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tNOX Serves as a Serum Marker for Detection and Monitoring of Disease

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CHICAGO -- A team of researchers at Purdue University has found a protein in the blood that may prove to be more reliable than the standard prostate specific antigen (PSA) test in measuring the extent of prostate cancer.

According to D. James Morre, Ph.D., distinguished professor of medicinal chemistry at Purdue, the protein -- called tNOX -- is a member of a family of proteins that are involved in cell growth. Normal cells express the NOX enzyme only when they are dividing in response to growth hormone signals. In contrast, cancer cells have gained the ability to express NOX activity at all times. This overactive form of NOX, known as tNOX -- for tumor-associated NOX -- has long been assumed to be vital for the growth of cancer cells, because drugs that inhibit tNOX activity also block tumor cell growth in culture.

Morre's group -- in collaboration with colleagues at NOX Technologies in West Lafayette, Indiana, and Marshall Edwards Inc. in New York -- wanted to determine if the tNOX protein could be used to monitor disease progression in prostate cancer. That is, could tNOX serve as a biomarker for not only detecting the cancer, but also in gauging the amount of disease.

Results were presented at the first meeting on Molecular Diagnostics in Cancer Therapeutic Development, organized by the American Association for Cancer Research.

Prostate cancer can be difficult to detect and track because of inaccuracies in current testing methods. The PSA test gives false-positive readings at least 20 percent of the time, resulting in unnecessary biopsies to confirm disease. The digital rectal exam in which a doctor physically checks the prostate is also plagued with reliability problems. At the same time, relying on changes in PSA levels to correlate with disease progression -- whether with treatment or not -- can be problematic.

In the study, Morre's group collaborated with Marshall Edwards Inc., which was conducting a phase II clinical trial in Australia with an experimental drug called phenoxodiol in late-stage metastatic prostate cancer. Blood samples were taken prior to, midway, and at the end of the 12-week treatment, and analyzed for tNOX. They were compared to PSA levels in the blood that were taken at the same times.

Of 19 patients in the trial, nine -- who had prostate cancer that was continuing to grow based on PSA levels -- showed on average a 60 percent greater amount of circulating tNOX protein compared to those patients who had stable (7) or falling (3) PSA levels.

“It’s the first demonstration that we have – assuming that PSA levels indicate major tumor burden in some fashion – that tNOX levels also reflect tumor burden during and after therapy for prostate cancer,” said Morre. “That is, the more prostate cancer present as evidenced by PSA levels, the more tNOX protein that is present.”

He said that tNOX would probably find greater use in estimating the amount of cancer, rather than in detection, and could be another useful marker for monitoring an individual’s response to therapy.

While rising PSA levels are usually associated with worsening disease, PSA scores can be erratic, he said. Individuals with substantial disease can still have a low PSA score, and those with moderate or even non-existent disease can show a high PSA.

“We think our marker may be more closely aligned to tumor burden than PSA,” Morre said. “It looks like it stands a better chance of being proportional to tumor burden and may be more reliable. It seems to be more uniform in terms of disease severity.”

In future work, the researchers hope to conduct more extensive clinical trials to try to link tNOX and PSA levels as estimates of tumor burden and to monitor responses to therapy of patients with late-stage metastatic disease.