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Aggressive search for an aggressive tumour test

Hepsin accurately predicts prostate tumour aggressivity

BY EMILY ANDREWS

An international team of researchers based in Toronto, Berlin and Athens, hope that their work on hepsin protein, a substance present in unusually large quantities on the cell surfaces of prostate and other tumours, may eventually lead to a blood test that can assess the malignancy of prostate cancer.

In an article published in the January issue of the Journal of Urology, Dr Stephan Carsten and colleagues report that measurements of hepsin expression from prostate cancer cells correlated with other predictors of tumour aggressivity such as Gleason score, tumour stage and WHO tumour grade. Hepsin expression measured in tumour tissue was higher than that in non-cancerous cells in 81 of 90 patients undergoing radical surgery. Although levels did not correlate significantly with prostate specific antigen (PSA) or most individual predictors, the researchers found that establishing a cutoff at the 75th percentile delineated which patients were at high vs low risk.

The study used real-time reverse transcriptase polymerase chain reaction (RT-PCR), which allows rapid amplification of a DNA sequence, and built on prior complementary DNA (cDNA) microarray studies which showed that the hepsin gene and its corresponding enzyme (a protease) plays important roles in cell growth and function and in blood coagulation via human factor VII activation. Hepsin is found in the liver, pancreas, testes, prostate, lung, thyroid and pituitary gland and is highly overexpressed in prostate, ovarian and renal cancer tissues.

Speaking from his office at Mount Sinai Hospital in Toronto, Dr Eleftherios Diamandis expressed caution regarding any eventual therapeutic applications. "We may find a small molecule that switches off the hepsin and that could be a therapeutic molecule if the hepsin is involved with cancer progression."

He and his team are working to develop a serum measure of hepsin which could be used prior to surgery to help determine the best therapeutic approach for a given patient. A better marker is needed because the currently used PSA is also elevated in benign prostatic diseases such as benign prostatic hyperplasia. Importantly, PSA does not predict cancer aggressiveness.

He also outlined plans towards developing a hoped-for serum test for hepsin expression: develop recombinant protein from the messenger RNA (mRNA), raise antibodies against the recombinant protein and develop an ELISA assay (comparable to the PSA test) incorporating the antibodies. Provided that serum hepsin elevation is in proportion to hepsin expression on cancer cells, the ELISA assay would then be able to detect hepsin overexpression.

The proviso is important. Dr Laurence Klotz, Chief of the Division of Urology at Sunnybrook and Women's College Health Sciences Centre in Toronto, offered some words of caution. "There may or may not be a correlation between serum levels and the degree of expression," he said, noting that many tissue markers have been found that correlate with prognostic criteria for prostate cancer, but none has yet "panned out."