

Cutaneous and T-cell Lymphoma: Research and Treatment

We've learned more about cancer in the past two decades than at any other point in the history of medicine, thanks to advances in fields such as genomics, immunology, and data science. That understanding has led to outcomes that were unthinkable just a few years ago. Many patients with advanced disease once considered to be universally fatal—are in remission thanks to new treatments—and the pace of discovery is accelerating toward more precise, curative therapies.

Stanford's Multidisciplinary Cutaneous and T-Cell Lymphoma Program (MCTLP) has played a critical role in this monumental shift. Under the direction of Youn H. Kim, MD, the Joanne and Peter Haas, Jr., Professor of Cutaneous Lymphoma Research, and professor (by courtesy) of medical oncology, the program has become an international leader in rare skin lymphomas. Today our team sits on the precipice of understanding the genetic and immunologic underpinnings of this disease—the keys to developing targeted therapies that provide long-suffering patients lasting relief.

Thanks to a foundational gift from Ginnie and Pete Haas to support the MCTLP's core research operations, every additional gift we receive goes directly to developing a cure—a moonshot to create a novel immunotherapy for cutaneous lymphoma that would serve as a model of the power of personalized medicine for other cancers.

Over the next five years, we have set a goal to raise five million dollars to accelerate this groundbreaking immunotherapy research. We invite you to help us achieve this vision—to give patients with this rare cancer a fighting chance.

WORLD-LEADING PRECISION MEDICINE FOR RARE CANCERS

The human body contains as many as 40 trillion cells divided into 200 different cell types that work together with extraordinary precision. Each cell performs a specific function as new cells replace old ones at regular intervals. When even a small group of cells goes awry, the results can be disastrous.

In cutaneous T-cell lymphoma (CTCL), abnormal cells migrate to the skin and then multiply and accumulate excessively. In a healthy body, these cells, called T-lymphocytes, travel throughout the bloodstream to fight infections and disease. In patients with CTCL, the result is itchy, scaly red eruptions and tumors that can cover the whole body and spread. Symptoms look like an allergic reaction or simple rash.

Because cutaneous lymphoma is so rare—approximately ten cases per one million people—most doctors have never encountered it, leaving many patients to suffer for years before receiving a correct diagnosis.

The most common type, called mycosis fungoides (MF), is not life threatening in its early stages. But in more advanced stages, patients with tumors and other organ involvement have shortened life expectancy. Sézary syndrome is a more aggressive, leukemic form of CTCL with increased risks for infections and death. Both are chronic conditions, and although there are treatments with notable symptom relief, they do not result in durable benefit or curative outcomes.

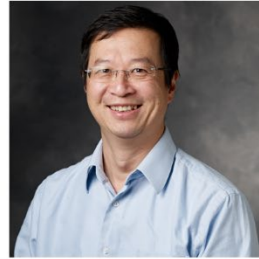
Youn Kim first encountered the cancer as a dermatology resident at Stanford working with her mentor Richard Hoppe, MD, the Henry S. Kaplan-Harry Lebeson Professor of Cancer Biology, and co-founder of the MCTLP. Frustrated by the difficulty in diagnosing cutaneous T-cell lymphoma and the lack of effective treatments, Kim dedicated her career to finding solutions for her patients. Today, the MCTLP has advanced the standard of care—pioneering breakthrough therapies and providing hope and relief for patients worldwide.



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An interdisciplinary team that brings together dermatologists, medical oncologists, radiation oncologists, and experts in blood stem cell transplantation, the program has collaborated with cutting-edge investigators in dermatology to identify key genetic alterations in patients' diverse manifestations of the disease. By gaining a clearer picture of the genetic and immunologic factors, the team is better able to develop targeted treatments that kill the cancer cells but spare the healthy cells.

“We can now design drug trials in a smart, evidence-based way that is specific to the patient,” says Kim. “Before we had this data, it was trial and error—we were totally flying blind.”

COLLABORATING ACROSS THE GLOBE

Deciphering the cause of any disease is exponentially more difficult when that disease is rare and diverse in expression. Even doctors who focus on CTCL don't see enough cases to build a robust tissue bank or database. To solve this issue, Kim organized an international coalition of experts, the Cutaneous Lymphoma International Consortium (CLIC), headquartered at Stanford. The consortium includes more than 81 academic institutions committed to producing a large-scale clinical and pathology database linked with many patients' tissue and blood samples, establishing the mechanism to share data and material cohesively across five continents. This innovative mobile app and data center is linking the world toward a cure for CTCL.

Collaborations like this are essential to making progress against orphan diseases like cutaneous lymphoma. To further refine diagnosis and treatment, Kim has been instrumental in revising the cutaneous lymphoma classification staging system, which guides clinical trial design and patient management worldwide.



CLINICAL RESEARCH

Clinical trials are often the only hope for patients who have exhausted other avenues of treatment. Such trials help ensure that new drugs, new uses for existing drugs, new surgical approaches, new radiotherapy alternatives, new vaccines, and new medical devices are safe and effective.

“Dr. Kim has been at the forefront of bringing new therapies to patients and she’s run a clinical trial on almost every single new agent that can be used in caring for this cancer,” said Paul Khavari, MD, PhD, the Carl J. Herzog Professorship in Dermatology, and chair of the Department of Dermatology.

Radiation therapy remains the most effective weapon in the arsenal against cutaneous lymphoma. Stanford developed the original total skin electron beam therapy (TSEBT), where radiation generated by electrons can be delivered to optimize treatment of the entire skin surface. An innovative approach led by Hoppe uses a significantly lower dose of radiation, allowing patients to receive therapy multiple times with fewer side effects and with dramatic clearing of disease. The low-dose TSEBT approach can be combined with immune therapies to prolong the duration of response in patients.

BREAKTHROUGHS IN IMMUNE THERAPIES

Stanford is a recognized leader in immunology, with major contributions in the development of technologies to examine human immune function, and in the development of new therapies that boost patients’ own immune systems to attack cancer cells directly. Researchers here made seminal contributions in the early years of cancer immunotherapy, particularly in the field of lymphoma. Today, cellular immunotherapy is a new frontier that holds great promise to enhance our arsenal against cancer.

Groundbreaking research, led by MCTLP member Michael Khodadoust, MD, PhD, assistant professor of medicine (oncology) and of dermatology, includes immune checkpoint inhibitors, where antibody therapy releases the brakes in the immune system, enabling dormant immune cells to be unleashed and eliminate cancerous cells. Other immune approaches in development are vaccine-type therapies to fight against patient-specific abnormal T-cell receptors.

Another member of the cutaneous lymphoma program, Wen-Kai Weng, MD, PhD, associate professor of medicine (blood and marrow transplantation and cellular therapy), led the development of a novel blood stem cell transplant regimen, replacing CTCL patients’ defective immune cells with healthy cells from a compatible donor. By creating an original regimen, the team has reduced the risks of difficult, sometimes fatal side effects such as graft-versus-host disease, and preserved cells’ ability to attack cancer. Weng also helped develop a tool capable of detecting a single cancer cell among a million cells—a nearly 1,000-fold increase in sensitivity compared to older technologies—which allows doctors to detect, track, and respond to recurrences with greater speed and precision.

NOVEL INVESTIGATOR-INITIATED TRIALS

Developing promising new therapeutics for patients requires a robust investigator-initiated trials program. Phase 0 and phase 1 trials are based on novel concepts that come from Stanford laboratories but are not funded by industry. Once these early discovery trials show promising data, they may ultimately be sponsored by industry. In the interim, researchers need access to highly specialized technical expertise in drug development and assistance with outsourcing, data management, and analytics to move their best ideas forward.



By conducting early-phase clinical trials at Stanford, researchers can provide powerful proof-of-concept evidence for the viability of novel therapies—and further mitigate the risks involved with advancing them to late-phase trials, which can take several years and involve hundreds or thousands of patients.

In cutaneous lymphoma, a novel immunotherapy vaccine that can ignite the T-cell receptor (TCR) has shown promising results in mouse models and is now ready for a human clinical trial. Our goal is to develop a personalized TCR vaccine to treat patients with mycosis fungoides.

Researchers have designed a phase 0 trial to test the vaccine at a low dose in 15 to 20 patients, which will be followed by a larger phase I trial to test for vaccine efficacy. This will be the first Stanford immune therapy innovation in T-cell lymphoma. Physicians will be able to combine the new vaccine with Stanford's radiation therapy approaches and/or novel small molecules to optimize patients' long-term outcomes.

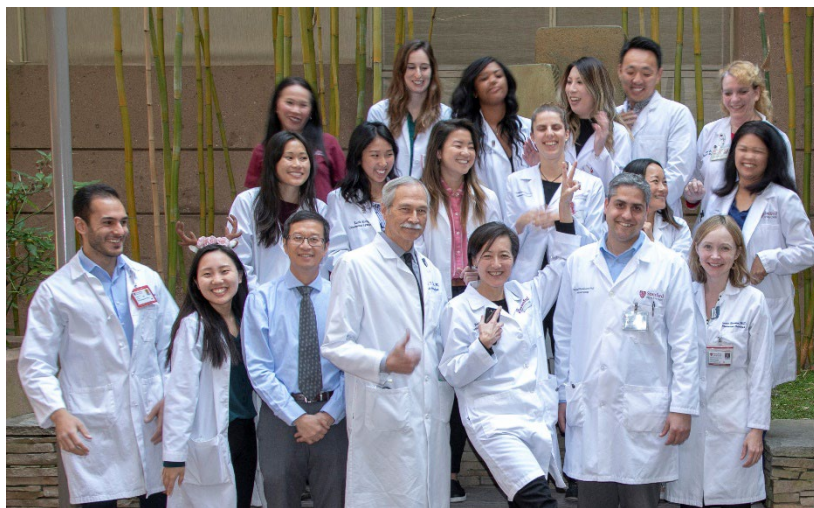
Research plans are often refined during these investigator-initiated trials, as they learn more with correlative clinical samples acquired from patients while on treatment. Without critical philanthropic support at this early stage, research can languish, be left unexplored, or be compromised due to pharmaceutical industry involvement.

JOIN US

Thank you for your interest in helping advance the field of cutaneous lymphoma. With increased knowledge about the genetics and biology of CTCL, coupled with sustained funding for investigator-initiated trials, the Stanford MCTLP team will be able to pursue the most promising areas of research to improve the lives of patients affected by this rare disease.

Your support is vital to this effort. There has never been a more exciting time to make progress in biomedical research, but never has it been more costly to do so. Pharmaceutical companies, beholden to shareholders, do not typically invest in developing highly personalized therapies. Thanks to a foundational gift from the Haas family, every dollar you give will go directly to support groundbreaking immunotherapy research toward a cure.

We welcome your partnership as we seize this unique moment in medicine and the power of T-cell vaccine technology to expand our research, encourage collaborations, and develop new therapeutics to provide lasting solutions for patients everywhere.



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