Team finds two new and very large classes of RNAs linked to cancer biomarker

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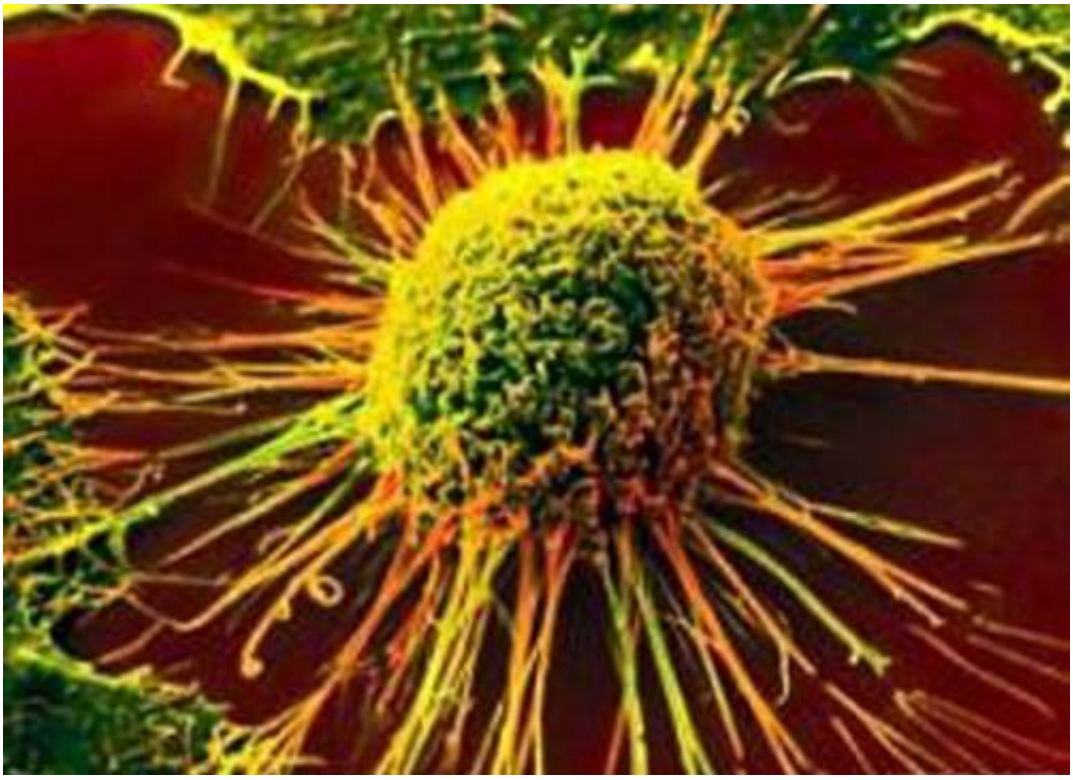

Researchers at the University of Pittsburgh School of Medicine have identified two new classes of RNAs that are closely associated with a protein known to be a prognostic biomarker for breast cancer and could play a role in progression of prostate cancer. Their findings were published in the June issue of the scientific journal *RNA*.

Levels of human Y-box binding protein 1 (YB-1), which is involved in many cellular functions, have been shown to correlate with drug resistance and poor patient outcomes in a variety of cancers. The observation that this cancer biomarker is tightly linked to a surprisingly large and diverse class of RNAs, and the known associations of some of these RNAs to cancer opens an opportunity to discover a potentially very important pathway in human biology and cancer, said senior investigator Bino John, Ph.D., adjunct professor, Pitt School of Medicine, where the research was conducted.

Intriguingly, one of the abundant RNAs that the team discovered was found to originate from the widely known DNA region of the Dicer1 gene and was determined to control multiple genes involved in cancer progression.

"Many small RNAs known as microRNAs already have been shown to correlate with different grades of prostate cancer and could potentially serve as biomarkers for diagnosis and treatment," Dr. John said. "We did this study after computer models led us to hypothesize that there was a connection between YB-1 and microRNAs. What started out as a curiosity-driven experiment ended up being an exhilarating treasure hunt over four years, culminating in the discovery of two big molecular finds from human cells."

The Pitt scientists discovered that YB-1 associated with many microRNAs, and were surprised by the realization that YB-1 associated with thousands of RNAs that were never before known. The team grouped the RNAs into what they called YB-1 associated short non-coding RNAs, or shyRNAs, and their smaller, processed counterparts, dubbed YB-1 associated small RNAs (smyRNAs).

"We conducted functional assays on one of these RNAs, and found that it had the ability to suppress cancer cell growth when it interacted with

YB-1," said co-senior author Donald B. DeFranco, Ph.D., professor of pharmacology and chemical biology, Pitt School of Medicine. "More work must be done to determine how these shyRNAs interact to influence cancer progression and perhaps influence other diseases."

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