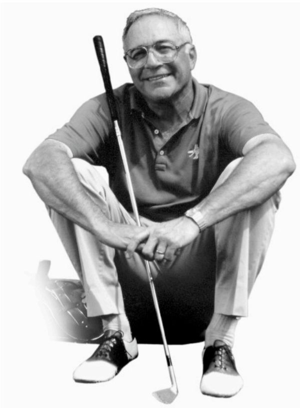


Jake Gittlen

CANCER RESEARCH FOUNDATION

Warren Gittlen celebrates thirty-nine years of giving. The 39th Annual Jake Gittlen Memorial Golf Tournament raised a record $830,000 in support of the Gittlen Cancer Research Foundation at Penn State Hershey Medical Center.

When my dad, Jake, died of cancer in 1970, I wanted to do something in his memory. Having been captain of Penn State's Golf Team and a tournament player, I started a golf tournament, The Jake Gittlen Memorial. I wanted to have the best golfers in Central PA come together each year and try to raise some money for cancer research.

The first year I raised $2,500 and gave it to a young scientist at Penn State's Hershey Medical Center, Dr. John Kreider. In the years to follow, Kreider would become one of the top cancer researchers in the world. We now formed the Jake Gittlen Cancer Research Foundation.

Our fund raising skyrocketed over the years with help from companies like ABC 27, Giant Foods, SYSCO Metro NY, AT&T, and many others. We have raised over $14 million since we began in 1970.

If you've contributed to our cause, those cancer survivors — and their families — have you to thank.

Warren Gittlen

Gary A. Clawson, M.D., Ph.D.

■ There are two major arms of research in the Clawson laboratory: basic science and applied science. The basic science effort seeks to better understand how and why cancer begins, i.e. how and why does a cell become cancerous and grow into a tumor. A "domino effect" of events in a cell is set in motion by factors that can cause cancer (such as certain chemicals, viruses, inherited diseases, UV rays, etc.). This is much like pushing a starting domino, causing a whole path of dominos to fall. The "dominos" here would lead a path to cancer.

The goals of the Clawson laboratory basic science initiative are:

- To understand any differences that occur in the first "domino" (there are many possible causes of cancer; they may push the same starting domino in a cell, or there may be many possible starting dominos that begin a path to cancer)
- To identify some of the first dominos to fall
- To determine the pathway along which the dominos fall

If these goals are achieved, it may be possible to develop strategies to prevent the dominos from falling, even after the starting domino is pushed.

The applied science arm is pursuing development of nanotechnology for early detection of cancers. Initial clinical trials are currently underway for early detection of melanoma.

Diane M. Thiboutot, M.D.

■ If I don't have acne, why should I care about acne research? To date, the most effective treatment for acne is a drug known as 13-*cis* retinoic acid (13cRA). The same drug is also used to treat certain types of cancer. Although the drug is very effective, the specific details of how it works are not yet known and, because of its potentially serious side effects, its use is regulated in the U.S. by the Federal government. Our research has shown that the one of the effects of the drug is to kill cells within the gland that is involved in acne, the sebaceous gland. During treatment, the size of the gland shrinks due to the death of the cells and the acne clears up. In cancer, tumors develop because mutated cells, which would normally be able to be destroyed by the body aren't killed and uncontrollably divide and form masses. Studies in the field of cancer research have shown that retinoic acids like 13-*cis* retinoic acid can kill these cells as well. Our goal is to determine how the drug works to destroy cells so that we can find an alternative drug that will still kill the cells but not have the potentially harmful side effects of the retinoic acids.

Neil D. Christensen, Ph.D.

■ The Christensen lab has a long-standing interest in the immune response to infectious agents (such as those caused by viruses and bacteria) and cancer. The role of the immune responses to these diseases is to clear the infection from the body and to prevent cancer growth. A better understanding of how the immune system works, and why it can fail, provides us with opportunities to improve general health and protect against the most dangerous of these foreign invaders. We currently work with a virus known as the human papillomavirus (HPV), which can cause cancers in humans. We use modern molecular biology research techniques to determine how the virus enters our body and how the virus causes disease. In addition, we use pre-clinical models to develop and test improved vaccines to help protect against virus infection, and to help eradicate existing infections after the virus has successfully invaded.

Keith C. Cheng, M.D., Ph.D.

■ Our instruction book of life, our DNA, sets down the basic rules of cooperation between our cells to create the miracle of bodies. Normal cells begin on the road to becoming cancer cells when their rule books start to accumulate too many mutations. Normal cells are able, by and large, to take care of their DNA. When they can no longer properly take care of their DNA as a result of mutations in "caretaker" genes, they have a greater chance of becoming cancer cells. My lab is using the power of zebrafish genetics to find those "caretaker" genes. The more we learn about them, the better we will be at designing ways to fight cancer.

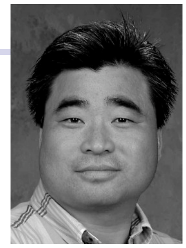
We know that UV light from the sun causes mutations in DNA. We also know that skin cancer is particularly common in people of European ancestry. This susceptibility is due to the relative lack of melanin pigment, which absorbs harmful UV light in people of darker complexion. One of the mysteries is why people of East Asian ancestry (Chinese, Japanese, Amerindians) are not nearly as susceptible to skin cancer despite their lighter skin. Somehow, East Asians must be able to better protect the DNA in their skin despite having relatively little melanin. We reason that if we can understand the mechanism of lightening skin in both Europeans and East Asians, we may be able to learn how to better protect European skin from the sun. In 2005, our lab discovered one of the key genes involved in lightening European skin (our ancestral color was dark). However, that gene is not involved in lightening East Asian skin. We are currently in on a quest to find the genetic key to the light skin of East Asians, which will simultaneously complete a circle of understanding of variations in human skin color.

Kristin A. Eckert, Ph.D.

■ The long-term goal of research in the Eckert laboratory is to understand one of the fundamental processes by which a normal human cell becomes a cancer cell. This process is known as mutation, and it results in changes to a cell's DNA sequence (also known as the genome). Mutations are critical events that occur naturally throughout a person's lifetime. The accumulation of many different mutations within a single cell eventually results in the creation of a cancer cell. Mutations serve as the fuel that powers the development of all types of cancers; therefore, it is of utmost importance to understand where, why and how they arise. Each cell in our body contains 6 billion building blocks of DNA, any one of which may be changed during the mutation process. One research project in our laboratory is to discover precisely where within the genome cancer-causing mutations can happen. We are focused on identifying those regions of our genome's DNA that are more susceptible to mutations.

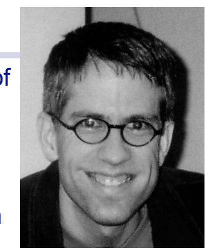
■ Because the precise sequence of everyone's genome is slightly different, each individual person will accumulate harmful mutations at a different rate. Cancer-causing mutations in cells can also be caused by exposure to chemicals in a person's diet or in the environment. Another project in our laboratory is focused on identifying how the chemicals present in tobacco smoke and chemotherapy drugs damage a cell's DNA and cause mutations. Finally, scientists in our laboratory are discovering how specialized proteins in a cell act to prevent mutations from arising in DNA. This research has helped to explain why some individuals, whose cells contain defective proteins, have an increased risk of developing cancer.

Jong K. Yun, Ph.D.



■ Our cancer research studies are dedicated to the development of a new class of novel drugs for the treatment of cancer. We have identified a protein, called Sphingosine Kinase 1, which has the unique ability to convert a cell death signal into a cell growth signal. We have evidence that this protein is highly expressed and more active in cancer cells than in healthy normal cells and might be responsible for the uncontrolled growth of cancer cells. We have indentified 4 "inhibitors", or agents that block the activity of Sphingosine Kinase 1. These inhibitors are the only known "drug-like" agents that block the activity of this protein. We are currently refining these inhibitors to make them more effective. Once we have finished optimizing these agents, we will begin clinical testing of their ability to treat human patients making the transition "from bench to bedside". With this new class of drugs, we can not only block the growth of cancer cells, but at the same time directly kill cancer cells. This ability to "kill two birds with one stone" makes Sphingosine Kinase 1 inhibitors an extremely powerful and very novel method of targeting cancer cells and should give doctors a revolutionary new tool in the fight against cancer.

Edward J. Gunther, M.D.



■ Breast cancer is so prevalent that nearly all of us have friends or family who have battled the disease. Strikingly, drugs essential for treating breast cancer, such as Tamoxifen and Herceptin, would not exist without basic research performed using laboratory rodents in the 1970's and 1980's. The Gittlen Foundation recognizes that basic laboratory investigation is an essential investment that holds the best chance of improving breast cancer care. As a practicing medical oncologist, I am privileged to participate in caring for breast cancer patients in the here and now. But in my role on the Gittlen team, I aim to improve treatments for our children's generation of breast cancer patients. Toward this goal, my laboratory seeks to unravel the basic biology of breast cancer using the power of mouse genetics.

■ Breast cancer is unusual in that it can recur years after surgical treatment renders a woman free of detectable disease. Presumably, microscopic disease persists in a dormant state during these long periods of disease remission. So-called "adjuvant therapy" - treatment administered after breast cancer surgery - is aimed at eradicating these undetectable dormant cancers. How breast cancers become dormant and how they ultimately "awaken" and give rise to disease relapse remains a mystery. Our laboratory has engineered breast cancer-prone mouse strains that are programmed to enter a state of tumor dormancy. Using further genetic modifications, we recently programmed mouse breast cancers to express bioluminescent molecules that literally make the tumor cells glow. These mice render dormant breast cancer cells visible for the first time, providing a new window into the biology of breast cancer in remission. We hope to use the insights provided by our mouse models to develop improved strategies for preventing breast cancer relapse.