

Unraveling the Mysteries of Liver Cancer

By Kim Irwin

LIVER CANCER IS THE MOST DEADLY CANCER. It remains shrouded in mystery for physicians and laboratory scientists toiling to understand it and find better ways to treat it.

Conventional treatments — surgery, chemotherapy, radiation, radiofrequency ablation (burning) and cryosurgery (freezing) — unfortunately do little to stop liver cancer, which kills up to 1 million people worldwide every year, including 10,000 Americans.

To study the causes and development of liver cancer and create new therapies that cure this largely unexplored disease, or at least significantly increase survival rates, officials at UCLA's Jonsson Comprehensive Cancer Center last year launched the Dumont-UCLA Liver Cancer Center, directed by Dr. Ronald W. Busuttill, a world renowned surgeon specializing in liver transplantation. A \$2 million gift from the Dumont Foundation provided initial funding for the project.

The new center brings together many of UCLA's best surgeons, laboratory scientists, medical oncologists, radiologists and pathologists. It is among the few organizations in the world attacking this deadly disease through a multidisciplinary treatment approach and a focus on basic science.

Members of the liver cancer center offer the latest in experimental and traditional treatments and conduct the most advanced research.

An important obstacle to liver cancer research is the shortage of laboratory models to illustrate the development and natural course of liver cancer in humans. Developing new laboratory models to facilitate the study of liver cancer is a priority for Dumont-UCLA scientists.

The center is uniquely positioned to attack this disease. Although no one understands why, unusually large numbers of Asians in the U.S. and abroad are infected with hepatitis B and C viruses, which cause liver cancer. Los Angeles' extensive Asian population, coupled with the city's Pacific Rim location, provides access to an important patient base.

Busuttill says the timing couldn't be better to focus on liver cancer.

"Liver cancer is the No. 1 cancer in the world [both in frequency of cases and in fatalities]," Busuttill says. "Right now, the fight against this disease is woefully inadequate. We'll be using a multidisciplinary treatment approach and cutting-edge clinical trials to get a hold on this deadly killer.

"We'll provide the best in care and the latest research. Our goal is to find a cure for liver cancer, to bring new treatments from the basic science labs to the bedsides of patients."

Liver cancer experts across the nation welcomed the opening of the Dumont-UCLA Liver Cancer Center. Dr. Goran Klintmalm, chair of the Baylor Institute of Transplantation Sciences at Baylor University Medical Center in Dallas, Texas, says UCLA became a

leader in liver cancer treatment and research with the opening of the new center.

"This is exactly the way we need to go to foster the development of liver cancer therapies," says Klintmalm, an internationally recognized authority on liver transplantation. "What we know about liver cancer now is not enough. To become more successful, we need to know more. Clearly, this is the way of the future. Those like UCLA that have the foresight to develop these centers will point the direction forward for the rest of us."

Dr. Rafael Amado is on the team of elite Dumont-UCLA scientists working to unravel the mysteries of liver cancer in order to find effective treatments.

"Once you develop liver cancer, it's almost always a death sentence guaranteed," Amado says. "We need to find out what causes this disease, what are the changes the liver cells go through to become malignant, what genes are turned on or turned off in liver cancer. This is virgin territory."

Worldwide, as many as 1 million new cases of liver cancer are diagnosed every year, with the highest incidence rates in China, Southeast Asia, and South and West Africa.

Amado and other UCLA researchers expect the number of liver cancer cases in the United States to increase as a result of hepatitis B and C infections. About 2 percent of Americans are infected with the hepatitis C virus, Amado says. Of those, 5 to 10 percent are expected to develop liver cancer.

U.S. Census Bureau figures show that Asian populations, which have a high incidence of hepatitis B and C, are one of the fastest-growing minority groups in this country. In the last decade, the nation's Asian population grew by 43 percent, with most of that growth occurring in California, which is now home to more than 4 million Asians.

"There is the potential for a big increase in liver cancer in the Western world," Amado says. "Los Angeles County, populated by growing numbers of Chinese, Koreans and Southeast Asians, already has the highest incidence of liver cancer in the United States."

If it could be detected early, liver cancer could be more easily treated. But this disease is difficult to diagnose early because patients often exhibit few symptoms. And the liver is a difficult organ to examine manually due to its location under the rib cage.

Removing the entire tumor surgically is the only way to cure liver

The Dumont-UCLA Liver Cancer Center is among only a few centers worldwide that are attacking this deadly disease through a multidisciplinary treatment approach and a focus on basic science. For more information, call **(310) 825-5318**.

cancer. However, if the cancer has spread beyond the liver, surgery is not an option. Surgery also won't work on a very large tumor, or if multiple small tumors are growing in different parts of the liver.

Dr. Pauline Chen, a surgeon and a Dumont-UCLA scientist (See related story on page 10.), is confident that help for liver cancer patients is within reach.

"I think we have a chance of finding a cure for this disease, of understanding how this kind of tumor works," Chen says. "We're taking what is now known and pushing the envelope. Our multidisciplinary focus will give us added insight. We're attacking liver cancer on all fronts."

A variety of new procedures for treating primary and secondary liver cancers is available to patients at the liver cancer center. For example, the center is testing an experimental drug that cuts off the blood supply to tumors, depriving them of oxygen and nutrients needed to promote growth. The drug, SU5416, has been tested on other tumor types with varying degrees of success. UCLA researchers hope it will prove effective against liver tumors.

Other experimental therapies offered to patients at the liver cancer center include treatments that target the biological mechanisms of cancer cells rather than all rapidly dividing cells. These specific, or targeted, approaches result in less severe side effects than those associated with traditional

therapies such as chemotherapy and radiation.

One kind of targeted treatment available at the liver cancer center employs a class of new medications called farnesyl transferase inhibitors. These inhibitors target a key step in a cancer cell's production of proteins needed to sustain cell life.

The center also plans to attack liver cancer using blockers of specific cell molecules that trigger tumor growth, as well as angiogenesis inhibitors, a class of drugs that attack cancer by cutting off a tumor's blood supply.

Jonsson Cancer Center Director Judith Gasson says the new liver cancer center furthers her goal to expand research and broaden treatments offered for cancer.

"The strength of our cancer center is bringing together discovery research and compassionate patient care," Gasson says. "I applaud Dr. Busuttill for launching this program that will impact so many lives worldwide."

Dr. Gerald Levey, UCLA's provost for the medical sciences and dean of the UCLA School of Medicine, called the Dumont-UCLA Liver Cancer Center "the essence of what UCLA is all about."

"We're recognized worldwide for our innovation and translating science into better patient care," Levey says. "This center will bring the latest in treatments to the patients." ★

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