



Henri Matisse, Blue Nude (IV), 1952. © 2003 Succession H. Matisse, Paris/Artists Rights Society (ARS), New York

## Prevention:

### *Breast Cancer's Next Chapter*

Immediately after breast cancer is diagnosed, all thoughts focus on treating the tumor. The physicians will chart their offensive like generals attempting to repel an attack by the most implacable foe. Lumpectomy or mastectomy? Chemotherapy, hormonal therapy, radiation, all or none? Are lymph nodes involved? If so, how many?

Take a step back from the front lines, however, and you find another set of medical team combatants, the members of what one might call the intelligence gathering community. These are physicians and scientists who try to figure out how to prevent abnormal growths from occurring in the first place. With the tumor already present, however, their task is to stop it before it metastasizes—before it gains the ability to spread throughout the body.

Drs. Jeffrey Pollard, deputy director of the Cancer Center and Thomas Rohan, chairman of epidemiology and population

health, are prominent physician/scientists in the cancer “preventive strike” arena.

Dr. Pollard is changing the way the scientific world has traditionally viewed the immune system’s role in coping with cancer. His particular specialty is the link between breast cancer and a previously unrecognized function of immune system cells known as macrophages.

Generally, macrophages carry out many helpful protective roles, from engulfing foreign cells outright to displaying bits of the offending invaders as flags to alert other immune cells that an intruder requires attention. Macrophages also secrete various potent substances that activate and empower other immune cells. They are also important in embryonic development—paving the way for new blood vessels, shaping tissue into its proper form and carving out space for growing tissue. For example, macrophages play an essential role in

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removing the webbing between digits, allowing babies to be born with discrete fingers and toes.

The traditional view holds that macrophages also help to combat cancer—that they're able to recognize cancer cells as foreign and then attack the cancer, just as they mobilize against viruses or bacteria. Experimental anti-cancer vaccines, for example, are based on this principle. Increasingly, however, new research is challenging this simplistic view of cancer and the immune system: Dr. Pollard's work indicates that tumors can actually enlist macrophages in a way that promotes, rather than prevents, the spread of the disease.

Indeed, especially aggressive breast cancers tend to have many macrophages associated with them. (The abundance of macrophages is at least partly due to the fact that these aggressive tumors also pump out generous amounts of a compound called CSF-1 that promotes macrophage growth.) The assumption had been that macrophages were there to fight the cancer. Now the evidence points to a different role for them—a malevolent role, in fact.

"We had the idea that instead of these macrophages being there to reject the tumor, they were actually helping the tumor grow," says Dr. Pollard. The macrophages are now suspected of digesting tissue to make way for the growing tumor and stimulating the formation of new blood vessels to feed the tumor—strikingly similar to the constructive role macrophages play in normal development of the fetus. But

now, this macrophage activity has the very negative effect of promoting the growth of cancer.

"The prevailing idea has been that the tumor is really foreign," says Dr. Pollard. "But it's not foreign so much as treasonous. And the macrophages open the gate for those tumor cells to escape from their constraints and then to metastasize."

Recent microscopy work done at the Einstein Cancer Center lends support to these suspicions. These images show how normal tissues break down in the presence of macrophages, freeing tumor cells bound up within them. In addition, microscopy of living tissue done in

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collaboration with Dr. John Condeelis, co-chair of anatomy and structural biology and director of Einstein's Analytic Imaging Facility, has revealed macrophages and tumor cells moving synchronously toward blood vessels. Once they are in the blood stream, tumor cells can easily travel to other parts of the body, resulting in metastases.

To further test this "macrophages-gone-bad" hypothesis, Dr. Pollard and his colleagues carried out studies with genetically engineered mice. In one experiment, they bred mice predisposed to develop breast cancer with mice that have no macrophages. "When we looked at the offspring, we found that the incidence



Dr. Jeffrey Pollard  
Betty and Sheldon Feinberg  
Senior Faculty Scholar

Dr. Jeffrey W. Pollard wears so many Einstein hats he might wish for a second head. And he recently added another hat to his collection: Dr. Pollard was named Deputy Director of the Albert Einstein Cancer Center, succeeding Dr. Matthew Scharff. Dr. Scharff, who remains a distinguished member of Einstein's faculty as professor of cell biology and of medicine and the National Women's Division's Harry Eagle Professor of Cancer Research, served as both the Director of the Cancer Center (1986-1995) and as Deputy Director (1995-2001).

Dr. Pollard, professor of developmental and molecular biology and of obstetrics & gynecology and women's health, is also Director of the Center for Reproductive Biology, faculty supervisor of Einstein's transgenic mouse facility (where mice with novel and useful genes are actually created) and the Betty and Sheldon

Feinberg Senior Faculty Scholar in Cancer Research. In addition, he recently guest-edited an issue of the *Journal of Mammary Gland Biology and Neoplasia*, a scientific publication devoted solely to breast cancer research. "Jeff is the College's and the Cancer Center's indispensable man," says Cancer Center Director David Goldman. The outside world agrees: Dr. Pollard's research has been featured on the cover of three scientific journals in the last year, a rare achievement.

Dr. Pollard comes from England, where he received his doctorate in 1974 from the Imperial Cancer Research Fund. After a postdoctoral fellowship at Toronto's Ontario Cancer Institute, he returned to England for a faculty position at the University of London. Einstein became his home in 1988. ■