Body's Immune Protein Fights Breast Cancer

By Nathan Seppa

The body's cancer-fighting defenses include an immune protein that seems able to distinguish between normal and malignant breast cells. When confronted with a malignant cell, the protein instructs it to self-destruct, but leaves normal cells unaffected, scientists find.

This quality suggests that the protein, interleukin-25, has potential as a breast cancer treatment, says study coauthor Saori Furuta, a molecular biologist at the Lawrence Berkeley National Laboratory, in California. The report appears in the April 13 *Science Translational Medicine*.

Furuta and her colleagues focused on breast epithelial cells, which form part of the milk-producing mammary glands and are the cells that turn malignant in the vast majority of breast cancers. To test the role of interleukin-25, they implanted 15 mice with breast tumors and injected the tumors with either IL-25 or a saline placebo daily. After a month, the tumors in the untreated animals had tripled in size whereas tumors in the IL-25–treated mice were virtually unchanged.

IL-25 works by binding to a receptor protein embedded in the membrane of a cell. Receptors act as docking stations and, when bound, send signals to the control center, or nucleus, of the cell. When four cell lines of breast cancer grown in lab dishes were exposed to IL-25, this protein-to-receptor binding triggered destruction of malignant cells - which is apparently what happened in the mice. IL-25 had no effect on healthy breast cells.

The findings suggest that IL-25 might be one of the body's many homegrown cancer-suppressing proteins, Furuta says. The body generates thousands of potentially malignant cells every day and routinely kills them, she says, sometimes through the same sort of programmed cell suicide triggered by IL-25.

Samples of human breast cancer tissues revealed plenty of IL-25's receptor protein, but no IL-25 itself. When breast epithelial cells turn cancerous, they seem to lose the ability to make IL-25, the researchers report. But the IL-25 receptor remains, and in a curious twist it can be bound by another interleukin, called IL-17b, that contributes to the cancerous cycle of cell proliferation.

That cross-reactivity between receptors and other proteins is not uncommon, says Michael Lotze of the University of Pittsburgh Cancer Institute. For the most part, interleukins are specific to their receptors, he says, "but there are individual examples of this cross talk."

The new study adds to the growing knowledge of interleukins, which are members of an immune-messenger club called cytokines that play a wide variety of roles in the body. "Here was this cytokine, IL-25, just waiting for somebody to figure out what it does," says Lotze, a physician and immunologist. The growing roll call of interleukins is now up to IL-38, he notes.

Now the challenge remains to sort out whether IL-25 can beat cancer beyond the simple cell lines used, he says, since real tumors are a complex organization of proliferating cells with their own blood vessel networks.

Furuta hopes that companies will take interest in translating these lab findings into usable IL-25 versions that are testable in people as an anticancer drug. Other cytokines have succeeded as drugs. Interleukin-2 is the basis of drugs for fighting kidney cancer and melanoma, says Lotze, and another cytokine, interferon, is a frontline drug against hepatitis.