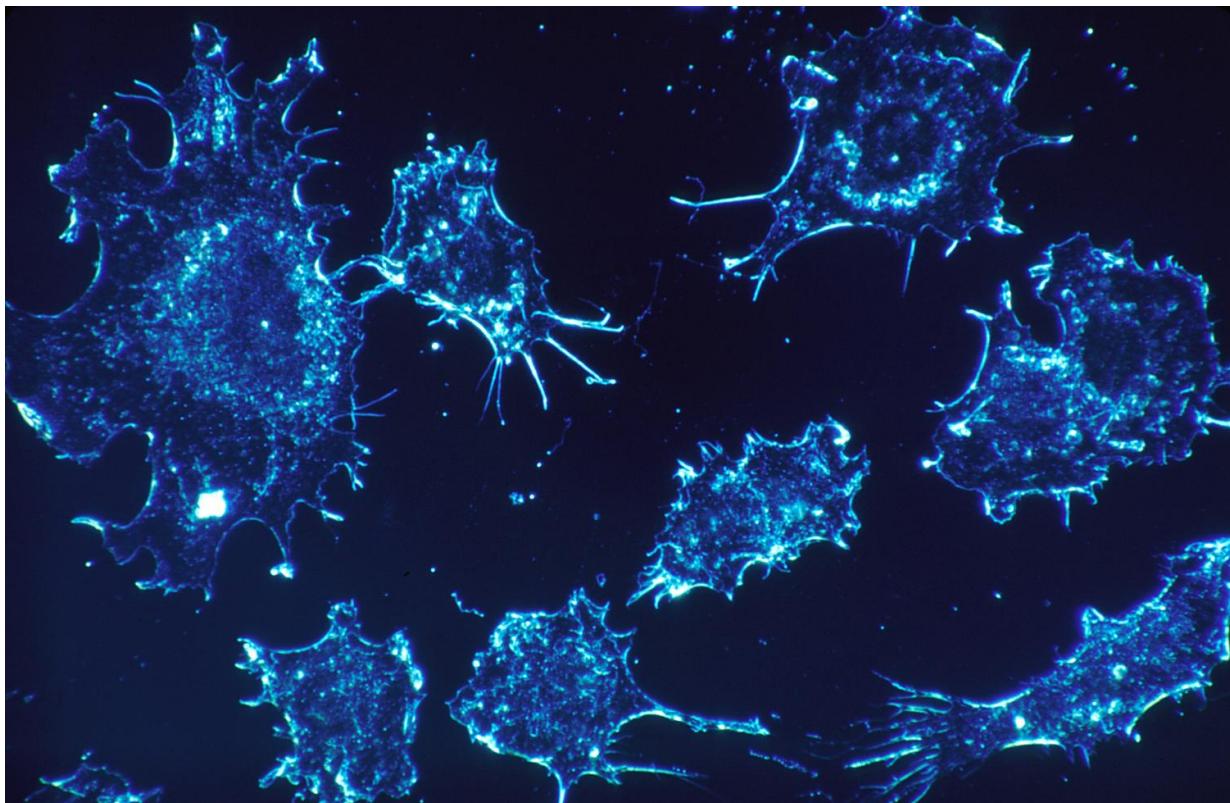


Biomarker indicates tumor aggressiveness and poor prognosis in men with prostate cancer

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Mortality due to prostate cancer is usually related to its likelihood to metastasize, especially to bone. Prognostic biomarkers are urgently

needed to predict disease aggression so that appropriate treatment can be selected. A report in *The American Journal of Pathology*, published by Elsevier, indicates that CCN3, a protein secreted into the extracellular matrix between cells, may be an important factor that promotes prostate cancer invasion of bone and may aid in identifying prostate cancer patients at higher risk of poor outcomes.

"Our work indicates that CCN3 functions to promote the formation of [prostate cancer bone](#) metastases and supports its use, after further validation, as a biomarker that predicts metastasis to bone," said lead investigator Peter M. Siegel, Ph.D., of the Goodman Cancer Research Centre, McGill University, Montreal, Canada.

Investigators analyzed [prostate](#) cancer specimens to assess CCN3 content and compare the levels to patients' clinical data. In the first series consisting of 285 patient specimens obtained from a biobank, high CCN3 expression (measured by histochemistry) correlated with shortened [overall survival](#) and the development of bone metastases at 10 years. The risk of dying from prostate cancer was also found to be greater in patients with high CCN3 expression.

A second group of tissue samples was acquired through five medical centers that belong to the Canadian Prostate Cancer Biomarker Network, which yielded 1,259 primary prostate cancer specimens. Findings were similar to those from the first group of samples, in this case using histofluorescence. Patients with the highest CCN3 expression were more likely to develop bone metastasis after 15 years and were more likely to develop biochemical relapse at three and five years compared to the low-CCN3 group. However, no significant differences in survival rates were found between CCN3-high and -low expressing groups. "Our results indicate that CCN3 expression correlates with aggressive disease and negatively correlates with the expression of prostate specific antigen (PSA), a marker of androgen receptor signaling," explained Dr. Siegel.

The investigators also measured CCN3 levels in different types of prostate cancer [cells](#). They observed that CCN3 expression was highest in prostate cell lines known to form osteolytic (bone destroying) bone metastases *in vivo* and lowest in cell lines known to be less aggressive. The researchers also found that the C-terminal (CT) domain of the CCN3 protein, thought to be crucial to CCN3's role in cell proliferation, plays an important functional role in metastatic bone destruction.

CCN3, also known as nephroblastoma overexpressed gene (NOV), is a member of the CCN family of signaling proteins secreted into the [extracellular matrix](#), which is the space outside of cells that supports cells, like a scaffold, and hosts intercellular communication. This family of proteins is thought to be involved in a wide range of biological processes, such as cell proliferation, motility, invasiveness, and angiogenesis (blood vessel formation). Other scientists have shown that CCN3 promotes breast cancer metastasis to bone.

"Our PC tissue microarray data confirms that CCN3 is positively correlated with prostate cancer aggressiveness and is not consistent with a tumor suppressor role for CCN3 in patients with prostate [cancer](#). Our work supports further investigation of CCN3 as a prognostic biomarker to predict PC recurrence to bone," observed Dr. Siegel.

More information: "CCN3/Nephroblastoma Overexpressed Is a Functional Mediator of Prostate Cancer Bone Metastasis That Is Associated with Poor Patient Prognosis," *American Journal of Pathology* (2019). [DOI: 10.1016/j.ajpath.2019.04.006](https://doi.org/10.1016/j.ajpath.2019.04.006)

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