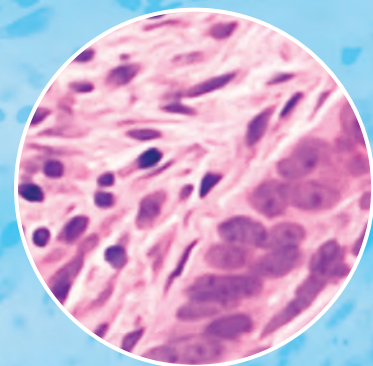


stopping the most common cancer

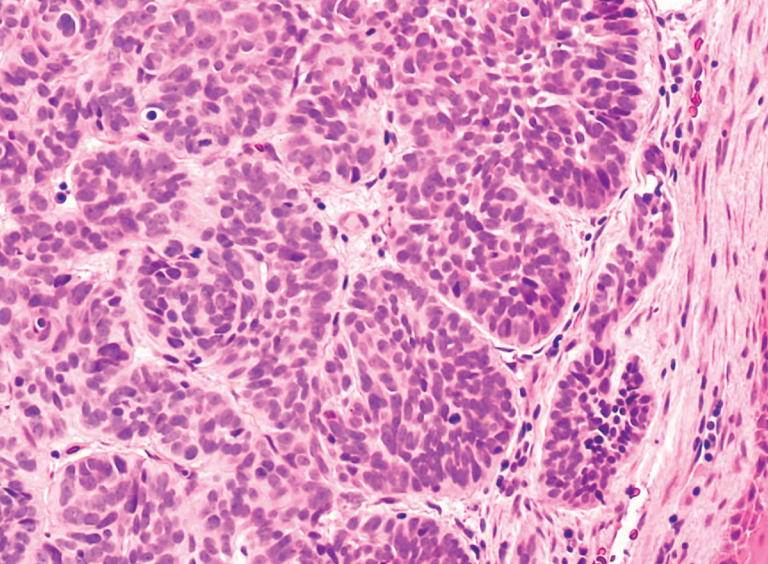




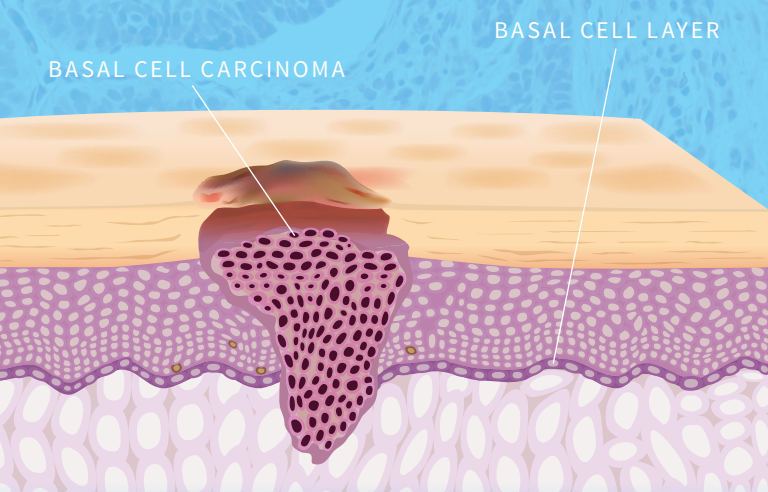
There are more than **5 million** new cases of skin cancer every year—that's more than twice as many as all other cancers combined

Skin cancer is everywhere. One in five Americans will develop it in his or her lifetime, and we all increase our risk every time we build castles in the sand, play tennis in the sun, or mow the lawn on a hot summer day. Basal cell carcinoma (*pictured at left and in the sky*), squamous cell carcinoma, and melanoma are the three most common types of skin cancer. Sun exposure is the primary cause. We can protect ourselves, but prevention isn't always enough. At Stanford, the world's leading scientists are on the case. And what we learn about skin cancer, which occurs right in front of our eyes, will help us fight other cancers that are more difficult to detect and treat. Stanford's Dermatology Department is working to make sure skin cancer—and all other cancers—have no place in our future.





BASAL CELL CARCINOMAS start in basal cells, which form the bottom layer of our skin. These cells constantly divide to replace cells lost to wear and tear. Basal cell carcinomas grow very slowly, and they can be very serious if they invade other tissues. More than four million cases are diagnosed in the United States each year, most caused by overexposure to the sun—and people with fair complexions are especially susceptible. Most basal cell carcinomas occur on the face, ears, lips, arms, and shoulders. Early diagnosis and intervention can prevent damage to areas around the cancer and decrease the risk of recurrence.



There's more to skin cancer than you think.

We can see it on the surface, but the lessons that we can learn from it run so much deeper. Accessible and usually curable, it offers insight into the inner workings of almost all cancers.

Skin cancer starts when a cell goes rogue. Like all cancers, it's a disorder of uncontrolled cellular growth. One cell decides it's going to grow however it wants and wherever it wants. That's why a tumor can go from one cell to a mass big enough to kill a person. Whether it's breast, prostate, or skin cancer, tumors start as single cells that multiply exponentially. One cell becomes two, then four, then sixteen—and before you know it, there are millions of them.

Ninety percent of all cancers start in the same kind of cell. Called epithelial cells, they cover us inside and out. They make up our skin and line all our organs—and they're ground zero for the majority of solid tumors. We used to think of cancer in terms of where it arises, but we've learned that cell type matters more than location. Two tumors can have many similarities even if one is in the colon and one is in the skin.

The principles that drive skin cancer are the same principles that drive other cancers. The difference is we have a much better view of what's going on with skin cancer. Dermatologists can study tumors directly, treat them,

and watch how they respond in a way that's not possible in other specialties. What we learn about skin cancer—which grows right in front of our eyes—will help us understand other cancers that grow out of sight.

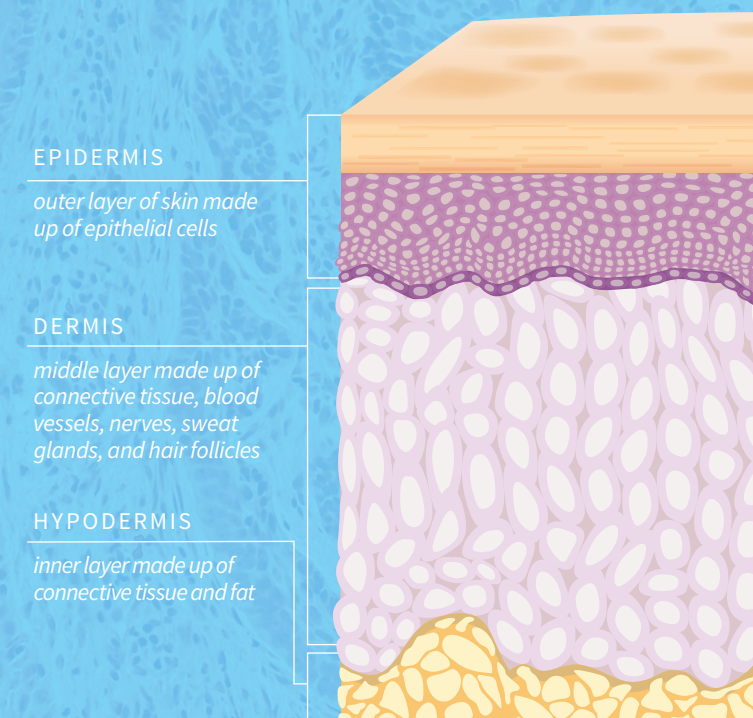
We're discovering how skin cancers—and all cancers—start and spread.

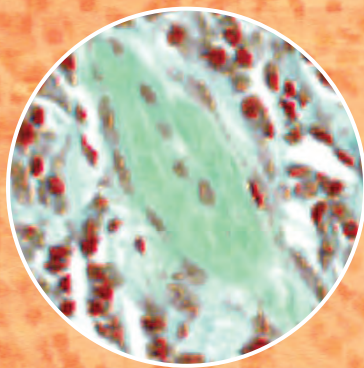
By collaborating with geneticists, molecular biologists, data scientists, and other experts, we're unraveling the fundamental mechanics of skin cancers. We're developing new therapeutic strategies based on our discoveries. And we're conducting clinical trials to see how well these strategies work in patients. Our dermatology researchers and clinicians are producing more new knowledge than any of our peer institutions. We publish more high-impact studies than the next top ten dermatology departments combined.

As part of an academic medical center, we tackle the problem from all sides. We have an integrated set of clinical programs to take care of our patients, a full spectrum of research programs to innovate for the future, and a comprehensive range of educational programs to train the next generation of leaders. That combination is critical. If our clinical programs stood alone, we couldn't develop new therapies. If our research stood alone, we wouldn't have the hands-on experience needed to guide our investigations. And if we don't train our young scientists and clinicians to be tomorrow's leaders, we'll never reach a future free of skin cancer.

We're working hard to make this bright future a reality. Leveraging the latest breakthroughs and technologies, we'll find new and better ways to stop skin cancer. And stopping the most common cancer may be the key to stopping *all* cancers.

WE ARE ALL COVERED IN EPITHELIAL CELLS, inside and out. The most prolific type of cell in the body, epithelial cells form our skin and line every internal organ. In our lungs, stomachs, and bladders, these cells are involved in everything we do. Unfortunately, they are also the starting point for 90 percent of all malignancies, including lung, breast, and colon cancers. To unlock the mysteries of these cells, we created Stanford's Epithelial Biology Program, which brings together more than 75 leading researchers with expertise in 26 subspecialties. These scientists are shedding light on the basic biology of these cells, how they give rise to cancer, and how we can intervene to keep them—and all of us—cancer-free.



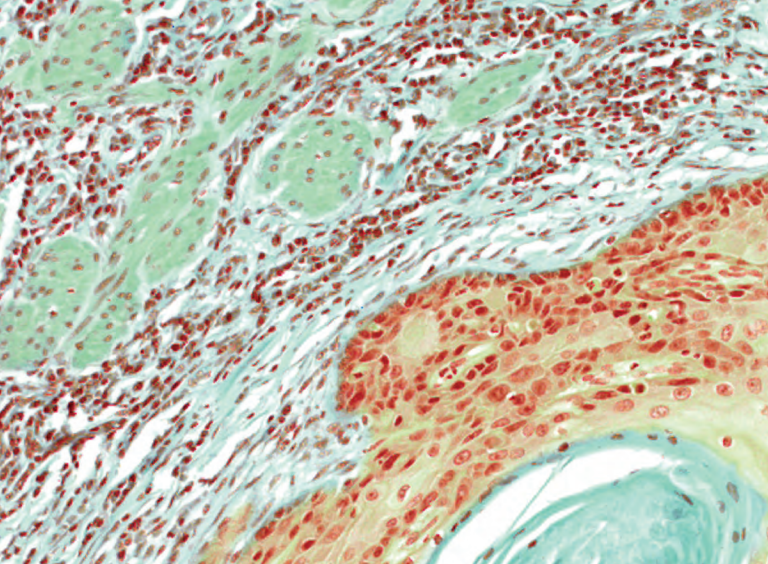


Since the 1970s, the incidence of squamous cell carcinoma of the skin has increased by more than

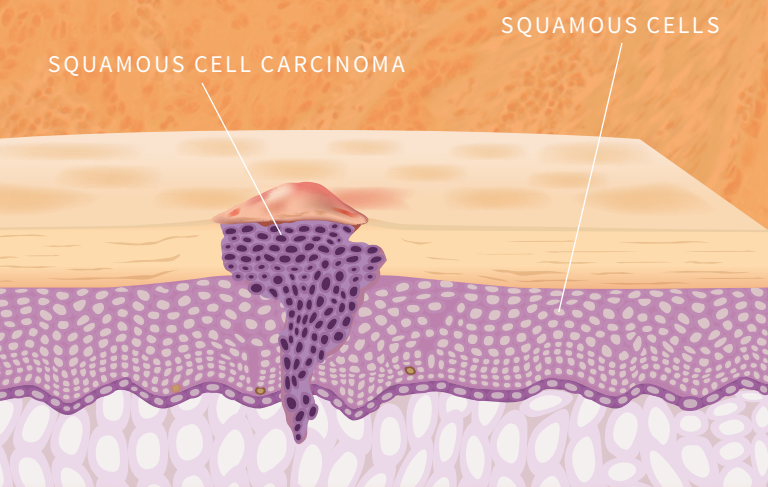
250%



Stanford Medicine gives us an unbeatable advantage. Our physician-scientists can leverage the outstanding resources of Stanford Health Care and the Stanford Cancer Institute. And hundreds of the world's best scientific minds are just a few steps away, including seven living Nobel laureates. Stanford is famous for the preeminence of our research, our unique atmosphere of multidisciplinary collaboration, and our entrepreneurial spirit. Stanford Medicine brings it all together in a new way of thinking about lifelong wellness called Precision Health. We precisely tailor treatment and prevention strategies to each patient's unique biology and circumstances to stop disease before it starts—or cure it decisively if it does.



SQUAMOUS CELL CARCINOMAS start in squamous cells, which make up most of the skin's upper layers. They're more genetically complex than basal cell carcinomas and can be more serious. Caused by sun exposure, as well as by skin damage from burns, ulcers, chronic infections, or other injuries, squamous cell carcinomas can occur anywhere basal cell carcinomas do. But they can also occur on less exposed areas. Each year, more than a million Americans are diagnosed with squamous cell carcinoma and it will kill as many as 8,800 of them. Its incidence has increased more than 250 percent over the past 30 years and it's the most common skin cancer among African Americans.



We were the first to create cancer in a lab.

When Stanford dermatologists converted healthy skin into basal cell carcinoma in 1997, it was the first time anyone anywhere created any kind of cancer from normal cells.

By turning human skin directly into cancer, we greatly expanded our capacity to study the disease. Now we can dictate the pace. By recreating a process that normally unfolds over a lifetime in just a few weeks, we can quickly create and study thousands of tumors without putting a single patient at risk. We can apply a therapy, see how the cells respond, analyze the data, and reiterate—again and again. This has transformed cancer research around the world.

We did it by activating the Hedgehog pathway. A cascade of biochemical signals, this pathway regulates cell growth and differentiation. It's critical for embryonic development and helps renew tissues and maintain organs in adults. Stanford scientists were the first to connect this pathway to basal cell carcinoma. When we recreated the process in the lab, we proved that triggering the Hedgehog pathway was enough in an experimental model to turn skin into cancer. Then we focused on what was causing the pathway to drive cancer, and what we could do to make it stop.

Our research resulted in the first drug that interrupts this pathway and our scientists led the clinical trials that resulted in FDA approval. While

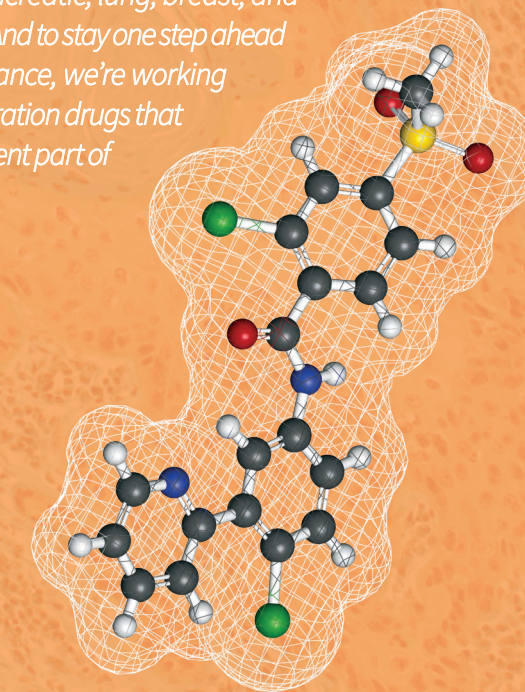
physicians in our clinics—and around the world—are treating patients with the first Hedgehog pathway inhibitor, we're developing the next generation of these drugs to hit different parts of the pathway.

We've radically increased the number of potential targets for new therapies. We've identified not just one or two, but thousands of new targets. And the more targets we have, the more chances we have to develop effective treatments. For example, one-third of all human cancers are driven by mutations in a family of genes called *RAS*. Add in all the receptors and proteins associated with it, and *RAS* may be responsible for 70 percent of all cancers. We identified a six-fold increase in the number of *RAS*-interacting proteins that could lead to new therapeutic targets.

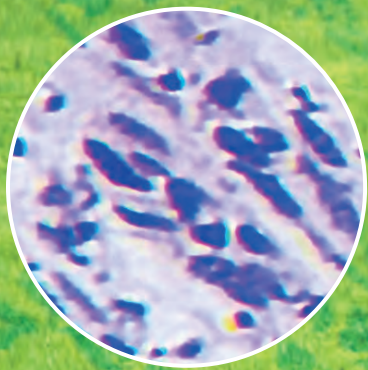
We're looking for other places to intervene. By sequencing the genomes of squamous cell carcinomas, we've started to understand what makes them spread regionally and metastasize, which is when this cancer really becomes lethal. And we've discovered that exposure to UV light can mutate a gene called *KNSTRN* and cause squamous cell carcinoma. With melanoma, we've discovered what parts of a tumor's genome turn on and off when it's responding to treatment—and what parts turn on and off when it becomes resistant. By figuring out how skin cancers start and spread at the genetic level, we hope to find new mechanisms to interrupt the process.

Our work enhances the way everyone studies cancer. Researchers around the world are building on our scientific breakthroughs and using tools we invented. For example, we developed new tools that are a million times faster, more sensitive, and more accurate than other technologies used to analyze the genomes of tumors.

THE HEDGEHOG PATHWAY is a cascade of biochemical signals that regulate cell growth and differentiation. Stanford researchers were among the first to understand its connection to basal cell carcinoma. By investigating every aspect of this pathway, our scientists developed vismodegib, the first Hedgehog pathway inhibitor, a pill that halts the signaling between cells and shrinks tumors. After we demonstrated its efficacy in clinical trials, the FDA approved it for patients whose basal cell carcinoma can't be treated with surgery. It's also being tested on other Hedgehog-dependent cancers, including pancreatic, lung, breast, and brain cancer. And to stay one step ahead of drug resistance, we're working on next-generation drugs that target a different part of the pathway.



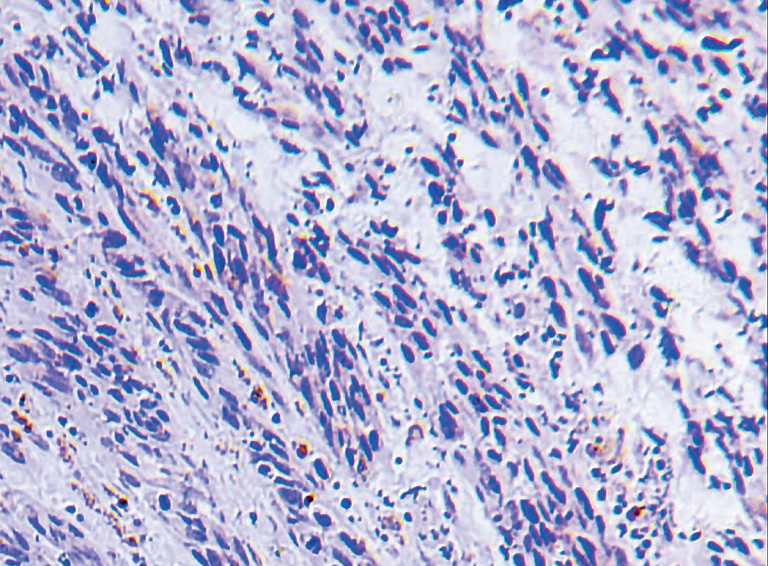
Molecular structure of the drug vismodegib, the first Hedgehog pathway inhibitor. Atoms are represented as spheres with conventional color coding: hydrogen (white), carbon (grey), oxygen (red), nitrogen (blue), sulfur (yellow), and chlorine (green).



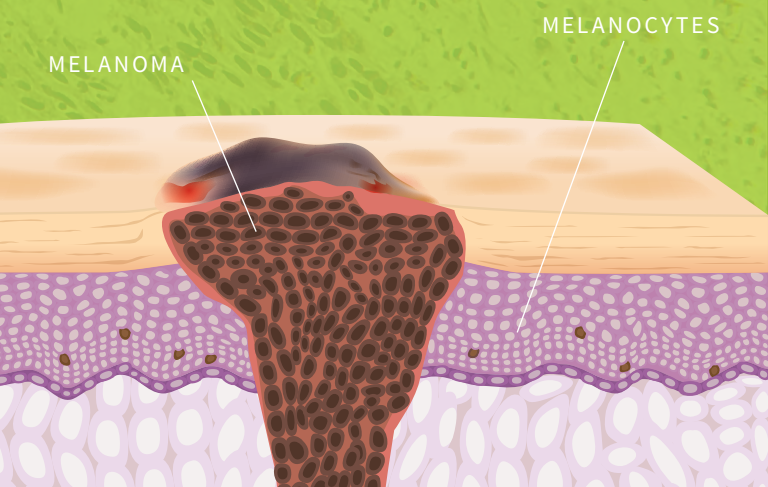
Melanoma kills **90%**
of its victims if it's not caught before
it spreads to other parts of the body



We're part of an NCI-designated Comprehensive Cancer Center, which means our scientific impact is felt by our patients every day. All of our skin cancer experts are members of the Stanford Cancer Institute, one of only 49 cancer centers to earn top designation from the National Cancer Institute for depth and breadth of research, ability to translate breakthroughs into new treatments, and seamlessly coordinated multi-disciplinary care.



MELANOMA is the deadliest skin cancer—and one of the deadliest of all cancers. It starts in melanocytes, cells that make the pigment melanin, which gives your skin its tan or brown color and acts as the body's natural sunscreen. Prone to metastasize (or spread) to other parts of the body, melanomas are caused by sunburns, particularly in those who are genetically predisposed. If recognized and treated early, melanoma is often curable. If not, it can spread to the liver, lungs, or brain and become much more difficult to treat. Melanomas account for less than one percent of skin cancers, but the vast majority of skin cancer deaths. About 90,000 new cases are diagnosed in the United States each year and every 54 minutes it claims another life.



Practice makes perfect. Because we treat so many patients, we see even the rarest skin cancers at all stages—over and over. If we didn't, we couldn't see the whole picture or be as precise in prescribing treatments.

The best time to stop skin cancer is before it starts, so we have a range of innovative prevention initiatives, including genetic testing by our Skin Cancer Genetics Program to determine hereditary risk, and SUNSPORT, a program that's educating student athletes, coaches, and spectators about risk and sunscreen use. We have a High-Risk Skin Cancer Clinic focused solely on patients who are especially susceptible, including those with genetic predispositions, histories of radiation therapy, or suppressed immune systems. We also conduct free skin cancer screenings throughout the Bay Area.

Early detection is critical, so we help patients stay ahead of the problem. Our NIH-sponsored Pigmented Lesion and Melanoma Program offers the most advanced preventive strategies and treatments for patients with precursor lesions and all stages of this aggressive and deadly cancer. And we were among the first institutions to use positron emission tomography (PET) for detection of metastatic disease in melanoma patients. Now we routinely use it combined with *computed tomography* (CT) scans to identify cancer cells throughout the body that might otherwise go undetected.

Successful treatment requires precision, so our Mohs and Dermatologic Surgery Center offers patients extremely precise surgical removal of skin cancers to conserve healthy tissue and performs reconstruction to minimize scarring. Our Advanced Basal Cell Carcinoma Clinic offers precise multimodal treatment of skin cancers that can be difficult to treat by surgery alone. And our Skin Cancer Genetics Program leverages Stanford's expertise in genomics and computer science to identify the best treatment options based on the unique genetic makeup of each individual—and his or her tumor.


Standing with every patient over the long haul, our Cancer Survivorship Program helps people transition from cancer diagnosis, through treatment, to wellness. With personalized care, we help them deal with long-term issues like reproductive health and fertility, body composition, bone health, sleep disorders, anxiety, and depression. We also monitor for metabolic changes that can signal cancer recurrence or the development of other conditions associated with cancer, like diabetes and heart disease. And our Supportive Dermato-Oncology Program is one of only a few in the nation dedicated to managing chemotherapy-related skin reactions, radiation dermatitis, and other side effects from therapies that are used to fight many kinds of cancer.

We also have a robust clinical trials program. At any given time, we have more than 35 open trials to test the latest therapies. Essential to translating the breakthroughs made here and elsewhere into safe and effective interventions, these studies are at the heart of our research and clinical efforts to stop not just skin cancers, but all cancers.

MOHS MICROGRAPHIC SURGERY is a precise surgical technique in which cancerous cells are removed one layer at a time. We mark each layer with special stains and examine it under a microscope to see if we've cleared all the afflicted cells. If we haven't, we continue the process until we're certain that every cancer cell has been removed and only cancer-free tissue remains to minimize the chance of recurrence. At the Stanford Mohs and Dermatologic Surgery Clinic, we use this technique to remove basal and squamous cell carcinomas. For patients with potentially deadly melanomas, we use special antibodies in an advanced version of Mohs. Once we've made sure there's no cancer left, we can use simple to advanced reconstructive techniques to make it look like it was never there.

Sumaira Z. Aasi, MD, professor of dermatology and director of Mohs and dermatologic surgery, saving the world one cancer cell at a time.



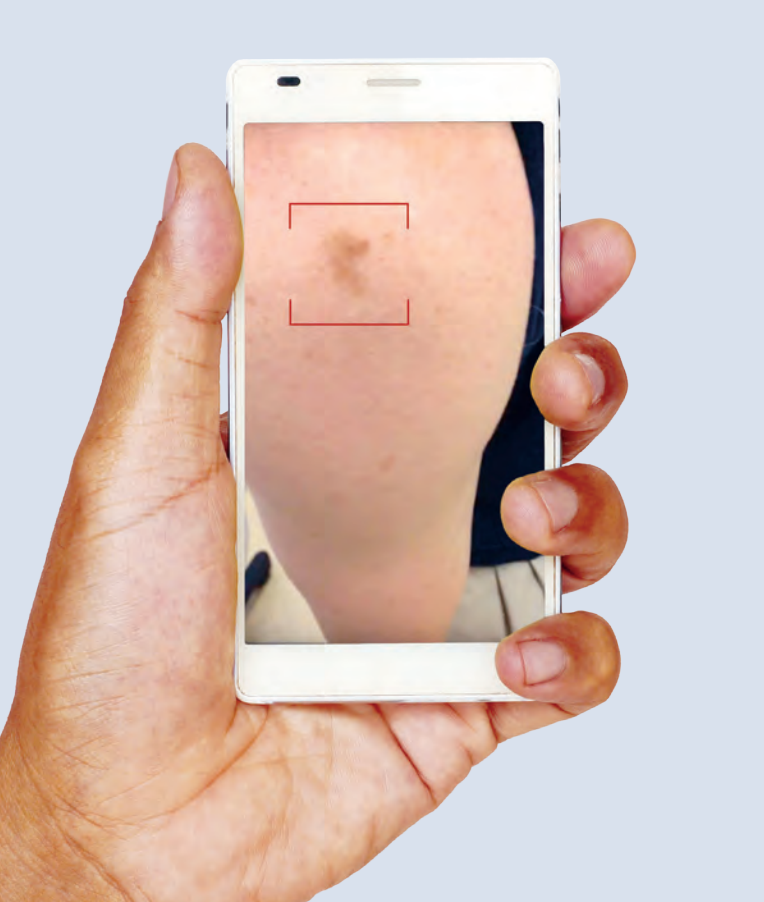
An aerial photograph of three skiers descending a vast, snow-covered mountain slope. The skiers are positioned diagonally across the frame, from the upper left towards the lower right. The skier in the foreground is wearing a red jacket and black pants, leaving a trail of white snow behind them. The middle skier is wearing a yellow jacket and black pants, and the third skier, further back, is wearing a blue jacket. The sun is low in the sky, casting long, dark shadows of the skiers onto the snow. The overall scene is bright and crisp, with a cool color palette dominated by whites and blues.

The annual cost of treating skin cancers in the U.S. is estimated at

\$8.1 billion

Now is the most exciting time to be working to end skin cancer.

Over the past two decades, biomedical knowledge has grown exponentially. We're making new discoveries and developing new tools that will allow us not only to heal disease, but to predict and prevent it. Here at Stanford Dermatology, we have a culture of innovation, a history of success, and a unique ecosystem where multiple generations of physician-scientists challenge and inspire one another to set—and achieve—higher and higher goals.



WHAT IF YOUR SMARTPHONE COULD DETECT SKIN CANCER? Stanford scientists have made an app for that. In collaboration with the Stanford Artificial Intelligence Laboratory, we created a deep learning algorithm that accurately diagnoses skin cancer from a smartphone. A major breakthrough in machine-assisted medicine, this technology may extend high-quality, low-cost diagnostic capabilities to the furthest reaches of the globe. We tested the app against 25 nationally recognized and well-respected dermatologists. It performed as well as—or better than—all but one. Because early detection is so important for surviving skin cancers, this app will help doctors everywhere make life-saving decisions by determining if that funny little spot is freckle or foe.

A future without skin cancer. Every day in our clinics, we teach patients how to reduce their risk. And every day in our labs, we search for better, more reliable ways to make sure their risk never becomes reality.

Prevention has to be a team effort. We're training the next generation of skin cancer researchers and clinicians while educating the public. Because athletic fields are often drenched in cancer-causing UV rays, we're enlisting athletes, coaches, and fans in the fight to end skin cancer. With our SUNSPORT program, we're teaching people of all ages how to identify their risk and protect themselves. This university-wide program can be reproduced in any community and scaled for any population. We've also developed technology (see *left*) to put the power of artificial intelligence in every physician's pocket to help them diagnose skin cancers with extraordinary accuracy.

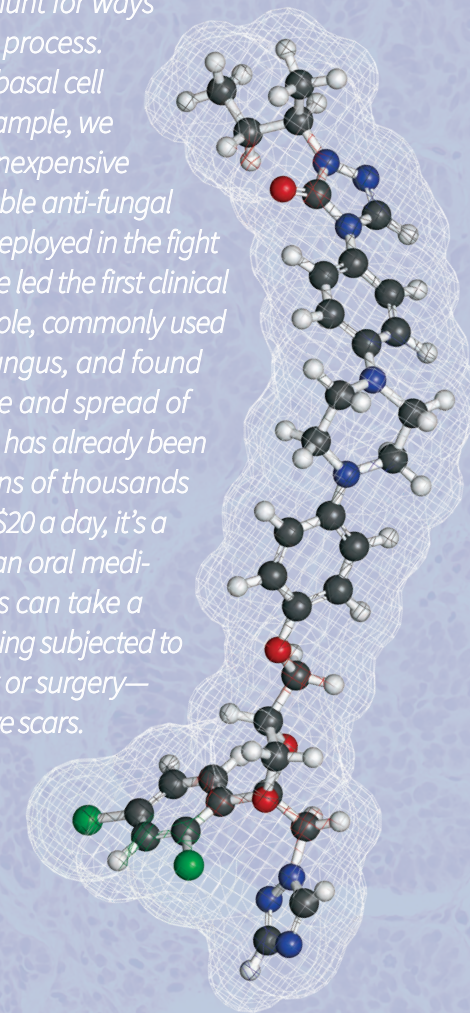
We're making prevention easier for everyone. Stanford scientists were the first to reveal that calcium, Vitamin D, a low-fat diet, and even aspirin can play important roles in preventing melanoma. Our researchers also tested a common anti-fungal drug and found it reduced the size and spread of basal cell carcinoma tumors. We're currently evaluating a topical gel version of the drug (see *right*) for its effectiveness.

We're applying personalized genomics to improve prediction, prevention, and treatment. Our scientists use the most advanced gene sequencing technologies to investigate the genetic aspects of skin cancer risk, progression, and response to therapy. By analyzing vast data sets, we can identify genetic alterations associated with susceptibility to skin cancer. And we utilize genomic data from the tumors themselves to predict which new therapies will be most effective in each patient.

We're providing the most precise treatments possible, individually tailored to each patient. Our scientists created tools that allow us to investigate how genes are switched on and off at the level of a single cell. We can see what's happening on a genetic level when a tumor is responding to treatment and when it becomes resistant. If we know how tumors escape therapy and come back to hurt the patient, we can take steps to make treatments effective for longer periods of time.

Our research on skin aging may stop the clock on skin cancer. Global demographics are shifting toward an older population. And as all of us age, our risk of developing skin cancer naturally increases. The benefits of slowing the aging process are not merely cosmetic. If we can slow the aging process, we can slow—or even eliminate—the risk of skin cancer. Stanford researchers are uncovering the genetic and epigenetic mechanisms that cause skin to age so we can find new ways to make sure that an aging population can also be a cancer-free population.

CURING CANCER ISN'T CHEAP and developing new drugs always takes too long. To cut costs and timelines, our researchers hunt for ways to accelerate the process. For patients with basal cell carcinoma, for example, we realized that an inexpensive and widely available anti-fungal drug could be redeployed in the fight against cancer. We led the first clinical trials on itraconazole, commonly used to treat toenail fungus, and found it reduced the size and spread of tumors. This drug has already been given safely to tens of thousands of people, and at \$20 a day, it's a bargain. Plus it's an oral medication so patients can take a pill rather than being subjected to radiation therapy or surgery—both of which leave scars.



Itraconazole antifungal drug (triazole class), chemical structure. Atoms are represented as spheres with conventional color coding: hydrogen (white), carbon (grey), oxygen (red), nitrogen (blue), sulfur (yellow), and chlorine (green).



A future free of skin cancers—and all cancers—is within sight.

At Stanford Dermatology, we're unraveling cancer's mysteries. We're translating our discoveries into safe and effective treatments. And we're helping thousands of patients every year. We're passionate about our work and committed to alleviating human suffering—in today's patients, and tomorrow's.

Our team has accomplished so much. Yet we can do so much more.

If we invest enough energy, effort, time, and resources, we will create this bright future. We have a community of brilliant physician-scientists eager to spend the energy, effort, and time. But the resources are not guaranteed. Federal funding for research, in real dollars, has been going down for more than a decade. And costs keep rising.

There's never been a time when we've needed philanthropic support more. And there's never been a time when the opportunity to make progress is greater

We have incredible momentum. We're producing new knowledge at an unparalleled pace. We're sharing it with our colleagues around the world. And we're training the next generation to lead.

With help from visionary partners like you, we'll accelerate our progress, recruit and retain the most talented researchers, acquire cutting-edge equipment and technologies, and pursue the kinds of high-risk, high-reward research that will make sure skin cancer has no place in our future. **Please join us.**

A handwritten signature in black ink, appearing to read 'Paul A. Khavari'.

Paul A. Khavari, MD, PhD

Carl J. Herzog Professor and Chair
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