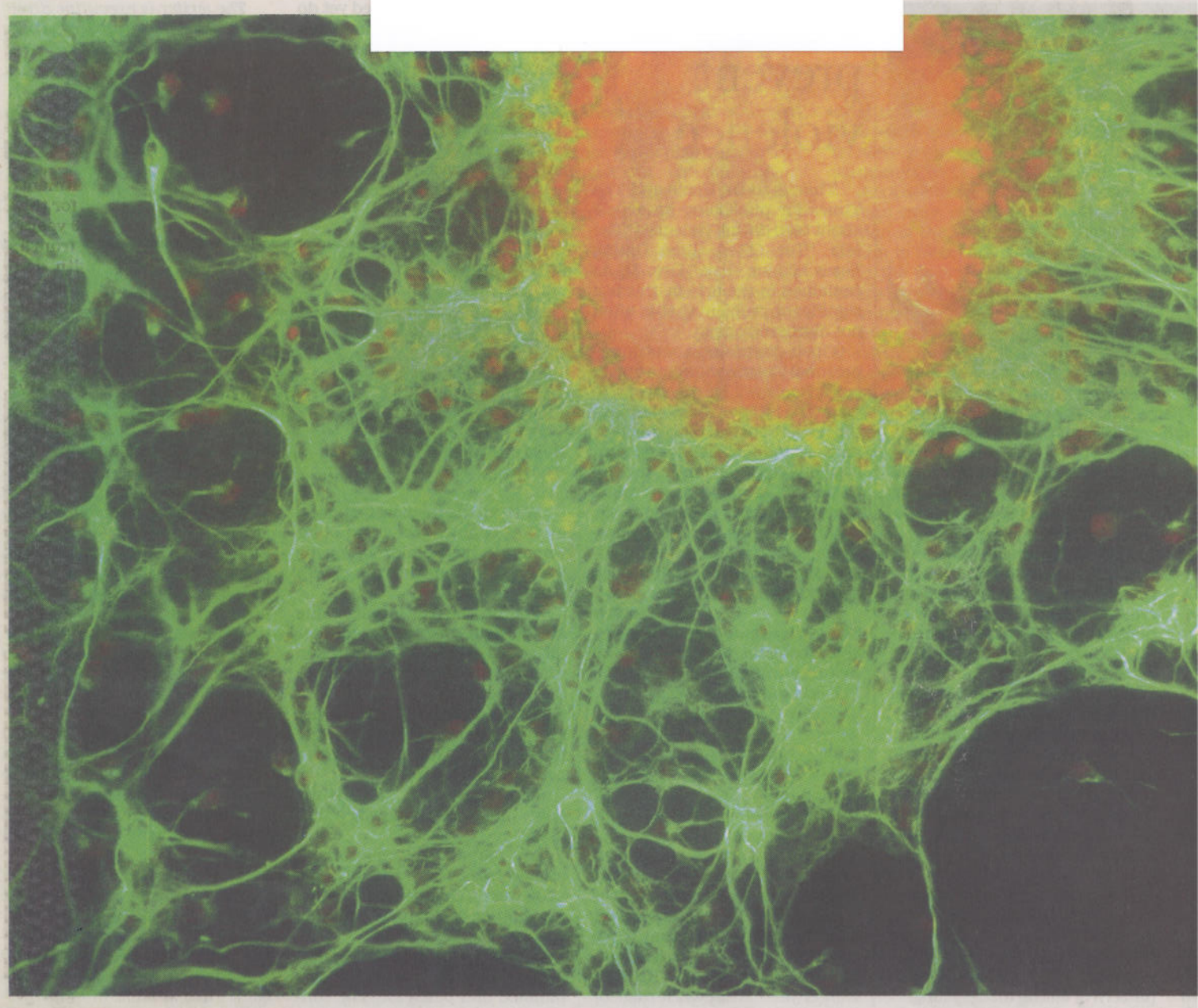
MEDICINE

Chandra Shekhar, Ph.D.
science writer

(609) 921-7180 (home)
(609) 477-8028 (cell)
chandra@nasw.org



ROOT CAUSE? *Scientists hope that if drugs are designed to kill or disable "cancer stem cells" like this one, they could eradicate the tumor.*

A cell's 'neighborhood' might make it go bad

By Chandra Shekhar
Special to The Times

The realization that cancers may be driven by stem cells isn't the only new concept in oncology. Scientists are also taking a closer look at the role of the "neighborhood" in which a cell resides — its microenvironment.

"A healthy or unhealthy microenvironment may determine if a stem cell is normal or cancerous," says Mark LaBarge, a postdoctoral fellow in life sciences at the Lawrence Berkeley National Laboratory.

Every cell, be it normal or cancerous, lies among a multitude of other cells, attached to a support structure known as the extracellular matrix. The space outside of a cell teems with a variety of chemicals. Studies offer intriguing clues to the role of this chemical-rich microenvironment in cancer.

In the 1980s, experiments with chickens showed that an embryo carrying a so-called oncogene — a genetic mutation associated with cancer — could develop into a normal, cancer-free adult bird. When cells from the bird were cultured in the lab, however, they quickly turned cancerous. And if such a bird was wounded, a tumor developed at the site of the injury.

These and similar findings suggest that oncogenes alone can't form tumors — a microenvironment marred by wounding, swelling, aging, or other causes may also play a part. The findings also suggest, conversely, that a healthy microenvironment may act to suppress tumors.

LaBarge and his colleagues are testing the idea further by comparing the response of normal human breast stem cells and mutated, cancer-prone breast stem cells to different microenvironments. (They've created a variety of microenvironments in the lab using combinations of proteins present in breast tissue.)

A microenvironment link to cancer may explain why many Japanese women who were in puberty during the nuclear attacks on Hiroshima and Nagasaki went on to develop breast cancer 20 to 30 years later, LaBarge says. The radiation fallout would have damaged the victims' breast stem cells, which would have turned cancerous as the breast microenvironment deteriorated with age. "Mutated stem cells may very well be the root of cancer," LaBarge says. "But we don't think they turn nasty until something goes wrong with the microenvironment."

Many compounds that affect the tumor microenvironment have shown promise in treating cancer. The drug bevacizumab (Avastin), which starves tumors by blocking the formation of blood vessels in them, was approved in 2004 for treating some types of colon and lung cancers. Nonsteroidal anti-inflammatory drugs such as aspirin also seem to protect against colon cancer when given in large doses. A type of chemical called bisphosphonate that binds to bone tissue may prevent breast, prostate and other tumors from spreading to the bones. These and various other compounds are in human trials.