

## A protein is pivotal in prostate cancer

Prostate cancer can be a Jekyll-and-Hyde disease. Some cases progress slowly, and some aggressively. Cancers initially contained by treatment can later become fierce and deadly.

Scientists at Memorial Sloan-Kettering Cancer Center in New York now link the dual identity of prostate cancer to a protein encoded by the *p27* gene. Degradation of this cancer-suppressing protein has been implicated in other malignancies, and the new research confirms that rampant destruction of *p27* protein occurs commonly in the most aggressive prostate cancers.

The study, described in the Sept. 2 *JOURNAL OF THE NATIONAL CANCER INSTITUTE*, also suggests that benign prostatic hyperplasia (BPH), an enlargement of the prostate in older men, isn't necessarily a precursor of cancer, as often feared.

Normally functioning cells make *p27* protein nonstop. Instructions from the *p27* gene are carried by messenger RNA to the molecular machinery that makes the protein. Enzymes regularly chop up the *p27*, leaving just enough to keep the cell from dividing. When it comes time for cell division, the enzymes destroy all available *p27* protein. More is made an instant later.

"We don't know the specific enzymes of *p27* degradation," but their function seems clear, says Michele Pagano, a cell biologist at New York University and the Kaplan Comprehensive Cancer Center in New York. "You need specific traces of [*p27* and other] proteins, but you also need to get rid of them fast."

The new study indicates that in aggressive prostate cancer, "the tumor is getting rid of [*p27* protein] all the time," allowing unchecked cell growth, says Massimo Loda, a pathologist at the Dana-Farber Cancer Institute in Boston.

To explore the protein's role, researchers examined samples of prostate tissue from 4 healthy men, 14 BPH patients, and 130 men whose cancerous prostates had been removed—including 32 in whom the cancer had spread beyond the prostate. Of this last group, 78 percent had unusually depressed or undetectable concentrations of *p27*. Among the other cancer patients, 64 percent had low or undetectable levels of *p27*. The healthy subjects and 32 percent of all the cancer patients had normal amounts of *p27* in their prostate tissue.

The results suggest that prostate cancer can develop along two distinct pathways—one in which a loss of the protein *p27* allows unbridled cell proliferation and another that circumvents the growth-suppressing effects of *p27*—says study coauthor Carlos Cordon-Cardo, a pathologist and cell biologist at Memorial Sloan-Kettering.

"We're not saying [degradation of] *p27* is *the* cause of prostate cancer," Cordon-Cardo cautions. "Probably, there are other mechanisms there already."

The researchers note that the 14 patients who had BPH, a noncancerous proliferation of muscle cells in the prostate, also lacked *p27* protein—but not because enzymes were chopping it up. Instead, the BPH patients had little or no *p27* messenger RNA.

None had cancer, indicating that a simple lack of the protein may result in this benign cell proliferation but not malignancy. "These two conditions were very different," which suggests BPH isn't a precursor for cancer, says Cordon-Cardo.

The cancer danger seems to arise when a person's cells make *p27* but then destroy it, he says, rather than when there are mutations in its gene. A prostate cancer patient's *p27* concentrations may tip off doctors as to the potential severity of the cancer, he says, better enabling them to decide on treatment.

—N. Seppa