NIH NATIONAL CANCER INSTITUTE

CENTER FOR CANCER RESEARCH

MILESTONES

Cancer Research with a Purpose

HIGHLIGHTS 2023–2024

U.S. Department of Health & Human Services | National Institutes of Health

CENTER FOR CANCER RESEARCH

The Nation's Cancer Center

The Center for Cancer Research (CCR) is the largest division of the National Cancer Institute's intramural research program with nearly 250 basic and clinical research groups located on two campuses just outside of Washington, D.C.

The CCR is home to an extraordinary group of scientists and clinicians exploring the cutting edge of cancer and HIV/AIDS research. Our scientists work on a wide spectrum of biological and biomedical problems that range from understanding genes, proteins and cellular pathways to using artificial intelligence and machine learning to explore large cancer datasets, developing novel methods for drug discovery, inventing biomedical devices and technology and creating innovative ways to treat patients.

Our scientists enjoy complete intellectual freedom and are expected to creatively and innovatively explore the most important questions in the field of cancer research and treatment. We support projects over a long time horizon, allowing our investigators to pursue some of the most difficult, high-risk problems in the field, and we are always on the lookout for new challenges and the most pressing problems in modern cancer research.

The success of CCR is grounded in an exceptionally strong discovery research program that provides the foundation for the seamless translation of insights into basic cellular and molecular processes to clinical applications and patient care. Examples of our success are the development of groundbreaking immunotherapy approaches, HIV/AIDS testing and the creation of a human papillomavirus vaccine.

The CCR is a unique place of science where we combine diverse expertise with the freedom to thoroughly pursue the most pressing questions in cancer biology and treatment.

For more about our science, our training programs and our clinical trials, visit **ccr.cancer.gov**.

Inside the NIH Clinical Center, all types of activities take place. The building is filled with everything from operating rooms and patient beds to laboratories buzzing with activity as represented on this year's cover. The work we do at CCR — where findings from a lab inform patient studies and treatments, and the results of patient studies inform the next batch of laboratory investigations — is the epitome of bench-to-bedside and back. Like the puzzle pieces seen here, they all connect to create the cancer medicines of tomorrow.

Credit: SPGM, FNL, NCI, NIH

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The **MISSION** of CCR is to improve the lives of all cancer patients by solving important, challenging and neglected problems in cancer research and patient care through:

- A world-leading basic, translational and clinical research and patient care program
- An institutional focus on high-risk and long-term projects, unmet needs and pursuit of unexplored ideas
- Research to eliminate cancer health disparities
- Leadership and coordination of national disease networks and development of technology resources for the cancer community
- Partnerships with academic institutions, commercial entities and patient advocacy groups
- Training of the next generation of a diverse and inclusive biomedical workforce

Contents

Director's Note

Cancer research comes in different flavors. To some it is the search to understand the fundamental molecular and cellular processes that go awry in cancer cells or to shed light on what causes and promotes cancer. To others it is to discover new ways to prevent and diagnose cancer or to develop novel cancer treatments.

No matter how cancer research is defined, all new cancer treatments are the result of putting individual puzzle pieces together, and they emerge from the synergy created by the seamless integration of basic discovery and clinical research. Without basic immunology, there is no immunotherapy; without a molecular understanding of DNA, there is no CRISPR technology; without programs to map gene expression, there is no precision medicine. At CCR, we pursue and collaborate across all facets of cancer research, and this issue of *Milestones* highlights the full spectrum of our activities.

In the past year, CCR scientists have overturned dogmas in our understanding of how cells proliferate, exposed how proteins end up in the correct location in the cell and harnessed bacterial proteins to deliver drugs. Work done in CCR has also uncovered a role of rare immune cells in liver cancer and identified metabolites that may lower the risk of developing it in the first place.

We have also found ways to learn about human cancer from pet dogs, and we have characterized new biomarkers that predict the response of ovarian cancer patients to treatment. Finally, delivering on our ultimate goal of bringing new therapies to patients, CCR scientists have developed new treatments for several cancer types, some leading to FDA approvals.

Success in cancer research requires the contributions of many with diverse skills and perspectives. Regardless of the flavor, cancer research is always about discovering better ways to care for all our patients. This is what we do in CCR.

Tom Misteli
Director
NCI Center for Cancer Research

TWO STRIKES AGAINST MESOTHELIOMA

Major prognostic and treatment advances are made against a rare and deadly disease.

Raffit Hassan, M.D.
Chief
Thoracic and GI
Malignancies Branch

Mesothelioma, an aggressive tumor that affects the lining of the lungs or abdomen, belongs to the unfortunate list of cancers that are aggressive, difficult to treat and have poor outcomes. But a combination of lab and clinical work in CCR now holds promise for a cancer that has been intractable for many years.

"The standard therapy for patients with mesothelioma is immunotherapy and chemotherapy," says **Raffit Hassan, M.D.**, who has been studying mesothelioma at CCR for decades. "But the median overall survival has been less than two years." Recently, however, his team uncovered genetic signatures that hint at a patient's prognosis and potential treatments, while results from a clinical study showed that a novel adoptive T-cell therapy can lead to tumor regression in some patients with treatment-resistant mesothelioma.

In one study, published in *Cell Reports Medicine*, Hassan and his colleagues analyzed blood and tumor samples of 122 mesothelioma patients and identified a group of 48 genes in which high expression was associated with worse survival. Higher expression of one gene in particular, *CCNB1*, which is involved in the growth of cells, was associated with significantly lower survival.

Then, in collaboration with Senior Investigator **Eytan Ruppin, M.D., Ph.D.**, they used a computational tool Ruppin's lab had developed, called SELECT, which analyzes the unique genetic makeup of a person's cancer to predict which existing drugs could potentially be an effective treatment for that individual. Using the tool, the researchers were able to predict with high accuracy which patients would have a partial or complete response to seven different immunotherapy and chemotherapy drugs.

In a second study, Hassan and his colleagues reported results from a phase 1 clinical trial exploring the safety and efficacy of a novel cell therapy called gavocabtagene autoleucel (gavo-cel), developed by the immuno-oncology company TCR^2 Therapeutics, now combined with Adaptimmune. The approach involves taking a patient's T cells, a type of immune cell, and modifying them so that they recognize the mesothelin protein, which is highly expressed on mesothelioma. With their ability to target the cancer boosted, the modified T cells are then infused back to the patient.

As reported in *Nature Medicine*, the study included 32 patients with either mesothelioma or advanced mesothelin-expressing ovarian cancer or cholangiocarcinoma, a cancer of the bile ducts. Twenty percent of patients who received gavo-cel experienced tumor shrinkage, and 13 percent had durable tumor regression.

"It was very exciting to see tumor shrinkage in some patients," says Hassan, recalling one patient with mesothelioma who had already been treated with four previous therapies. "Just before this study she was thinking of going to hospice, but she had a pretty dramatic response to treatment with gavo-cel — almost a complete response that was maintained for about one year."

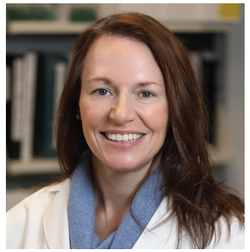
Hassan notes that, while not all patients responded to the therapy and some had serious side effects, this study shows proof of principle that it is possible to target solid tumors using adoptive T-cell therapy. He and his colleagues will continue investigating novel T-cell therapies with the hope that even more patients will respond as these therapies evolve.

Nair, N.U., et al. *Cell Rep Med*. 2023 Feb 21;4(2):100938.
Hassan, R., et al. *Nat Med*. 2023 Aug;29(8):2099-2109.

In one study, CCR researchers identified gene signatures that are associated with mesothelioma prognosis and can help determine a patient's response to therapy. In a second study, CCR researchers showed that it was possible to treat mesothelioma with adoptive T-cell therapy. These two strikes against mesothelioma, one from basic research, one from a clinical trial, will help fight this rare cancer. Credit: iStock

LEARNING FROM OUR PETS

Studying osteosarcoma in dogs may improve treatment options for people and pets.



Amy K. LeBlanc, D.V.M.
Senior Scientist
Molecular Imaging Branch

Studying osteosarcoma, an aggressive bone cancer that most commonly occurs in teenagers and young adults, is very difficult because it is diagnosed in fewer than 1,000 people in the United States each year. For that reason, scientists in CCR's Comparative Oncology Program (COP) are taking advantage of remarkable similarities between osteosarcoma in humans and dogs to improve treatment options for both people and pets.

In dogs, osteosarcoma is far more prevalent than it is in humans: U.S. veterinarians diagnose more than 10,000 cases of canine osteosarcoma annually. Senior Scientist and COP Director **Amy LeBlanc, D.V.M.**, says studying osteosarcomas in pets helps researchers learn how the disease behaves when it arises naturally, complementing studies in laboratory models. "Studying dogs with cancer provides another piece of a really complex puzzle and helps give us insight into how cancers form and respond to therapy," she says.

Twenty academic veterinary centers in the United States and Canada participate in the NCI's Comparative Oncology Trials Consortium, which runs clinical trials to assess novel cancer therapies in pet dogs. As they investigate experimental osteosarcoma treatments in their canine patients, their insights are informing the design of human clinical trials. One recent study, reported by LeBlanc and her team in *Communications Biology*, offers the most detailed description yet of clinical and molecular similarities between the human and dog form of the disease — and points toward potential treatment strategies for both.

LeBlanc and her colleagues examined how osteosarcoma's molecular makeup influences its behavior by analyzing tumor samples from nearly 200 dogs. Some of the dogs had better clinical outcomes than others, surviving longer after their osteosarcoma diagnosis or remaining disease-free longer following treatment. LeBlanc's team, led by postdoctoral fellow Joshua Mannheimer, Ph.D., found that these outcomes were related to patterns of activity of particular genes in the tumors. Remarkably, the same molecular signatures also correlated with clinical prognosis in human patients with osteosarcoma.

LeBlanc says the composition of those prognostic gene signatures provides clues about the biological factors that influence osteosarcoma outcomes. Many of the genes that comprise the signatures help shape tumor cells' interactions with the immune system, suggesting more anti-tumor activity occurred in the osteosarcoma patients that fared better. "That speaks to one of the big pictures that we're learning about cancer," LeBlanc says. "The more that your immune system is aware and active, the better the outcome you may have as a patient, whether you're four-legged or two-legged."

A next step will be to investigate why many patients, both human and canine, lack a strong immune response to osteosarcoma and how their immune systems could be empowered to control their cancer. Laboratory studies of immune cells' interactions with osteosarcoma tumors will complement NCI-supported clinical trials investigating immunotherapy treatments for canine osteosarcoma and could set the stage for more targeted therapies in dogs and humans. "There's a huge amount of value in studying dogs and the diseases they get, and we're just getting started," LeBlanc says.

Mannheimer, J.D., et al. *Commun Biol.* 2023 Aug 17;6(1):856.

We may not be able to teach old dogs new tricks, but studying cancer in pet dogs can teach us new ways to treat both dogs and humans. Osteosarcoma is rare in humans, which makes it difficult to study. Unfortunately, however, it is common in dogs. CCR researchers have long studied naturally occurring osteosarcoma in pets. They recently found that molecular signatures for immune activity in dogs that had favorable clinical outcomes matched the signatures and outcomes in human patients. This research paves the way for improving treatment options for both four-legged and two-legged patients. Credit: iStock

NO POINT OF NO RETURN

A new view of cell division changes the way we think about how some cancer drugs impact cells.

Steven D. Cappell, Ph.D.
Stadtman Investigator
Laboratory of Cancer Biology and Genetics

Looking at familiar processes in new ways sometimes overturns long-standing ideas about how biology works. That's what happened when Stadtman Tenure-Track Investigator **Steve Cappell, Ph.D.**, followed individual cells in real time as they proceeded through the cycle of cell growth and division. His team unexpectedly discovered that cells that are preparing to divide are not as committed to completing that process as previously thought. Instead, they reported in *Nature*, a cell's decision to divide can be reversed.

When cells receive growth-promoting signals, they begin to prepare for cell division by entering the cell cycle. That cycle is a precisely choreographed series of steps that culminates in a step called mitosis, which divides a cell in two. The textbook view of the cell cycle includes a point of no return after which growth signals would no longer be needed to drive cells to divide. But James Cornwell, Ph.D., a postdoctoral researcher in Cappell's lab, noticed that not all cells follow this rule. When he took growth signals away from growing cells, some of the cells managed to exit the cell cycle and return to a resting state, even when they had progressed beyond the supposed point of no return. Cornwell took advantage of the advanced imaging technology available in CCR to capture videos of thousands of cells and monitor each one's progression individually through the cell cycle. When cells stopped receiving growth signals, most continued through the cell cycle and eventually split, but cells that were still early in the cycle when they stopped receiving growth signals returned to a resting state.

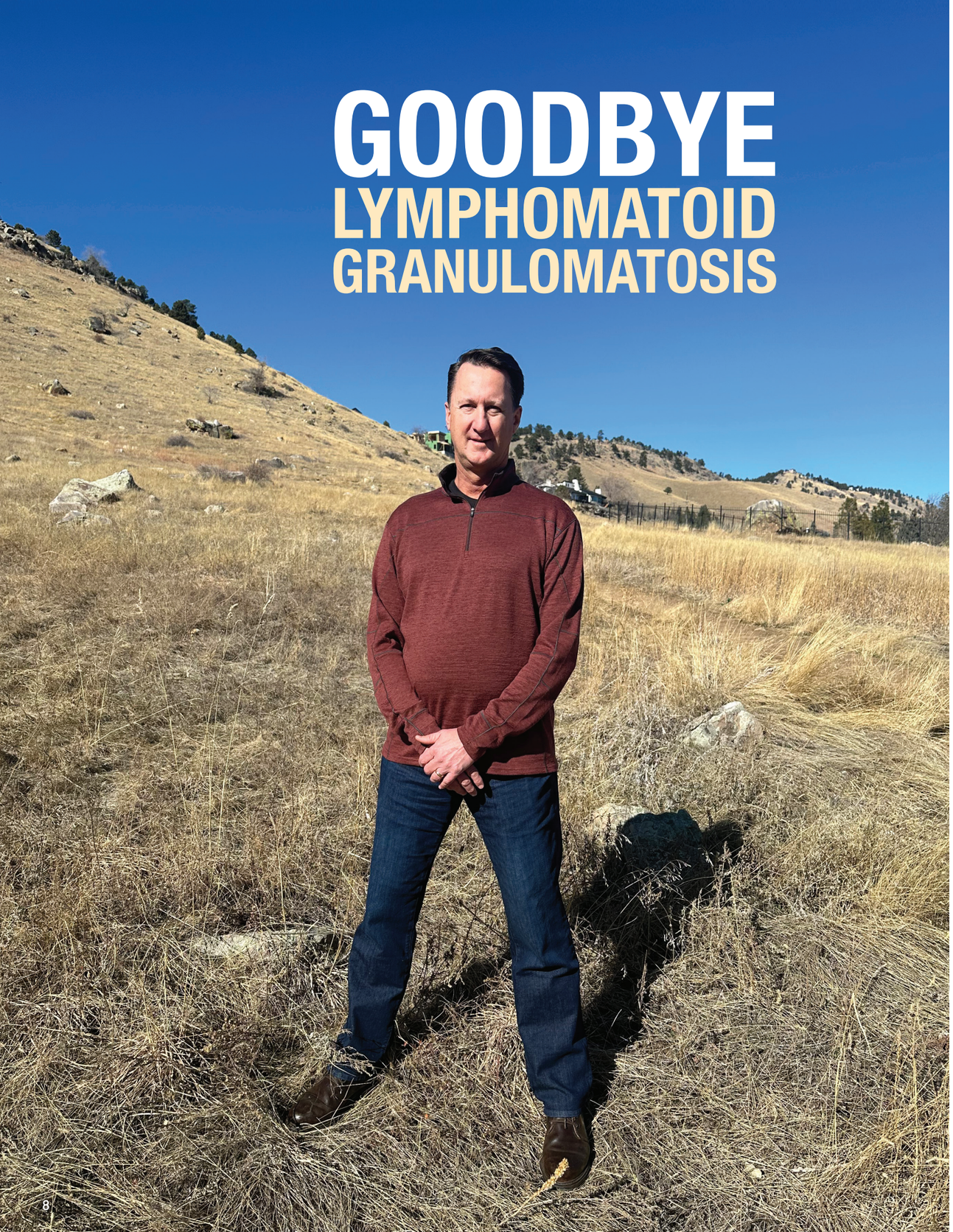
The team discovered that each cell's fate is essentially a race between the steps leading up to mitosis and the steps necessary for cell cycle exit. "What we found is that usually mitosis wins that race, but sometimes the exit will win," Cappell explains. Cells that had just started to prepare for mitosis had the best chance of completing the exit process before time ran out. But when the researchers stopped the clock by blocking mitosis entirely, even cells that were farther along when growth signals were interrupted managed to exit the cycle.

In addition to overturning a long-held dogma of how cells grow and divide, the team's discovery could lead to better cancer therapies. The researchers identified specific molecules that control the race between mitosis and cell cycle exit, and their findings suggest that drugs that work by inhibiting certain cell cycle regulators — CDK4 and CDK6 — likely affect cells' progression through the cell cycle differently than previously thought. "It turns out, we don't quite understand all the pathways that cells can take when we treat them with these drugs," Cappell says. Recognizing how such drugs might affect the fates of individual cancer cells could allow Cappell and his team to design combination therapies with longer-lasting benefits for patients.

Cornwell, J.A., et al. *Nature*. 2023 Jul; 619(7969):363-370.

Past a certain point in a cell's cycle of growth and division, it had been assumed that the cycle cannot be stopped and that a cell must undergo mitosis, or cell division, due to continuous CDK2 signaling. New research, however, shows that inhibiting the growth signaling proteins CDK4 and CDK6 can reverse the cell's decision to divide — if the signals are stopped early in the cell cycle. These two stopwatches show samples of cell activity over time, with yellow indicating progress toward mitosis and blue indicating a resting stage. In the group of cells treated with a CDK4/6 inhibiting drug (right), up to 15% of cells gradually lost CDK2 activity, returned to a resting state and did not enter mitosis. This did not occur when cells in the group to the left were untreated. Credit: James A. Cornwell, CCR, NCI, NIH; SPGM, FNL, NCI, NIH

GOODBYE LYMPHOMATOID GRANULOMATOSIS



A 30-year trial leads to a highly effective treatment.

Wyndham Wilson, M.D., Ph.D.
Senior Investigator
Lymphoid Malignancies Branch

Decades ago, nobody knew the cause of lymphomatoid granulomatosis, a rare and life-threatening disease that affects the immune system. But now, CCR researchers, in a clinical trial conducted over 30 years, have identified a treatment that cures the disease in a significant portion of patients and dramatically extends life expectancy by twenty years for others.

Lymphomatoid granulomatosis is a precancerous condition in which the body produces many abnormal immune cells that accumulate in and damage healthy tissues. "When I started studying this disease back in 1990, there was no standard therapy for it and the median survival was somewhere around 6 months," says Senior Investigator **Wyndham Wilson, M.D., Ph.D.**

At the time, emerging evidence suggested that the disease was triggered by the Epstein-Barr virus (EBV), which infects immune cells. Most people are infected with EBV by adulthood and face few, if any, consequences, because their immune system successfully suppresses it for the rest of their life. However, in extremely rare cases, the immune system fails to control the virus, which triggers the growth of abnormal immune cells, leading to lymphomatoid granulomatosis and the development of lesions in critical organs.

Shortly after Wilson joined NCI, some of his CCR colleagues were finding the first indications that lymphomatoid granulomatosis was due to defects in a type of immune cell called a B cell. Based on what was known about the disease, Wilson suspected that a relatively novel drug at the time — interferon, a form of immunotherapy — could help treat it. He tested this theory in a few patients, and "in three out of four patients, the disease went away," says Wilson, noting the effect was sustained after therapy was discontinued less than two years later.

Given the rarity of lymphomatoid granulomatosis, recruiting enough patients for a large clinical study to prove the therapy's efficacy was a major challenge. It took over 30 years to enroll 67 patients in his phase 2 trial.

"Nowhere else would you be able run a study for 30 years, bringing in two to three patients per year, and get the funding for it," says Wilson, noting that the trial was possible thanks to NCI infrastructure, funding and experts.

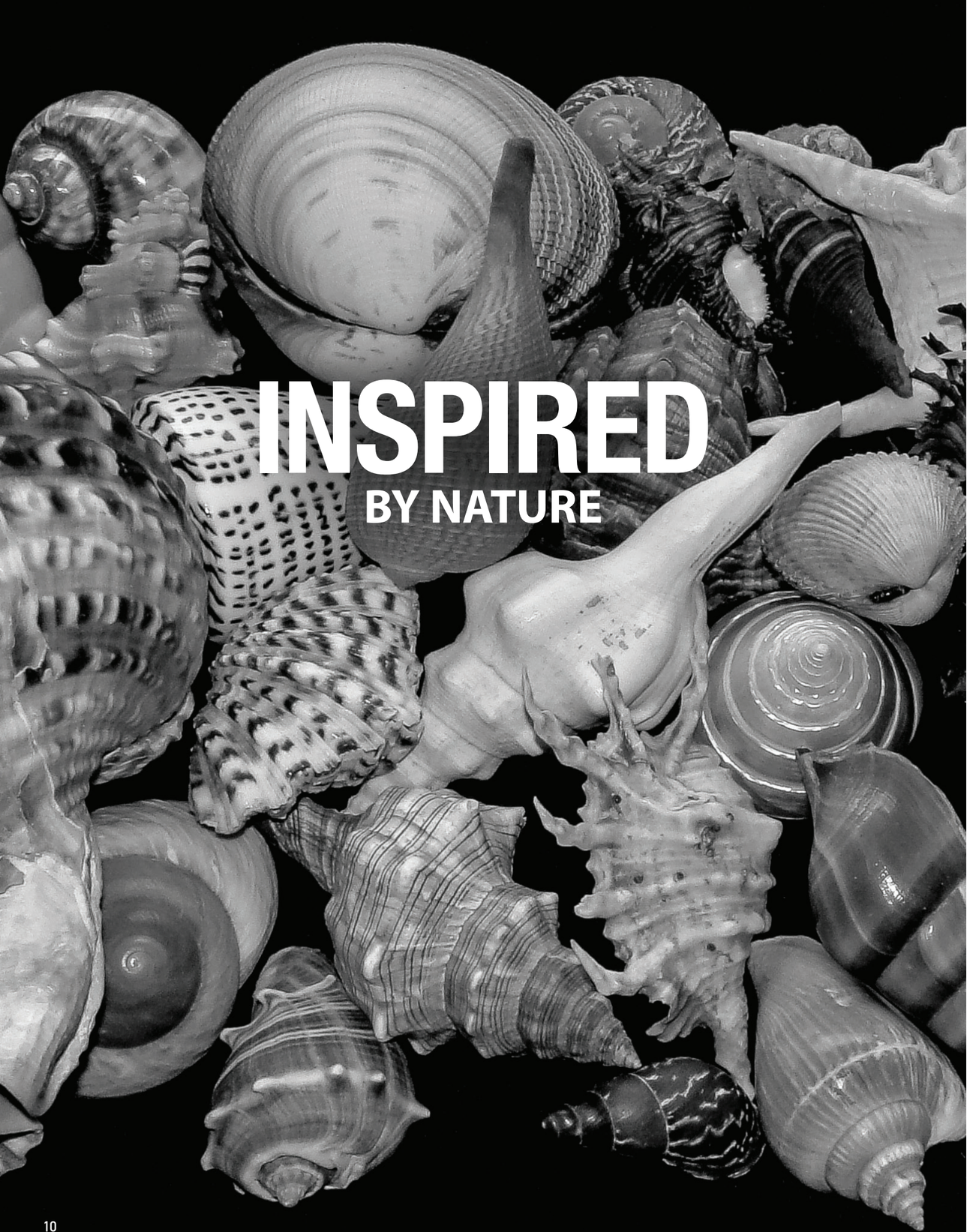
In the trial, 45 patients in the early stages of their disease were given the immunotherapy interferon alfa-2b, while 18 patients with more advanced disease were treated more aggressively with chemotherapy.

The results, reported in *The Lancet Haematology*, turned out to be a game changer for patients. Among those initially treated with interferon alfa-2b, 61 percent had a complete response, which meant their lesions shrunk substantially and no new lesions formed for at least three months. Among those treated with chemotherapy, 47 percent had a complete response. What's more, if a patient didn't respond to their initial treatment with immunotherapy or chemotherapy, they were given the other treatment in a cross-over experiment, which resulted in even more responses.

"In a nutshell, using this strategy, we changed the average survival time from six months to over 20 years! And we really were able to, for the first time, eradicate this disease in most folks," says Wilson, noting that two patients he treated in the initial study, who were in their 30s at the time, are still alive today. "It is very gratifying."

Melani, C., et al. *Lancet Haematol.* 2023 May;10(5)e346-e358.

In 2009, Troy Kamphuis learned that he had tumors on his lungs, liver, spleen and colon, but months of testing yielded no diagnosis. Suspicious that Kamphuis might have an extremely rare disease called lymphomatoid granulomatosis, his medical team sent tissue samples to the only doctor in the U.S. specializing in the disease at the time, Wyndham Wilson, who confirmed their hunch. Eager to learn more, Kamphuis called the number on Wilson's website. "Lo and behold, Dr. Wilson picked up the phone!" says Kamphuis. "That turned out to be my small miracle." Kamphuis decided to skip his first chemotherapy treatment the following Monday and instead fly from Boulder, Colorado, to the NIH Clinical Center in Maryland where he joined Wilson's clinical trial and received treatment with interferon. Within two months, Kamphuis' scans showed no lesions or tumors. He continued taking interferon for one year before stopping altogether. "I wrapped up treatment in early 2011 and have been fine ever since," says Kamphuis, emphasizing that his whole experience with NIH — including the faculty and staff — was excellent. Credit: Adam Kamphuis



INSPIRED BY NATURE

Can a survival mechanism used by bacteria create a better drug delivery system?

Kumaran S. Ramamurthi, Ph.D.
Deputy Chief
Laboratory of Molecular Biology

Kandice Tanner, Ph.D.
Senior Investigator
Laboratory of Cell Biology

David J. FitzGerald, Ph.D.
Senior Investigator
Laboratory of Molecular Biology

Delivering chemotherapy drugs to tumor cells can be a tricky task; oftentimes, the drugs get into the surrounding healthy cells and can cause side effects for a patient. A new approach inspired by nature offers a way to potentially address this problem.

The idea came from an unexpected source. Senior Investigator **Kumaran Ramamurthi, Ph.D.**, studies the basics of bacterial reproduction, which can involve the creation of dormant spores that will eventually spread and develop into new bacteria.

"To protect a developing spore, bacteria deposit a 'protein coat' to cover the spore's surface," explains Ramamurthi. To further shield the spore, two proteins develop a stable mesh around the coat, upon which other proteins and layers of protection are built. The spore can then hibernate until reaching ideal conditions before being released to germinate and produce new bacteria.

As part of their efforts to understand spore formation and function, the team recreated a stripped-down version of spores in a test tube. They identified the minimum number of protein building blocks needed to form the protective layer and called the structures SSHELs (short for synthetic spore husk-encased lipid bilayers).

Once the SSHEL was created, Ramamurthi realized that it could be used as a vessel to deliver cancer drugs. The team hypothesized that the SSHEL could be protective, just like a spore is, and shuttle drugs directly to the cancer cells.

To test the SSHEL as a drug delivery vehicle, Ramamurthi's team collaborated with Senior Investigator **David FitzGerald, Ph.D.**, to create a mouse model of ovarian cancer, which can be treated with the chemotherapy drug doxorubicin. They packaged silica beads soaked with doxorubicin into SSHELs covered with proteins selected to target proteins on the surface of the ovarian cancer cells and injected them into the mice.

Not only did the SSHELs reach the tumors, the team was surprised to discover that the cancer cell's own mechanisms triggered the next step: the SSHEL destabilized and released the drug, killing the cell. Compared to the typical doxorubicin delivery method, the SSHELs shrank the tumors more effectively and with fewer side effects. They then used a transparent zebrafish model provided by Senior Investigator **Kandice Tanner, Ph.D.**, to directly observe this process.

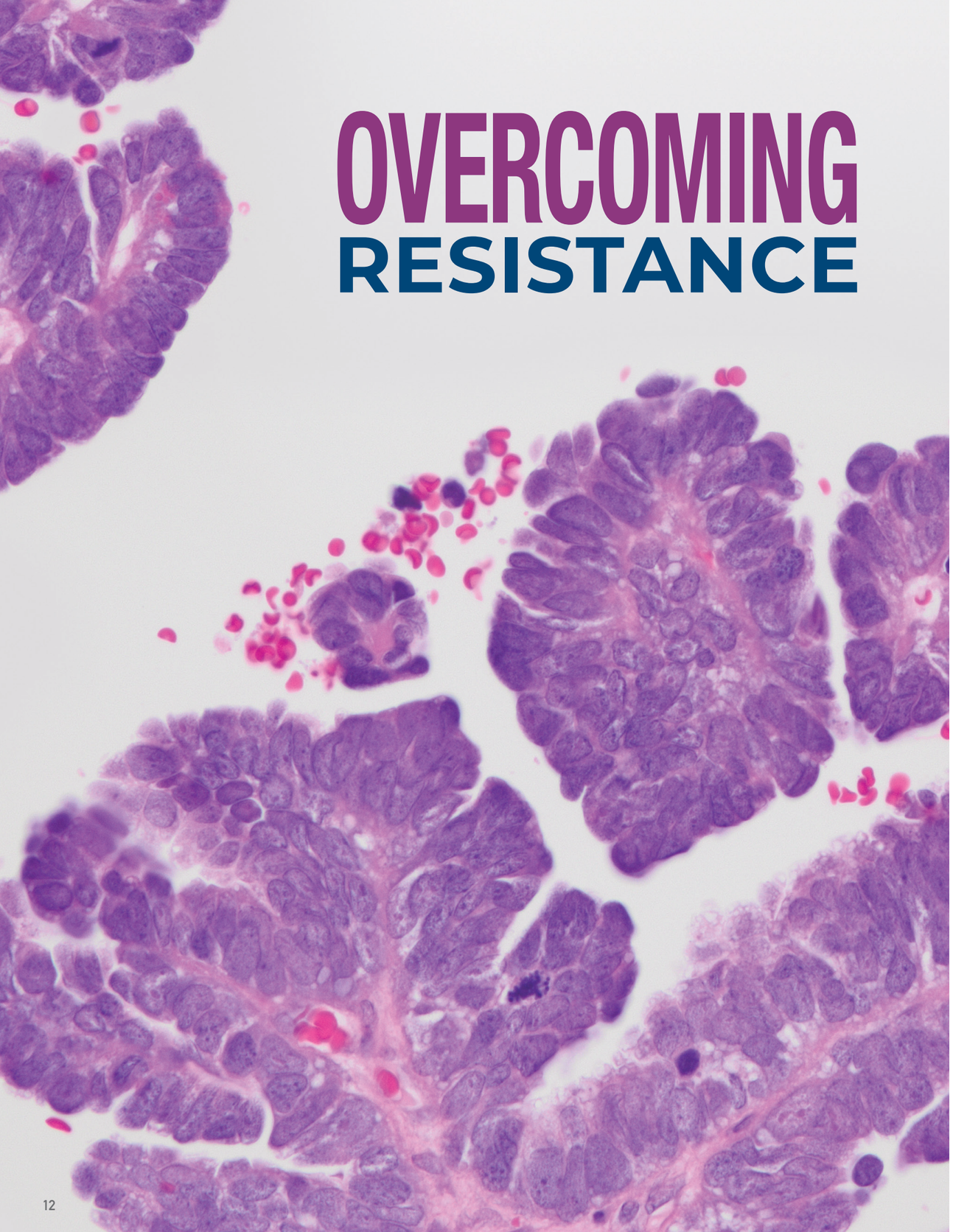
The team published the details of their SSHEL in *Cell Reports*. Encouraged by their findings, Ramamurthi and colleagues are now exploring the development of modified SSHELs for various clinical applications.

"CCR really provides a place where the whole of a research project can be greater than the sum of its parts," Ramamurthi says. "Not only is high-risk, high-reward exploratory research encouraged, we are surrounded by experts in other fields to whom we can turn when we want to translate our basic research into something practical."

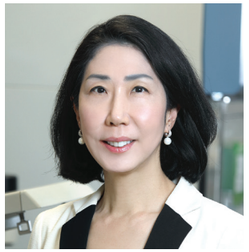
Kong, M., et al. *Cell Rep.* 2023 Jan 31;42(1):111955.

Sea creatures like snails and clams build shells around their soft bodies as protection against predators. Similarly, some bacteria shield their spores in a protein coat to protect them from a harsh environment and thus enhance their chances of survival. Inspired by bacteria, CCR researchers developed a technology they call SSHEL that could be used to help deliver drugs to cancer cells by protecting them from the outside environment and guiding them directly to the target cells. They hope that this will minimize side effects typically encountered with cancer treatments. Credit: SPGM, FNL, NCI, NIH

OVERCOMING RESISTANCE



Studies identify a marker of treatment response for patients with advanced, drug-resistant ovarian cancer.



Jung-Min Lee, M.D.
Lasker Clinical Research Scholar
Women's Malignancies Branch

Ovarian cancer often goes undetected until it has become advanced, and it is the most lethal of all gynecological cancers. Nearly a decade ago, the outlook for people diagnosed with ovarian cancer improved when drugs called PARP inhibitors were approved as a treatment for the disease. However, a new challenge has emerged for doctors who treat ovarian cancer: how to treat patients whose cancer has become resistant to PARP inhibitors, as most eventually do.

One doctor working to address this challenge is Lasker Scholar Tenure-Track Investigator **Jung-Min Lee, M.D.** Through laboratory and clinical studies, Lee has identified a class of drugs that may stop tumor growth for a subset of patients whose ovarian cancer no longer responds to PARP inhibitors. She and her team, including Medical Research Scholars fellow Nitasha Gupta, M.D., research fellow Tzu-Ting Huang, Ph.D., and biologist Jayakumar Nair, Ph.D., reported their findings in *Science Translational Medicine*.

PARP inhibitors interfere with cells' ability to repair damaged DNA. They are particularly effective at eliminating cancer cells whose DNA repair systems are already impaired due to mutations in *BRCA1* or *BRCA2* genes. Today, many patients with ovarian cancer use PARP inhibitors as maintenance therapy after their initial treatment, and the drugs can keep cancer at bay for years. Eventually, however, most cancer cells develop resistance to the drugs.

Lee worked with the National Center for Advancing Translational Sciences at NIH to determine how thousands of different chemicals affected the growth of ovarian cancer cells that, like many of her patients' cancers, are resistant to PARP inhibitors and have mutations in *BRCA* genes. One of the best killers of those cells was the experimental cancer therapy prexasertib, which inhibits an enzyme called CHK1.

Lee and her colleagues then tested prexasertib in a clinical trial involving 17 patients with PARP inhibitor-resistant ovarian cancer. Four patients saw their tumors shrink or stabilize for at least six months following the treatment. While not everyone in the trial benefitted from the drug, Lee reasoned that it might be possible to identify the best candidates for prexasertib treatment based on their tumors' molecular makeup.

Armed with data and tumor samples collected during the clinical trial, she went back to the lab. "Even if we don't see a dramatic response in the majority of people, when we have a biologically relevant hypothesis, we can learn from that," she says.

She and her team discovered that the cancer cells from patients who benefited from the treatment had unusually high activity in two genes: Bloom syndrome RecQ helicase (*BLM*) and cyclin E1 (*CCNE1*). They confirmed that PARP inhibitor-resistant *BRCA*-mutated ovarian cancer cells are more sensitive to CHK1 inhibitors when both *BLM* and *CCNE1* are overactive.

These findings have informed the design of a clinical trial that Lee is leading to evaluate prexasertib's effects in patients with ovarian, endometrial or bladder cancer. Because of the treatment's potential to address an urgent need for patients with advanced ovarian cancer, the U.S. Food and Drug Administration has granted a fast-track designation to speed prexasertib's evaluation.

"My ultimate goal is to improve the clinical outcome of my ovarian cancer patients," Lee says. "I feel like I have to figure out something for this critically important and emerging patient population I see in the clinic."

Gupta, N., et al. *Sci Transl Med.* 2023 Jun 21;15(701):eadd7872.

High-grade serous carcinoma ovarian cancer cells with hematoxylin and eosin (H&E) staining. Ovarian cancer is often diagnosed when it is already advanced, and treatment options are often limited. CCR researchers have now identified a drug that could be beneficial for a subset of patients whose cancer has grown after treatment with PARP inhibitors. They have also identified the gene activity that may indicate which patients are good candidates for the new drug. A clinical trial to evaluate its effects is underway. Credit: Maria Del Carmen Rodriguez Pena, M.D., CCR, NCI, NIH; Markku M. Miettinen, M.D., Ph.D., CCR, NCI, NIH; SPGM, FNL, NCI, NIH

HELP FOR A FATTY LIVER

An immune signal that reprograms fat metabolism could help control nonalcoholic fatty liver disease.

Daniel W. McVicar, Ph.D.
Acting Chief
Cancer Innovation Laboratory

Nearly one in three people worldwide are thought to have an excess accumulation of fat in their liver. The condition, known as nonalcoholic fatty liver disease, usually exhibits no symptoms of its own but it puts people at risk for diabetes and other metabolic disorders. When it becomes severe, nonalcoholic fatty liver disease can damage the liver and may lead to liver cancer.

The liver handles most of the breakdown of fats in the body. When high levels of fats are taken in through the diet, the liver can become overwhelmed, so patients with excess fat in their liver are usually advised to control their weight with diet and exercise. A discovery from the lab of Senior Investigator **Daniel McVicar, Ph.D.**, suggests it may also be possible to reduce fat deposits in the liver by directing liver cells to process fats more efficiently.

When high levels of fat are present in the liver, immune cells called macrophages are summoned to the organ, where they respond to the threat by releasing a molecule called itaconate. McVicar and his team reported in *Nature Metabolism* that itaconate helps the liver deal with the excess fat.

Staff Scientist Erika Palmieri, Ph.D., and Associate Scientist Jonathan Weiss, Ph.D., studied this process in mice. When laboratory mice are fed a diet that is high in fat, mimicking a typical Western diet, fat builds up in the animals' livers. When McVicar's team genetically manipulated mice so they could not make itaconate, their livers accumulated even more fat and the mice became obese. These mice also developed metabolic problems that did not arise in itaconate-producing mice that were fed the same food.

The researchers suspect itaconate helps mitigate fat accumulation in human livers, too. They found elevated levels of the compound in samples of liver tissue from patients with a severe form of nonalcoholic fatty liver disease called nonalcoholic steatohepatitis (NASH). In NASH, excess fat causes the liver to swell and become damaged. The researchers say the high levels of itaconate in the damaged livers could be a sign the immune system is trying to help the liver cope with the excess fat. "In disease, this loop gets overwhelmed and can't control the condition anymore," McVicar says. "But it's trying." Without itaconate, he says, patients' livers might have retained even more fat and accrued even more damage.

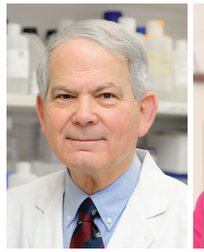
McVicar's team found that mice without their own itaconate became more resilient to the effects of a high-fat diet when they were administered an itaconate-like compound. The findings suggest similar compounds might help rein in fat accumulation in people whose diet promotes nonalcoholic fatty liver disease. Controlling that condition could reduce metabolic complications like diabetes and ultimately lower the risk of liver cancer.

Weiss, J.M., et al. *Nat Metab.* 2023 Jun;5(6)981-995.

This colored transmission electron micrograph shows a cross section of liver tissue with a case of fatty liver disease. If left untreated, fatty liver disease can result in scar tissue, reduced liver function and sometimes liver cancer. This study has now identified a molecule released by macrophages (a type of immune cell) that helps the liver cope with excess fat, and which could be harnessed to help control nonalcoholic fatty liver disease. Credit: IKELOS GmbH, Dr. Christopher B. Jackson, Science Source

STOPPING ASPS ASAP

NCI trial leads to first drug approval for a very rare cancer.



James H. Doroshow, M.D.
Senior Investigator
Developmental Therapeutics Branch
Deputy Director
Clinical and Translational Research, NCI

Alice Chen, M.D.
Head
Early Clinical Trials Development Program and the Developmental Therapeutics Clinic, NCI

John W. Glod, M.D., Ph.D.
Associate Research Physician
Pediatric Oncology Branch

Alveolar soft part sarcoma (ASPS) is a slow-growing cancer that starts in soft tissues. It is diagnosed in fewer than 100 people each year in the United States, most of whom are adolescents and young adults. ASPS does not respond to chemotherapy, and when patients' tumors cannot be removed surgically, it has been difficult to treat.

Many patients with ASPS are referred to the NIH Clinical Center, where a clinical trial recently led to the first FDA-approved treatment for advanced cases of the cancer.

Encouraged both by laboratory findings and reports of a few patients with ASPS who had improved following treatment with a type of immunotherapy called checkpoint inhibitors, **Alice Chen, M.D.**, Head of the Developmental Therapeutics Clinic in NCI's Division of Cancer Treatment and Diagnosis (DCTD), considered the use of the immunotherapy atezolizumab as an effective treatment for ASPS. So, Chen and her team launched a clinical trial.

The results of the trial, which was conducted at the NIH Clinical Center and at sites in the NCI's Experimental Therapeutics Clinical Trials Network, were reported in the *New England Journal of Medicine*. For 19 of the 52 participants, tumors shrank by at least 30 percent following treatment with atezolizumab. Most other patients were considered to have stable disease, meaning their tumors were not growing or shrinking.

The side effects of atezolizumab were mostly mild, and the treatment was generally well tolerated by patients. "I think we've made an impact for a majority of these patients' lives," says Chen. "They were able to continue to do their daily living."

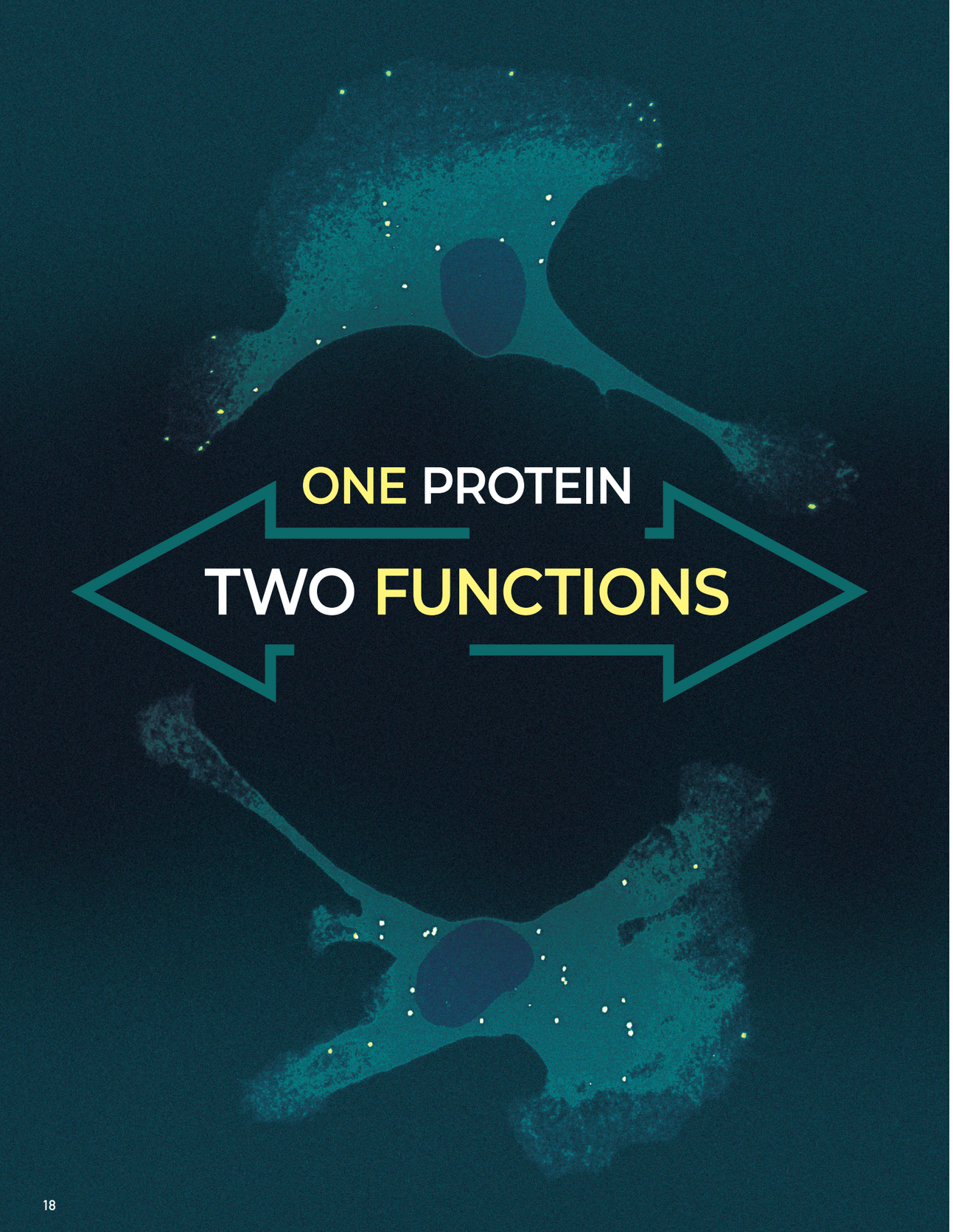
A collaboration with researchers in CCR's Pediatric Oncology Branch, led by Associate Research Physician **John Glod, M.D., Ph.D.**, enabled children as young as two to participate in the trial. Glod says that approach is crucial for advancing treatment options for children with very rare cancers like ASPS. "There just aren't enough pediatric patients to do a standalone study," he says, "so this is a way we can make more rapid progress for kids."

Tumor biopsies collected during the trial enabled the research team to investigate changes brought about by the treatment. Their findings suggest atezolizumab enabled patients' immune systems to attack their tumors as intended. "For many of the patients who had an objective shrinkage in their tumor after treatment, we could show that not only was the tumor now infiltrated with more T cells, the T-cell killing apparatus was activated," says DCTD director and CCR Senior Investigator **James Doroshow, M.D**.

Based on early reports from the trial, the FDA approved atezolizumab for adults and children with ASPS in 2022. It is the first pediatric approval of atezolizumab for any disease. The scientists stress that the success is the result of cooperation between DCTD, the CCR Pediatric Oncology Branch, the Experimental Therapeutics Clinical Trials Network and Genentech, a member of the Roche Group, which provided the drug through a cooperative research and development agreement with NCI.

Chen, A.P., et al. *N Engl J Med.* 2023 Sep 7;389(10):911-921.

When Tesu Kim had surgery to remove a mass in his leg that wouldn't stop growing, doctors told him he had alveolar soft part sarcoma (ASPS). He would need further treatment to keep the cancer under control. The NIH Clinical Center made the experience as easy as possible, he recalls, treating him kindly and providing transportation from his home in Columbia, Maryland. When the initial medications they gave him stopped working, he was invited to join a clinical trial investigating atezolizumab's ability to stop the rare cancer. The new drug not only kept his tumors in check but shrank them, and it caused none of the side effects he'd experienced with his previous treatment. Five years later, he remains on atezolizumab, and his cancer remains stable. He fits in regular visits to the Clinical Center in between work and classes at Howard Community College, and he even finds time for vacations. Here he is on a trip to Dubai in June 2023, having a unique dining experience about 150 feet up in the air at "Dinner in the Sky." Credit: Tesu Kim



Where and how fast a protein is made in the cell affects what it does.

Stavroula Mili, Ph.D.
Senior Investigator
Laboratory of Cellular and Molecular Biology

It has been generally assumed that where in the cell proteins are made does not matter much for their function, especially because proteins can move quite freely from one place to another. But new research by Senior Investigator **Stavroula Mili, Ph.D.**, and her colleagues now shows that the location and even the speed of how a protein is made in a cell influences what the protein ends up doing.

"If we understand more about the mechanisms that cells use to determine protein function, we could maybe manipulate these mechanisms and channel proteins to specific functions for therapeutic purposes," Mili says.

The instructions on how to construct proteins in the cell are encoded in messenger RNA (mRNA), which is distributed throughout a cell. Mili and her team were studying the mRNA that encodes a protein called NET1, which is associated with the spread of cancer cells, when they noticed that it can be found either at the center of the cell near the nucleus, or further away, in the cell periphery near the cell membrane. They were curious to understand if the location of the mRNA influenced the resulting protein's function.

Indeed, the researchers found the NET1 mRNA near the cell nucleus produced NET1 protein that interacted more with a protein known to help bring other proteins into the nucleus, called importin beta1. NET1 synthesized in this location was thus transported and sequestered into the nucleus, where it is thought to control cellular responses to DNA damage.

On the other hand, when NET1 mRNA was located further away from the nucleus, it gave rise to NET1 protein that interacted more with a different protein partner called CASK, which prevented its interaction with importin beta1 and transport into the nucleus. In this latter case, NET1's function could augment the cancer cells' ability to move, which is a property important for cancer metastasis.

But it is not only the location of where a protein is made that matters — the speed of protein production also seems to have consequences. Mili and colleagues manipulated the rate at which NET1 mRNA is translated into NET1 protein. Strikingly, slow synthesis — regardless of mRNA location — resulted in NET1 protein that interacted with importin beta1 and was carried into the cell nucleus, while relatively faster synthesis resulted in the opposite effect, decreasing importin beta1 binding and nuclear targeting.

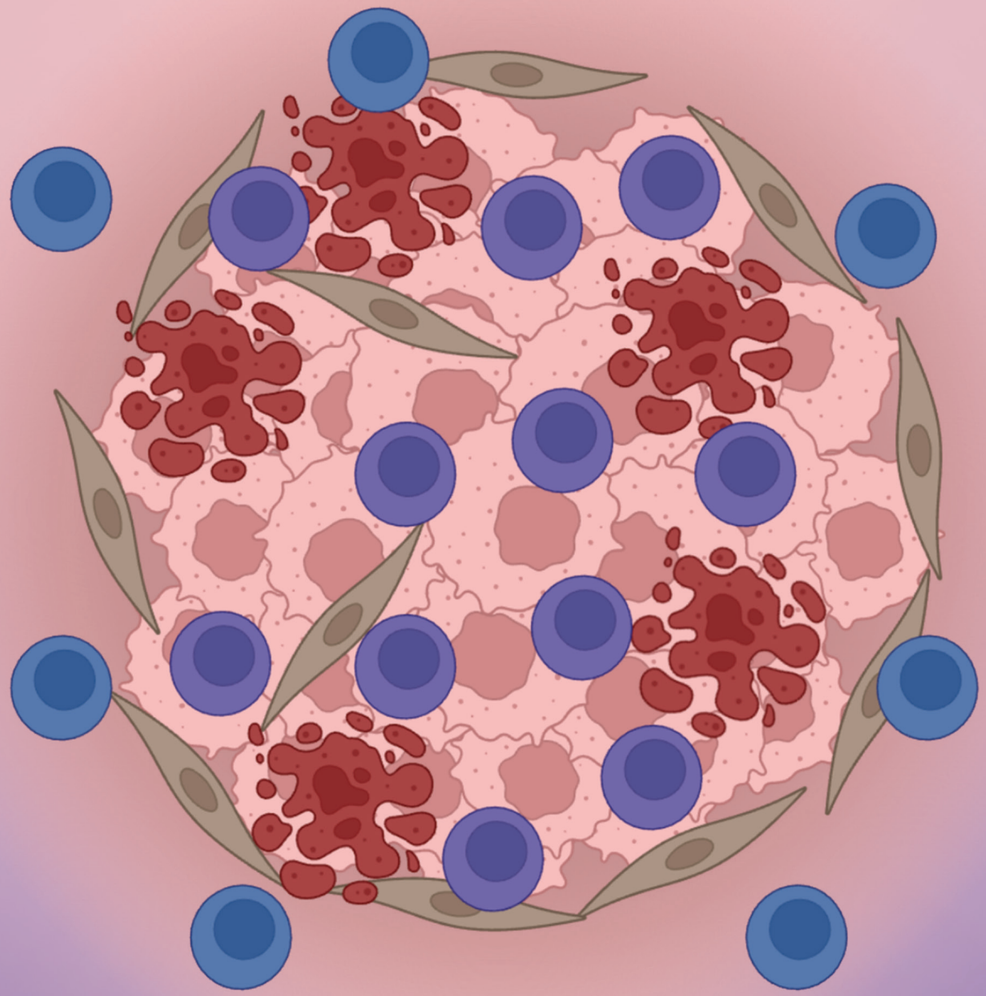
Together, these experiments, described in a study in *Molecular Cell*, suggest that both the location and rate of protein synthesis can affect which proteins interact with each other, which in turn influences a protein's function.

Moving forward, Mili plans to explore this phenomenon in greater detail. "We are trying to understand how widely applicable these mechanisms are — do they play a role in regulating other protein functions? We're also studying these mechanisms to see if we can use them to affect the ability of cancer cells to metastasize," she says.

Gasparski, A.N., et al. *Mol Cell.* 2023 Aug 3;83(15):2726-2738.e9.

Messenger RNA (mRNA, yellow dots) in the two breast cancer cells depicted here holds the instructions to make NET1 protein. New research has demonstrated that the location in a cell where this mRNA is turned into protein and the speed at which that process occurs affects what job the protein will have. By altering the location and speed of protein production, researchers may be able to control the protein's function and believe this could be harnessed for therapeutic purposes. Credit: Alexander N. Gasparski, CCR, NCI, NIH; SPGM, FNL, NCI, NIH

AN UNEXPECTED CANCER KILLER



An understudied immune cell can exhibit potent anti-tumor activity against liver cancer.

Tim F. Greten, M.D.
Deputy Chief
Thoracic and GI
Malignancies Branch

Researchers have discovered that an enigmatic type of T cell in the liver can be effective at attacking liver cancer cells, but its anti-tumor activity is suppressed in some patients. At the same time, the investigators have shown how treatment with immune checkpoint inhibitors can reverse this effect, helping this type of immune cell, called a mucosal-associated invariant T (MAIT) cell, better attack and infiltrate liver tumors. The finding could explain why some patients with liver cancer, but not others, respond to treatment with immunotherapy.

T cells are a type of immune cell that play a critical role in protecting the body by attacking and killing harmful pathogens or cancer cells. MAIT cells are a subtype of T cells typically only found in the liver, gut or lungs, and are not well understood.

Senior Investigator **Tim Greten, M.D.**, previously studied MAIT cells, and he was curious to understand the anti-tumor activity of these cells in the context of liver cancer, which remains difficult to treat and often involves a poor prognosis. His team used an array of detailed imaging techniques and RNA sequencing to analyze tissue samples from 37 patients with hepatocellular carcinoma (HCC), the most common type of liver cancer. Then they applied an artificial intelligence algorithm to help map out the function and location of MAITs, as well as neighboring cells.

"What makes this study distinct is that the tissue we analyzed contained the tumor, tumor rim and adjacent tissue, so we could actually study how the different cell types change from the tumor environment to the tumor," explains Greten.

As they report in *Cell*, Greten, Staff Scientist Firouzeh Korangy, Ph.D., and their team were surprised to see that many MAIT cells surrounded the tumors — but did not infiltrate them as one would expect. In the environment around the tumors, the researchers also observed a high number of immune cells called macrophages adjacent to the defective MAIT cells that were unable to penetrate and attack tumors.

Macrophages are notorious for emitting signals that suppress the ability of immune cells to attack cancer via a signaling pathway called PD-1/PD-L1. A common type of immunotherapy using immune checkpoint inhibitors works by blocking these signals. Through a series of follow-up experiments in mice and human tissue samples, the researchers confirmed that the macrophages were emitting PD-1/PD-L1 signals, and that blocking these signals with immune checkpoint inhibitors could boost the ability of MAIT cells to attack tumors.

Additional experiments showed that tissue samples from humans who had been treated with immune checkpoint inhibitors had greater MAIT infiltration in their tumors, and similar results were found in mice.

"This study shows very clearly that these MAIT cells can exert anti-tumor immunity," says Greten.

Based on these results, Greten says he is interested in exploring novel pathways beyond PD-1/PD-L1 that could be used to harness MAIT cells. He says, "Current therapy using immune checkpoint inhibitors only works in some patients. If we can find new therapies to boost MAIT cells, along with immune checkpoint inhibitors to better attack tumors, it could potentially lead to more effective cancer treatments."

Ruf, B., et al. *Cell*. 2023 Aug 17;186(17)3686-3705.e32.

Despite their potential to attack cancer cells, MAIT cells (shown here in blue) often surround liver tumors but fail to infiltrate them. New findings suggest that this is due to an interaction with macrophages that also surround the tumor, and that a common type of immunotherapy could block this interaction and thus release MAIT cells to be cancer killers. In this illustration, some MAIT cells have been able to infiltrate a liver tumor (pink) and are hard at work destroying cancer cells, which can be seen bursting (red). Also shown are stromal cells (tan). Credit: Ruf, B., et al.; BioRender.com

Faculty News

Brenda Adjei, Ed.D., M.P.A.

Brenda Adjei, Ed.D., M.P.A., has been appointed as Associate Director of the Office of Healthcare Delivery and Equity Research. In this role, she will direct CCR's institutional efforts to expand and improve the accessibility, equity and reach of our clinical research program.

Amiran K. Dzutsev, M.D., Ph.D.

Amiran K. Dzutsev, M.D., Ph.D., has been appointed as a Stadtman Tenure-Track Investigator in the Laboratory of Integrative Cancer Immunology, where he was previously a Staff Scientist. Dr. Dzutsev's research focuses on understanding the impact of microbiota on cancer development, cancer progression and responses to therapy.

Shuo Gu, Ph.D.

Shuo Gu, Ph.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the RNA Biology Laboratory. Dr. Gu's lab focuses on mechanisms of RNA interference and microRNA pathways and their applications in cancer treatment.

James L. Gulley, M.D., Ph.D.

James L. Gulley, M.D., Ph.D., has been appointed as NCI Clinical Director. In this role, Dr. Gulley will oversee the day-to-day operations of more than 350 active clinical trials as well as the regulatory aspects of CCR's clinical program. He will also continue to serve as Co-Director of the Center for Immuno-Oncology and as a Senior Investigator.

Stephanie A. Harmon, Ph.D.

Stephanie A. Harmon, Ph.D., has been appointed as a Stadtman Tenure-Track Investigator in the Molecular Imaging Branch, where she was previously a Staff Scientist. Dr. Harmon's research centers around the use of integrative biomarkers from various imaging scales to enhance the understanding of disease and expand the role of imaging in cancer diagnosis and treatment.

Sri Krishna, Ph.D.

Sri Krishna, Ph.D., has been appointed as a Stadtman Tenure-Track Investigator in the Surgery Branch, where he was previously a postdoctoral researcher. Dr. Krishna's research is focused on discovering and studying antitumor T cells, including those targeting neoantigens, antitumor T-cell receptors, human T-cell differentiation states and immune resistance by human tumors.

Diana C.F. Monteiro, Ph.D.

Diana C.F. Monteiro, Ph.D., has joined the Center for Structural Biology as a Stadtman Tenure-Track Investigator from the Hauptman-Woodward Medical Research Institute. She has also been named an NIH Distinguished Scholar. Dr. Monteiro's group develops and employs new methods to obtain high-resolution structures of medically relevant proteins.

Rosa Nguyen, M.D., Ph.D.

Rosa Nguyen, M.D., Ph.D., has been appointed as a Lasker Clinical Research Scholar and Tenure-Track Investigator in the Pediatric Oncology Branch. She has also been named an NIH Distinguished Scholar. The goal of Dr. Nguyen's research is to translate new and effective immunotherapies from the bench to the bedside and to understand the immunologic mechanisms that underlie tumor response and immune evasion.

Peter A. Pinto, M.D.

Peter A. Pinto, M.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Urologic Oncology Branch. Dr. Pinto is an expert urologic surgeon specializing in minimally invasive treatment, laparoscopic and robotic surgery for prostate, kidney, bladder and testicular cancer. His research focuses on developing novel diagnostic and treatment modalities for localized and locally advanced prostate cancer.

Arun Rajan, M.D.

Arun Rajan, M.D., has been named Director of the Medical Oncology Service. He leads the staff and fellows who support patients participating in CCR's clinical protocols at the NIH Clinical Center. As a clinical researcher, Dr. Rajan focuses on developing new therapies for patients with lung cancer and thymic malignancies.

Ramya Ramaswami, M.B.B.S., M.P.H.

Ramya Ramaswami, M.B.B.S., M.P.H., has been named a Lasker Clinical Research Scholar and Tenure-Track Investigator in the HIV and AIDS Malignancy Branch, where she was previously a Physician-Scientist Early Investigator. She has also been named an NIH Distinguished Scholar. Dr. Ramaswami's research is focused on developing novel diagnostic methods and therapeutic strategies for patients with HIV and cancer.

Nitin Roper, M.D., M.Sc.

Nitin Roper, M.D., M.Sc., has been appointed as a Lasker Clinical Research Scholar and Tenure-Track Investigator in the Developmental Therapeutics Branch, where he was previously a Physician-Scientist Early Investigator. Dr. Roper's research focuses on neuroendocrine tumors and aims to understand the relationship between Notch signaling and immunologic, epigenetic and molecular aspects of these tumors, with the goal of translating experimental data to the clinic.

Faculty News continued

Adam Sowalsky, Ph.D.

Adam Sowalsky, Ph.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Genitourinary Malignancies Branch. Dr. Sowalsky's lab conducts translational research focused on tumor evolution and treatment resistance with an emphasis on developing biomarkers for predicting responses in locally advanced prostate cancers.

Ramaprasad Srinivasan, M.D., Ph.D.

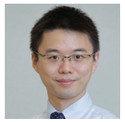
Ramaprasad Srinivasan, M.D., Ph.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Urologic Oncology Branch. Dr. Srinivasan is investigating a variety of mechanism-based treatment strategies in kidney cancers as well as hereditary kidney cancer syndromes.

Anish Thomas, M.B.B.S., M.D.

Anish Thomas, M.B.B.S., M.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Developmental Therapeutics Branch. Dr. Thomas' lab focuses on small cell lung cancer and understanding and targeting tumor plasticity, metastases and chemoresistance.

Nicholas P. Tschernia, M.D.

Nicholas P. Tschernia, M.D., has been appointed as a Physician-Scientist Early Investigator in the Center for Immuno-Oncology. Dr. Tschernia's research focuses on developing new cellular immunotherapy treatments for cancer patients, including CAR T-cell therapy. His lab is dedicated to identifying new potential targets on solid tumors and ways to improve the quality and fitness of the engineered cells.



Chen Zhao, M.D.

Chen Zhao, M.D., has been appointed as a Stadtman Tenure-Track Investigator in the Thoracic and GI Malignancies Branch, where he was previously an Assistant Clinical Investigator. Dr. Zhao's lab specializes in developing novel immunotherapeutics and using advanced tissue imaging techniques to understand the interactions among tumor cells, the immune system and the microbiota in the tumor microenvironment.

Joseph M. Ziegelbauer, Ph.D.

Joseph M. Ziegelbauer, Ph.D., has been appointed Deputy Chief of the HIV and AIDS Malignancy Branch. Dr. Ziegelbauer's research focuses on networks and pathways redundantly targeted by multiple viral microRNAs and circular RNAs. He is investigating human and viral gene expression patterns in normal tissue, in Kaposi sarcoma and in other Kaposi sarcoma-associated herpesvirus-infected pathological tissues.

Recently Retired

With appreciation for their service, we recognize these CCR Investigators who have recently retired.

Richard Hodes, M.D., Senior Investigator, Experimental Immunology Branch

Kathleen Kelly, Ph.D., CCR Deputy, Chief and Senior Investigator, Laboratory of Genitourinary Cancer Pathogenesis

Kenneth H. Kraemer, M.D., Senior Investigator, Laboratory of Cancer Biology and Genetics

Thomas Ried, M.D., Senior Investigator, Genetics Branch

William G. Stetler-Stevenson, M.D., Ph.D., Senior Investigator, Laboratory of Pathology

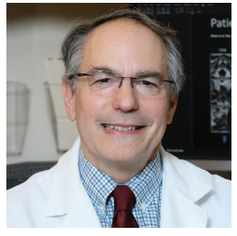
Allan M. Weissman, M.D., Senior Investigator, Cancer Innovation Laboratory

In Memoriam

S. Perwez Hussain, Ph.D., Senior Investigator, Laboratory of Human Carcinogenesis

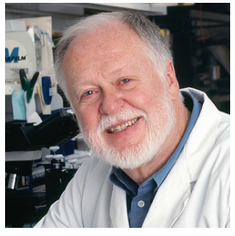
Faculty list is for calendar year 2023.

Awards & Honors

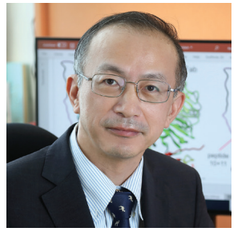


Peter L. Choyke, M.D., F.A.C.R., was elected to the Association of American Physicians.

C. Norman Coleman, M.D., received the D.A. Henderson Lifetime Achievement Award from NCI.

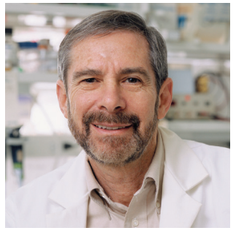


Curtis C. Harris, M.D., received the Golden Circle Founder Award and the Chairpersons' Circle Award at the 50th Anniversary Keystone Symposium.



Mitchell Ho, Ph.D., was elected to the American Institute for Medical and Biological Engineering.

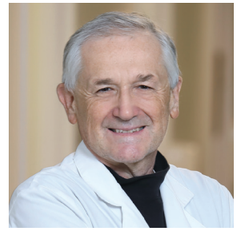
Elaine S. Jaffe, M.D., received the Federation of American Societies for Experimental Biology Excellence in Science Lifetime Achievement Award and a 2023 HHS Secretary's Award for Meritorious Service.



Douglas R. Lowy, M.D., received the 2022 Prince Mahidol Award in the field of Public Health.

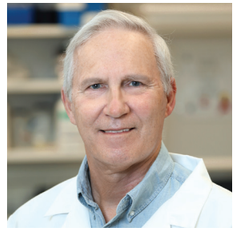
Tom Misteli, Ph.D., received the E.B. Wilson Medal from the American Society for Cell Biology.

Andre Nussenzweig, Ph.D., was elected to the American Academy of Arts & Sciences and was elected to the National Academy of Sciences.

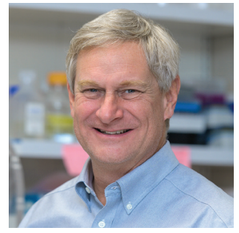


Steven Z. Pavletic, M.D., Ph.D., received the inaugural Lukas D. Wartman GVHD Achievement Award from the GVHD Alliance.

Steven A. Rosenberg, M.D., Ph.D., received the National Medal of Technology and Innovation from the President.



John T. Schiller, Ph.D., received the 2022 Prince Mahidol Award in the field of Public Health.



Joel P. Schneider, Ph.D., received the 2023 Cathay Award from the 17th Chinese Peptide Symposium.

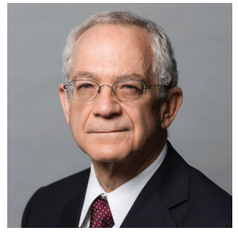
Awards & Honors continued

Louis M. Staudt, M.D., Ph.D., received a 2023 HHS Secretary's Award for Distinguished Service.

Kandice Tanner, Ph.D., received the Max Planck-Humboldt Medal from the Alexander von Humboldt Foundation and the E.E. Just Award from the American Society for Cell Biology.

Naomi Taylor, M.D., Ph.D., was elected to the Association of American Physicians.

Sandra L. Wolin, M.D., Ph.D., was elected to the American Academy of Arts & Sciences.



Robert Yarchoan, M.D., received a 2023 Career Achievement Award from the Department of Health and Human Services.

Howard A. Young, Ph.D., was elected to the 2022 class of fellows of the American Association for the Advancement of Science.

CCR Research Recognition Awards

These awards provide resources and recognition to our staff and fellows for their crucial contributions and dedication to cancer research.

CCR Excellence in Postdoctoral Research Transition Award

Recognizes exceptional CCR postdoctoral fellows and facilitates their transition to an independent research position at an academic institution:

Gwen Buel, Ph.D., Center for Structural Biology

Yilun Sun, Ph.D., Developmental Therapeutics Branch

CCR Outstanding Ph.D. Student Award

Recognizes outstanding Ph.D. students who conducted part or all of their thesis research at CCR:

Yevgen Levdansky, Ph.D., Max Planck Institute at the University of Tübingen, for work performed in the RNA Biology Laboratory

Katherine Masih, Ph.D., University of Cambridge NIH Oxford-Cambridge Scholars Program, for work performed in the Genetics Branch

Staff Scientist/Staff Clinician Scientific Achievement Award

For outstanding and novel research which has led to important contributions to the fields of basic, clinical or translational cancer research, technology development, computational biology or patient treatment:

Binwu Tang, Ph.D., Laboratory of Cancer Biology and Genetics

Staff Scientist/Staff Clinician Leadership Merit Award

In recognition of outstanding creativity and leadership in conducting any aspect of cancer research and patient care:

Matthew J. Anderson, Ph.D., Cancer and Developmental Biology Laboratory

Jennifer A. Kanakry, M.D., NIH Hematology Oncology Fellowship

Kathy McGraw, Ph.D., Laboratory of Receptor Biology and Gene Expression

Staff Scientist/Staff Clinician Outstanding Mentor Award

For exceptional dedication and commitment to the mentoring of junior physicians:

Sofia R. Gameiro, Ph.D., Center for Immuno-Oncology

David Peeney, Ph.D., Laboratory of Pathology

CCR by the Numbers

393 Open Clinical Trials

29 New Clinical Trials

1,686 New Patients

244 Principal Investigators

9 New Faculty Recruits*

5 Newly Tenured Investigators*

296/87 Staff Scientists/ Staff Clinicians

~600 Technical Lab Staff

832/115 Postdoctoral/ Clinical Fellows

375/75 Postbaccalaureate/ Predoctoral Students

207 Summer Students

>1,100 Articles in Peer-Reviewed Journals

64 Technology Facilities and Platforms

Technology Transfer Activities

85 New Employee Invention Reports

27 Issued U.S. Patents

31 New Cooperative Research and Development Agreements (CRADAs)

187 Active CRADAs

92 Clinical CRADAs

7 Umbrella CRADAs

10 New Clinical Trial Agreements (CTAs)

114 Active CTAs

125 New Licenses for CCR Technologies

675 Active Licenses

1 FDA Approval

1 FDA Orphan Drug Designation*

1 FDA Breakthrough Therapy Designation

The **NCI Technology Transfer Center (TTC)** works to enable and guide collaboration, invention development and licensing to advance today's discoveries into tomorrow's medical care. The TTC supports technology development activities for NCI in therapeutics, diagnostics, research tools, vaccines, devices and software and facilitates partnerships with outside organizations so that NCI discoveries can reach the public in a timely manner.

For information on licensing and co-development opportunities, contact the TTC Invention Development and Marketing Unit (**ncitechtransfer@mail.nih.gov**).

Numbers are for fiscal year 2023 unless otherwise marked.
**Numbers are for calendar year 2023.*

CCR Resources

For more information about CCR, the topics mentioned in these stories and the featured researchers, go to:

Center for Cancer Research
https://ccr.cancer.gov

CCR Clinical Trials
https://ccr.cancer.gov/clinical-trials

Developmental Therapeutics Clinic
https://dtc.cancer.gov

NCI CCR Liver Cancer Program
https://ccr.cancer.gov/liver-cancer-program

NCI CCR Comparative Oncology Program
https://ccr.cancer.gov/comparative-oncology-program

NCI Genitourinary Malignancies Center of Excellence
https://ccrod.cancer.gov/confluence/display/CoEGenMal/Home

NCI Center of Excellence in Immunology
https://ccrod.cancer.gov/confluence/display/COEI/Home

Search CCR Principal Investigators by Research Area
https://ccr.cancer.gov/staff-directory/principal-investigators/research-areas

Search CCR Principal Investigators by Disease Focus
https://ccr.cancer.gov/staff-directory/principal-investigators/disease-focuses

Center for Cancer Research

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