Researchers focus on potential tool for predicting survival, staging prostate cancer

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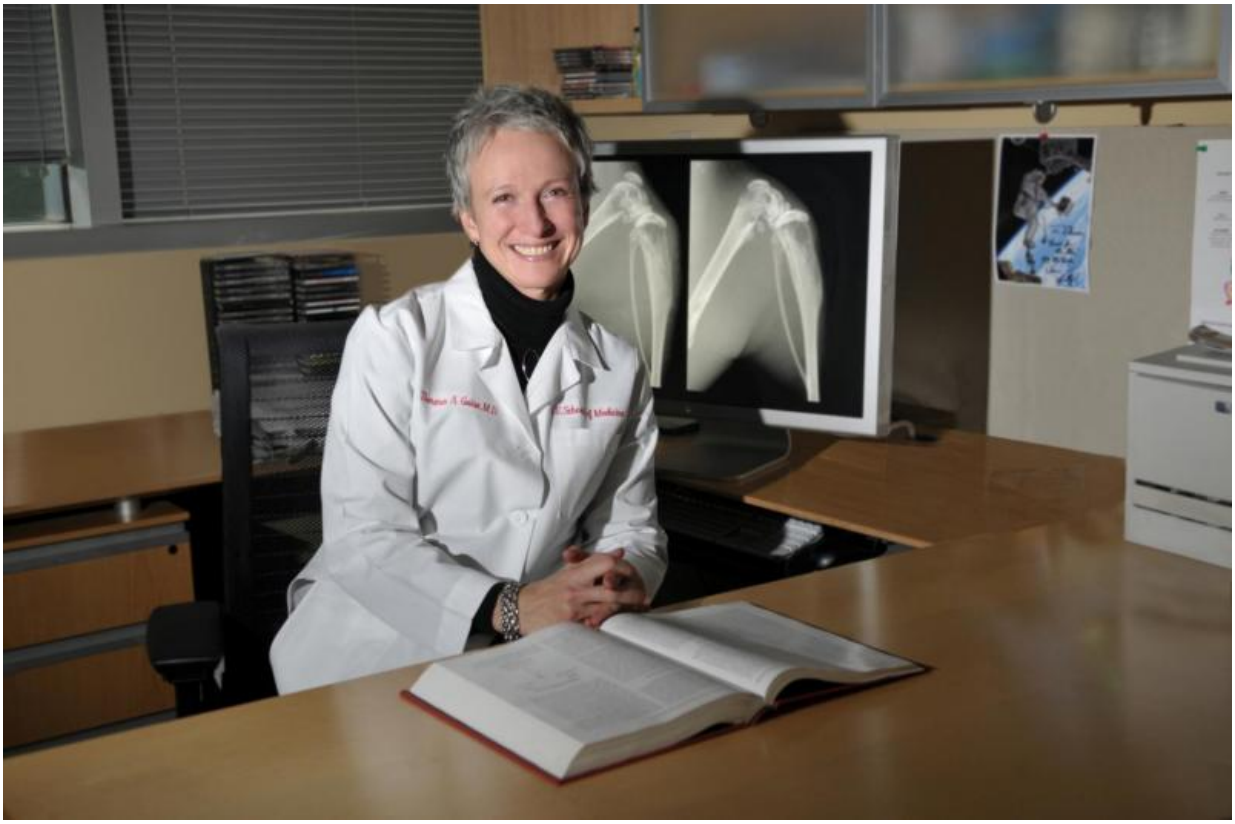

Theresa Guise, M.D.

Researchers with the Indiana University School of Medicine have identified a molecule that promotes metastasis of advanced prostate cancer to the bone, an incurable condition that significantly decreases

quality of life. The research, published online in the journal *Cancer Cell*, may offer new targets for diagnosing and treating this common disease.

The researchers homed in on a protein that is essential in multiple cell functions such as cell growth and proliferation and, in some cases, natural cell death. The protein, TGF-beta, also has been found to promote bone metastasis in patients with breast cancer and melanoma.

Prostate cancer is the second most common cancer among men, according to the American Cancer Society. More than 2 million men in the United States are prostate cancer survivors. ACS estimates that 220,800 new cases of prostate cancer are diagnosed annually in all age groups and that 27,540 men succumb to the disease each year. When diagnosed in the early stages, prostate cancer is often successfully treated. However, in advanced stages, metastasis to the bone is common. The tumors in the bone are incurable, cause increased pain and bone fractures, and potentially hasten death.

Bone disease experts Theresa A. Guise, M.D., senior author of "The TGF-beta Signaling Regulator PMEPA1 Suppresses Prostate Cancer Metastases to Bone," and lead author Pierrick GJ. Fournier, Ph.D., showed in earlier research that TGF-beta is active in the proliferation of metastatic disease. By inhibiting the action of TGF-beta, the researchers reasoned that bone metastases could be reduced in advanced disease.

By analyzing the genes present in patients with advanced disease, the researchers focused on the protein PMEPA1, which is abundant in primary prostate cancer cells but less common in advanced disease, including metastatic bone tumors.

To investigate the clinical significance of PMEPA1, the researchers compared its presence in normal tissue to primary tumors, finding that the gene was active in prostate, breast and lung cancer tumors. The

opposite was true of TGF-beta, which led the researchers to determine that the presence of TGF-beta regulates the activity of PMEPA1.

"Comparing data on patients with prostate or breast cancer, we found those with low amounts of PMEPA1 developed metastases faster and had shorter survival," Dr. Guise said. "By inhibiting TGF-beta, we believe we could reduce the spread of prostate cancer to the bone and increase survival."

Drs. Guise and Fournier think that with additional analysis, the presence of PMEPA1 may serve in the future as a diagnostic tool to predict the likelihood of prostate cancer metastases and serve as an indicator of survival, similar to the Gleason score and PSA counts currently used by physicians to stage prostate cancer and determine options for treatment.

"This finding could make a difference in how prostate cancer is treated in the future," Dr. Fournier said. "The unknown qualities of cancer frequently lead to aggressive treatments that are unnecessary. If we can determine a laboratory test that can serve as an indicator of the likelihood of progression or the severity of the disease, we could make better decisions about treatments and improve the quality of life for many patients."

More information: *Cancer Cell*, www.cell.com/cancer-cell/abstract/S1535-6108%2815%2900142-7

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