First biomarker discovered that predicts prostate cancer outcome

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Mayo Clinic researchers have identified the first immune molecule that appears to play a role in prostate cancer development and in predicting cancer recurrence and progression after surgery. The report on the B7-H3 molecule by Mayo Clinic Cancer Center appears today in *Cancer Research*.

“This discovery will allow physicians to individualize treatment and observation plans for prostate cancer patients,” says Timothy Roth, M.D., a Mayo Clinic urology resident and lead author of the study. “Being able to tell a patient his specific risk after surgery, and perhaps even prior to surgery, will be a huge step forward.”

Until now there were no strongly-predictive molecules for prostate cancer. The most notable other prostate biomarkers, prostate-specific antigen (PSA), and prostate-specific membrane antigen (PSMA) are useful to diagnose prostate cancer. However, PSA tends to leave prostate cancer cells and migrate throughout the body, making it a poor target for therapy.

In this study, Mayo researchers demonstrate that nearly all normal, pre-malignant and cancerous prostate cells have B7-H3 on their surface. Unlike PSA, B7-H3 stays attached to the surface of prostate cancer cells and does not appear to migrate, thus making B7-H3 a particularly attractive target for therapy. The researchers believe that B7-H3 kills or paralyzes immune cells that are trying to attack the cancer. Their findings indicate that B7-H3 may prove useful as a diagnostic,

prognostic and even therapeutic tool because it is stably or increasingly displayed by tumor cells as prostate cancers develop -- even after initiation of anti-hormone therapy, which is the most common treatment for advanced prostate cancer.

The physician-research team examined tissue from 338 consecutive patients who had cancers confined to the prostate and were treated exclusively with a radical prostatectomy (surgery to remove the prostate) between 1995 and 1998. All tumors and precancerous tissues displayed B7-H3, but patients with the highest levels of B7-H3 within their prostate tumors (19.8 percent) were four times more likely to experience cancer progression compared to those with weak levels of B7-H3 within their tumors. Moderate levels of B7-H3 also correlated with a slightly higher risk of recurrence (35 percent).

“Because B7-H3 is present in all prostate cancer tumors, and marked levels predict recurrence, we are able to forecast with much greater certainty the likelihood of cancer progression, regardless of therapeutic intervention,” says Eugene Kwon, M.D., a senior investigator and urologist at Mayo Clinic.

For some patients, a ‘watchful waiting’ clinical approach is sometimes used to manage prostate cancer prior to resorting to therapy to see if the cancer becomes increasingly aggressive. The researchers say that the evaluation of B7-H3 levels in prostate biopsies from patients may soon help to determine which patients may benefit from a watchful waiting strategy versus early aggressive treatment.

Mayo Clinic’s findings on biomarker identification may accelerate the development of new forms of therapy, say the researchers. Additionally, prostate cancer now joins kidney cancer as a malignancy that can be tracked and predicted based on the presence of B7-H immune molecules.

“This is the way of the future,” says Dr. Kwon, “We are becoming educated about ways to flesh out the molecular signatures of each patient’s cancer. Using such molecular signatures will facilitate, for the first time, a truly individualized approach to prescribing the most appropriate therapy for a given patient. We will soon be able to tailor-make therapies for each person’s cancer.”

To understand how B7-H3 affects the immune system, and whether a mutation of B7-H3 is involved in the anti-immune activity, more research is necessary. Mayo is planning clinical trials for a number of cancers in late 2008, and researchers are currently developing the necessary therapeutic antibodies to be used in these studies. Investigators expect that clinical laboratory tests for the B7-H proteins may become available at Mayo to assist with the assessment of patients with kidney cancer by late 2007 or early 2008, and then for prostate cancer patients shortly thereafter.

This study was possible because of Mayo’s unique patient registry for prostate cancer. The registry contains hundreds of discrete pieces of information, ranging from environmental factors to specific medical test results, for more than 15,000 prostate cancer patients, all followed prospectively since the first patient was entered into the database in 1970. The Mayo Clinic prostate cancer and kidney cancer registries represent the most detailed and complete cancer reference tools in the world. Using the latter registry, Mayo investigators were previously able to link high levels of another B7-H molecule, B7-H1, to poor kidney cancer outcomes, including significantly shortened survival times.

Without the key road maps provided by these registries, the recognition of important molecules that drive cancer would not be feasible, say the researchers. Use of these patient registries enables laboratory science to be directly linked to patient care and survival following treatment.

“To a large extent, working with these registries dramatically lessens the time, resources and effort that are required to link a candidate molecule to its role in cancer development and progression,” says Dr. Kwon, who is also the co-director of the Cancer Immunology and Immunotherapy Program in Mayo Clinic Cancer Center. “Our studies are the very first to provide a clear link between immune molecules and the behaviors of various cancers.”

Dr. Kwon and his fellow researchers have been charged by Mayo Clinic to investigate all cancers for immune molecules that may govern cancer behavior while doubling as new therapeutic targets -- identifying future research targets.

Mayo Clinic Cancer Center was the first to discover the B7-H family of immune molecules -- proteins that normally help regulate the immune response process. Mayo investigators showed that B7-H3 and other members of the B7-H family, such as B7-H1, can have an inhibitory function and actually protect cancers as they develop.

Mayo Clinic identified B7-H3 as a new molecule in 2001. Mayo researchers published the first research identifying an immune molecule’s role in cancer, with multiple publications pertaining to the role of B7-H1 in heralding a poor prognosis for patients with kidney cancer. Although a number of hypotheses predicted that these molecules might enable cancer development, no one had shown it clinically prior to these studies.

Thus far, the investigators have spent significant time researching the B7-H family of molecules. They have reviewed tens of thousands of samples from at least 30 different cancers, including cancers of the breast, colon, pancreas, brain and ovary, as well as mesothelioma.

Source: Mayo Clinic