Prestigious Grant Backs Major Lung Cancer Research

National Cancer Institute honors UCLA's Jonsson Comprehensive Cancer Center with a major grant to develop lung cancer treatments as fast as possible.

he word "spore" comes from the Greek term for sowing or seed, so it's a perfect acronym for the Specialized Program of Research Excellence sponsored by the National Cancer Institute.

The NCI recently honored UCLA's Jonsson Comprehensive Cancer Center with a \$13.9 million, five-year SPORE grant, one of only six SPOREs awarded nationwide for lung cancer research, and the first on the west coast.

"The SPORE is an honor for the cancer center. It means UCLA has been judged to be among the leaders in lung cancer research in the country. It is an honor that recognizes not only the excellence of our scientists, but also the teamwork among them that is making this collective effort a success," says Dr. Steven Dubinett, the program's lead investigator at the Jonsson Cancer Center. Dubinett works closely with Dr. Robert Figlin, a professor of medicine who oversees clinical research related to the SPORE.

SPORE programs fund projects that sow innovative research ideas and then cultivate them as quickly as possible to develop new cancer treatments and methods of cancer prevention. Or, in the official words of the NCI, SPOREs support "innovative, multidisciplinary translational research approaches that potentially may have an immediate impact on improving cancer care and prevention."

At the Jonsson Cancer Center scientists are tackling five SPORE projects targeting lung cancer, with more on the horizon.

Dubinett, a professor of medicine, is

working with Drs. Michael Roth, Raj Batra and Sherven Sharma in an effort to alter the human immune system so that it attacks non-small cell lung cancer, named for the kinds of cells it destroys.

Their plan is uncomplicated, but difficult to implement. They will remove cells called dendritic cells from patients with lung cancer. Ordinarily, in the presence of disease, dendritic cells activate the body's immune defenses. But lung cancer cells appear to destroy the effectiveness of dendritic cells.

"Therefore, we genetically alter the dendritic cells so that tumors can't poison them.

cells by starving them.

All cells feed off nutrients provided by blood. Cancer cells require more nutrition than most cells do, so tumors generate their own special blood vessels to assure sufficient nourishment.

Strieter, a professor at UCLA's School of Medicine, says a family of proteins called CXC chemokines that occurs naturally throughout the body, appears to play a critical role in generating tumors' blood vessel formation.

"We are working to develop ways to inhibit the role of CXC chemokines that cause new vessel formation, thereby destroying a tumor's ability to generate its own blood vessels," Strieter says. "Without

"The SPORE is an honor for the cancer center. It means UCLA has been judged to be among the leaders in lung cancer research in the country."

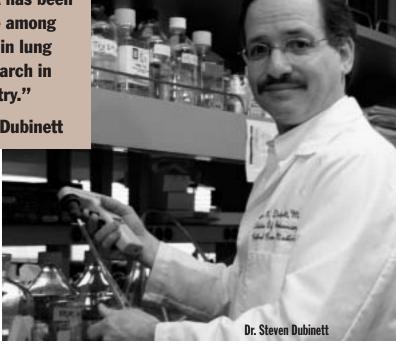
—Dr. Steven Dubinett

The altered dendritic cells induce an immune response throughout the entire body, encouraging white blood cells to attack lung cancer not only in the lungs, but also wherever else it has spread," explains Dubinett.

Laboratory experiments show Dubinett's work to be effective. He expects to begin experimental therapy with patients before the end of this year.

Dr. Robert Strieter leads another SPORE project. Strieter, who is UCLA's chief of pulmonary and critical care medicine, and his colleague, Dr. Lee Rosen, are attempting to kill non-small cell lung cancer those blood vessels, we think the tumor will die or shrink to an insignificant size. We expect to start clinical trials for cancer patients within a year."

Dr. Enrique Rozengurt, the Ronald Hirshberg Professor of Cancer Research at UCLA's Jonsson Cancer Center and chief of research in the Division of Digestive Diseases



"It's early in the game, but already I'm optimistic about where we're going."

—Dr. Robert Figlin

at UCLA, takes yet another approach to combating small-cell lung cancer. His project focuses on neuropeptides, which are short chains of amino acids that generate chemical signals promoting the growth of small-cell lung cancer cells.

"The neuropeptides are produced by the cancer cells and generate signals which stimulate proliferation of those cells," Rozengurt says.

Rozengurt and his colleagues are developing methods to block those signals, thereby preventing growth of the cancer cells. He says that without the growth-promoting signals generated by neuropeptides, small-cell lung cancer cells will either shrink or die, arresting or eliminating the cancer. Rozengurt hopes experimental treatments based on his work will begin on cancer patients within three years.

SPORE researchers Drs. Denise Aberle, Jonathan Goldin and Matthew Brown are developing the use of a new method to detect and characterize suspicious nodules in the lungs. They will work with a highly sophisticated new machine that melds computed tomography imaging (CT scanning), also known as computed axial tomography (CAT scanning), with Positron Emission Tomography (PET scanning).

CT scanning provides high-resolution images of a patient's anatomy and internal structure, including soft tissue, bone and blood vessels. PET scans show a person's cellular metabolism, or how the body is functioning, which is important to cancer patients because tumors have a generally higher rate of metabolism than healthy tissue, so they can be visualized through PET scans.

"For our work," Aberle says, "we will combine the ability of CT scans to detect increased blood flow engendered by tumors, and the capacity of PET scans to find increased metabolism indicated by high glucose content. By acquiring the two kinds of scans almost simultaneously instead of sequentially, we will get much

more accurate results because the patients' conditions and positions will not change. We'll make anatomy templates specific to each patient showing precisely where and how active tumors are and whether they are malignant or benign. We expect results to be more accurate than any now available anywhere in the world. Our goal is to be working with patients within a year."

Drs. Zuo-Feng Zhang and Donald Tashkin's SPORE project involves detective work based on the theory that lung cancer is caused by environmental exposures, genetic mutations and people's inherent genetic susceptibility to the disease. They are interviewing 600 people with lung cancer and 600 people without the disease, and analyzing cell samples painlessly taken from inside the mouth.

"When we finish our study in five years," Zhang says, "we hope to be able to identify potential genetic and environmental factors that will identify people at high risk for lung cancer. With that information, we will be able to recommend appropriate therapeutic and preventive measures."

Figlin, who is in charge of the SPORE's clinical aspects, has high hopes for the program. "Overall," he says, "our lung SPORE research is particularly exciting because it is designed specifically to benefit cancer patients and people at high risk for the disease. Our goal with every aspect of this program is to turn research results into cancer therapies and preventive measures with the utmost speed. It's early in the game, but already I'm extremely optimistic about where we're going."