researchers used a drug called clorgyline to inhibit the activity of the MAOA enzyme; the drug disrupted the signaling system that led to cancer cell invasion and proliferation. Similar drugs are used clinically as antidepressants, the authors write, and their effects on tumors in clinical settings are being investigated.

"To be sure, there have been no clinical studies reporting a lower risk of prostate cancer in people currently taking antidepressants," said Wu. "Our studies provide promising results in mice, which merit further investigation, such as adjusting the formulation, dose and delivery route of MAOA inhibitors, prior to ultimate clinical application."

The research is in keeping with WSU's Grand Challenges, major initiatives aimed at large societal problems. It is particularly relevant to the Sustaining Health challenge and its theme of changing the

course of disease.

More information: *Cancer Cell*, DOI: 10.1016/j.ccell.2017.02.003

Provided by Washington State University