

## Trailblazer drives new ways of cancer care

Valley doctor one of world's foremost researchers

By Anne Ryman  
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Many of Dr. Daniel Von Hoff's patients arrive at his clinic awaiting death.

They are losing their battle against cancer and have been told they have only months to live.

Von Hoff has defined his life around these patients. He specializes in the toughest cancer cases, for which conventional therapy has failed. He is especially focused on subduing pancreatic cancer, which kills most people within a

year of being diagnosed.

Von Hoff and his team, who work out of a clinic and a laboratory in Scottsdale, are one of the success stories in the decades-long, frustrating war against cancer, whose death toll in the United States is second only to heart disease.

He has been involved in the development of a half-dozen drugs that are routinely used to treat cancer, drugs that have extended people's lives by months and

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Dr. Daniel Von Hoff has worked over the years on more than 200 clinical drug trials, likely a record for one person.

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sometimes years.

In the quest to create the most effective medicine, he has worked with other scientists over the years on more than 200 clinical trials, which some cancer researchers say is probably a record.

The breadth of the research has made Von Hoff one of the foremost cancer scientists in the world. In June, the American Society of Clinical Oncology honored him with its most prestigious award in the field of cancer research.

In the past two decades, "he has done more to develop effective cancer drugs than just about anybody else," said Dr. Richard Schilsky, a professor of medicine at the University of Chicago who served on

### DR. DANIEL VON HOFF

**“**There are many, many people (with cancer who) if you don't try, you know what's going to happen. But if you try, sometimes there are breakthroughs.”

**Age:** 63.

**Born:** Oshkosh, Wis.

**Education:** Bachelor's in biology and chemistry, Carroll College, Waukesha, Wis., 1969; M.D., Columbia University College of Physicians and Surgeons, New York City, 1973. Also took a yearlong sabbatical in 1986 to work as a scientist in the Salk Institute's Gene Expression Laboratory.

the award-selection committee.

Colleagues describe Von Hoff as a doctor with a profound sense of urgency

who works non-stop to get promising drugs from the lab and into clinical trials.

The 63-year-old works nearly every day in his lab

**Current title:** Physician in chief, senior investigator and director of the clinical translational research division at the Translational Genomics Research Institute in Phoenix. He is also a clinical professor of medicine at the University of Arizona.

**Family:** Wife, Ann, and three adult children: Paul, Jane and Carol.

near Mayo Clinic in Scottsdale, in his clinic at Scottsdale Healthcare Shea Medical Center or at home. His employer is the



**Best known for:** His research in pancreatic cancer. He and his team were involved in the beginning of several anticancer drugs that are routinely used to treat various forms of cancer, including mitoxantrone, fludarabine, paclitaxel, docetaxel, gemcitabine and CPT-11.

**For more information on clinical trials:** Call Joyce Schaffer, patient-care coordinator, TGen clinical research services at Scottsdale Healthcare, 480-323-1339.

Translational Genomics Research Institute in Phoenix, or TGen, where he is physician in chief.

Von Hoff sleeps only

chance to know her instead of just a little baby sitting there seizing," Von Hoff said.

The experience had a profound effect on him. But he still wasn't planning to make cancer his life's work. His first choice was studying infectious diseases.

Then a random assignment came his way.

### A lesson learned

After medical school and an internship, he started a residency in 1974 at the University of California-San Francisco. Young doctors were assigned their rotations alphabetically based on their last names. He happened to get oncology.

Aspiring doctors viewed oncology, a relatively new specialty then, as too depressing because survival

three hours a night. He sees dozens of patients a month, advises other doctors on treating patients and oversees the research lab, which identifies potential "target" genes for cancer drugs.

He never loses sight of his patients, colleagues say.

"In the retail world, the customer is the king. For him, patients are the king," said Haiyong Han, who manages Von Hoff's lab.

Jeffrey Trent, president and research director of TGen, calls him the bravest person he has ever met because of the personal care and empathy Von Hoff maintains, year after year, for patients with only a few months to live. He is a kind of a "physician on steroids," Trent said.

"Most researchers say, 'Let's really understand this (drug) completely, and then we can perhaps use it for someone in the clinic.' Dan says, 'We need things for the clinic today. These people are in front of us today. Let's see if we can utilize that today.'"

To begin a clinical trial, researchers must show a drug has a high likelihood of success and a low likelihood of patient complications.

Von Hoff didn't set out with the goal of becoming a cancer doctor. In fact, it was purely an accident. He credits much of his success to a life lesson he learned as a young physician.

### Fascinating stuff

The oldest of five children, Von Hoff grew up in east-central Wisconsin, attending a one-room schoolhouse. His father was a bricklayer, and his mother a nurse's aide in a hospital.

He got interested in medicine around the fourth grade, when the polio scare was in full swing. Nurses came to the school to vaccinate the children. The large needles frightened him. He also was fascinated that a simple shot could prevent the dreaded viral disease, which crippled thousands of children in the early and mid-20th century.

After majoring in biology and chemistry in college, he was admitted to Columbia University College of Physicians and Surgeons in New York City in 1969. He soon saw firsthand how anti-cancer drugs could improve patients' lives.

One day, he tagged along with a pediatric oncologist who was treating a 3-year-old with a tumor mushrooming out of her head. The prognosis wasn't good; the child suffered from constant seizures.

The oncologist felt that the child might benefit from an experimental anti-cancer drug. He suggested the drug daunomycin to the girl's parents, who agreed to try it. Within a day, the child's seizures stopped. The next day, she rode a tricycle. Three days later, the parents took their daughter home.

She eventually died from the tumor, but she lived a lot longer than she would have without the treatment. That drug is still being used today.

"Her mom and dad got a

rates were poor, he said. At the time, U.S. deaths from all types of cancer numbered 199 per 100,000 population, compared with 181 in 2006, the most recent year for which figures are available, according to the National Center for Health Statistics.

The biggest killer was lung cancer. While overall rates have fallen only 9 percent since 1975, more patients live longer.

Von Hoff learned that while the cancer patients were very sick, there was always something he could do to help, be it alleviating pain or simply caring. He got hooked.

After his residency, he trained in oncology at the National Cancer Institute in Bethesda, Md. Colleagues who trained with him said his "off the charts" work ethic was apparent early on. While others went home in the evening, he would stay at the lab until well past midnight.

While he was training, he learned an important lesson that has guided him ever since.

A psychiatrist began shadowing him on the job, studying how young doctors respond to the loss of their patients.

While the psychiatrist observed him, Von Hoff learned from the psychiatrist during their conversations.

The psychiatrist taught him that no matter how much time he needed to spend with a patient, he should push all other concerns out of his mind.

"If you listen, they will help you help them," Von Hoff remembers the psychiatrist saying.

It wasn't easy. There was a tendency to think about the next appointment or an earlier patient. He really had to concentrate to do a good job of listening. But his listening became more focused, something that would benefit his research greatly within a few years.

### The KFC factor

In the late 1970s, Von Hoff was recruited to start a new drug-development program at the University of Texas Health Science Center in San Antonio.

He studied anti-cancer drugs in the lab and then conducted clinical trials with those that showed potential. Outside of work, he and his wife, Ann, were raising two daughters and a son.

One day, around 1987, he was treating a man whose advanced-stage pancreatic cancer had spread to his liver. The pancreas, a pear-shaped organ behind the stomach, produces enzymes that aid digestion and regulate metabolism. Pancreatic cancer spreads quickly, with symptoms often not appearing until the tumor is too far advanced to operate.

Von Hoff started the man on an experimental drug called gemcitabine. During one visit to monitor his condition, the man's wife started scolding the doctor.

"Dr. Von Hoff, you're late again," she said as he

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walked into the room. "I've got to get my husband over to Kentucky Fried Chicken. He really likes to eat Kentucky Fried Chicken."

Von Hoff, always attentive, stopped short. People with pancreatic cancer often lose weight because the tumor kills their appetite. He flipped through the man's chart. The patient had gained weight rapidly, putting on 11 pounds.

"How are you feeling?" Von Hoff asked him.

"Geez, you know doc, I feel better. The pain is gone," the man said.

Von Hoff looked down and noticed the man wore Adidas track shoes.

"Walking a lot?" Von Hoff asked.

"Oh, I've got energy," the man said. "I got these new shoes."

All the signs, taken together, indicated for the first time that gemcitabine was proving effective in clinical trials for pancreatic cancer. The drug went on to get FDA approval and became the first to improve one-year survival rates for pancreatic cancer. It also was approved, in combination with other drugs, to treat breast, lung and ovarian cancer.

Gemcitabine works by inserting itself into the tumor's DNA, causing the tumor cells to get confused about how to reproduce. The man whom Von Hoff had treated lived about another year, when average survival was only two to three months.

When giving lectures to other doctors or students, Von Hoff recalls that moment in the exam room and urges the students to remember the "Kentucky Fried Chicken factor."

"The KFC factor is 'Listen to your patient,'" he says.

### Ongoing challenges

In 1999, Von Hoff was recruited to the Arizona Cancer Center in Tucson. He continued his research there, and seven years ago began working at TGen in an emerging area of medicine known as genomics, in which DNA research of diseases is leading to advances in cancer treatment.

In applying genomics research to cancer, doctors analyze the molecular structure of the patient's tumor, trying to pinpoint vulnerabilities and come up with treatments to match.

Today, he and his team conduct clinical trials in partnership with Scottsdale Healthcare. More than 30 clinical drug trials are under way.

He sees patients in clinical trials every Monday. When they arrive, they are greeted in the lobby by

oversized stuffed animals handpicked by Von Hoff. The animals help create a comfortable atmosphere for the adults in clinical trials.

Von Hoff deals with death all the time, but colleagues say his mood remains upbeat. His focus is on extending lives and learning something to help future patients.

"He's the spark plug and the bulldog, and the one who is always keeping the spirits up," said Mark Slater, Scottsdale Healthcare's vice president of research.

Von Hoff sees patients all day on Mondays. He returns to his Scottsdale home around 7 or 8 p.m., eats a salad at his desk there and goes back to work, dictating notes until 2 a.m.

He grabs a few hours of sleep and is up by 5 a.m.

Colleagues often open their e-mails in the morning and find messages sent by him overnight.

He credits good genes for being able to get by on little sleep; his mother is the same way.

When he is not at the clinic at the Virginia G. Piper Cancer Center in Scottsdale, he checks in with his lab, consults with doctors and nurses on patient cases and participates in conference calls about new cancer treatments and therapies. He also travels to medical conferences at which the latest cancer treatments are discussed.

His schedule is planned weeks in advance. But patients say he is never too busy to take their calls, even giving them his cell-phone number.

Despite his and other research and new drug therapies, pancreatic cancer remains a formidable challenge.

Only 20 percent of people with pancreatic cancer are alive one year after being diagnosed. Less than 4 percent are still living after five years, according to the American Cancer Society.

Pancreatic cancer is the fourth-leading cause of cancer deaths in both males and females, with only lung, prostate, colon and breast cancer killing more people.

Von Hoff is the first to admit that progress to extend survival has been too slow.

Last year, his research got a boost. TGen, in partnership with the University of Pennsylvania, received a three-year, \$18 million grant from a philanthropic group, Stand Up to Cancer, to develop tests to better understand the nutrients that allow pancreatic cells to grow and survive. The aim is to cut off the supply.

Von Hoff and his team also are conducting clinical trials that combine gemcitabine with another

anti-cancer drug called nab-paclitaxel. Earlier this year, they reported a one-year survivorship of 52 percent, double the rate for patients who took only gemcitabine. A larger clinical study is under way.

Von Hoff's goal is to find a cure for pancreatic cancer before he retires.

If that doesn't happen, he hopes to have advanced the research far enough to set the stage for other scientists to find a cure.

He is optimistic that all cancers can be wiped out within 25 years.

"The advances are coming fast and furious," he said. "I'm not sure I will live to see it, but I know for sure my kids will."

Reach the reporter at [anne.ryman@arizonarepublic.com](mailto:anne.ryman@arizonarepublic.com) or 602-444-8072.