Biomarker predicts malignancy potential of HG-PIN lesions in the prostate

May 1 2008

Men whose prostate cancer screenings show high grade prostatic intraepithelial neoplasia (HG-PIN) may find themselves in limbo, "stuck" between diagnoses – they are told prostate cancer has not yet developed, but it might, and they are advised to undergo repeated needle biopsies as a precaution.

Investigators from Spain have found a means of distinguishing between HG-PIN lesions destined to become cancerous and those which will remain benign. Their findings, reported in the May 1 issue of *Clinical Cancer Research*, a journal of the American Association for Cancer Research, could spare patients the discomfort and inconvenience of unnecessary needle biopsies.

The Spanish team found that expression of the PTOV1 gene in HG-PIN lesions is linked to prostate cancer development, and that the higher the expression, the more likely it is that subsequent biopsies will find cancer. The reverse is also true—lack of PTOV1 reduces the risk of prostate cancer.

"This is the first HG-PIN biomarker to be associated with prostate cancer development," said the study's lead author, Rosanna Paciucci, Ph.D., a researcher at the Vall d´Hebrón Hospital Research Institute in Barcelona. She says that when the results of this study are validated, the PTOV1 gene marker could be used to determine which men with HG-PIN are at substantial risk of developing prostate cancer.

“Those patients with a high PTOV1 score should undergo an immediate repeat biopsy,” Paciucci said. On the flip side, men who test low for PTOVI may not need to receive future “annoying and useless” biopsies, she said. “We estimate that we can save 40 percent of unnecessary biopsies - those that are repetitively negative and contain HG-PIN lesions that do not develop into cancer.”

While the researchers do not know the precise biochemical function of PTOV1, they say they have found this protein promotes the proliferation of cancer cells when it is over-expressed, as it occurs in prostate cancer cells.

HG-PIN is defined as a pre-malignant lesion present in most cancerous prostates. Although a pre-malignant lesion shows many of the typical cellular changes observed in cancer, the lesion has not yet progressed fully to disease. Since HG-PIN lesions are also associated with the presence of cancer in many patients, men whose biopsies show HG-PIN are often re-biopsied until cancer is detected, Paciucci says.

In most recent studies, the average risk of cancer following a diagnosis of isolated HG-PIN in biopsy ranged from 20 percent to 30 percent, the researchers say. And while other researchers have found markers in HG-PIN lesions, none have been able to discriminate between lesions that will progress to cancer, the researchers say.

In this study, the research team analyzed HG-PIN lesions from 140 patients: the positive control group comprised 79 patients diagnosed with prostate cancer who had their prostate glands surgically removed and who had been earlier diagnosed with HG-PIN; the negative control group included 11 patients with bladder cancer who had both their diseased bladder and healthy prostate removed; and the study group comprised 50 patients diagnosed with HG-PIN but not prostate cancer. The study group had an average of 2.5 biopsies each between 2000 and 2004.

Finding that PTOV1 gene expression was elevated in HG-PIN associated with cancer, the investigators used tissue microarray and immunohistochemical analyses to see whether PTOV1 protein levels could discriminate these pre-malignant lesions from HG-PIN that did not develop into prostate cancer.

They considered both the number of cells that express the protein and the intensity of the expression, and derived a quantitative score (Hscore) that ranged from 0 to 300. From this, they calculated that an Hscore of 100 represented a highly sensitive malignancy threshold. “This means that when PTOV1 Hscore is equal or above 100 the possibility to find cancer in the subsequent biopsy is 90 percent,” Paciucci said. “Currently, the diagnosis of cancer is made only when the cancer lesion is seen in the biopsy.”

By adding the analysis of PTOV1, the positive predictive value (the chance that the HG-PIN lesion will become cancerous) of all samples, including those with a score of less than 100, is 34 percent, and the negative predictive value (the chance that the HG-PIN lesion will not become cancerous) is more than 95 percent, Paciucci says.

Paciucci cautions that the study results need to be confirmed among a larger study group. “From this validation we can expect to improve the current rate of early detection of cancer,” she said.

Source: American Association for Cancer Research