NIH NATIONAL CANCER INSTITUTE

CENTER FOR CANCER RESEARCH

MILESTONES

Cancer Research with a Purpose

HIGHLIGHTS 2022–2023

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**.

Often, answering one question in science leads to many more. Like the doors on this year's cover, every piece of research that we conduct at CCR leads to new frontiers, paths and questions to explore in cancer research, many as vast as the open sky. All of our research eventually contributes to progress developing new methods of cancer prevention and toward developing new treatments for people with cancer worldwide.

Credit: *iStock*

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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

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Director's Note

Every piece of research we do in CCR opens doors. The basic discoveries made in our laboratories unlock unexplored new areas of cancer biology and every drug and therapy we test in the clinic gives cancer patients access to new cancer medicines.

This issue of *Milestones* features some of the major scientific advances CCR teams have made in the past year that reveal new aspects of cancer biology and treatment.

The discoveries highlighted here are but a small selection of the broad palette of the meaningful work done in CCR. They all contribute towards our ongoing quest for better, more precise medicines for all people suffering from cancer and to prevent cancer in the first place.

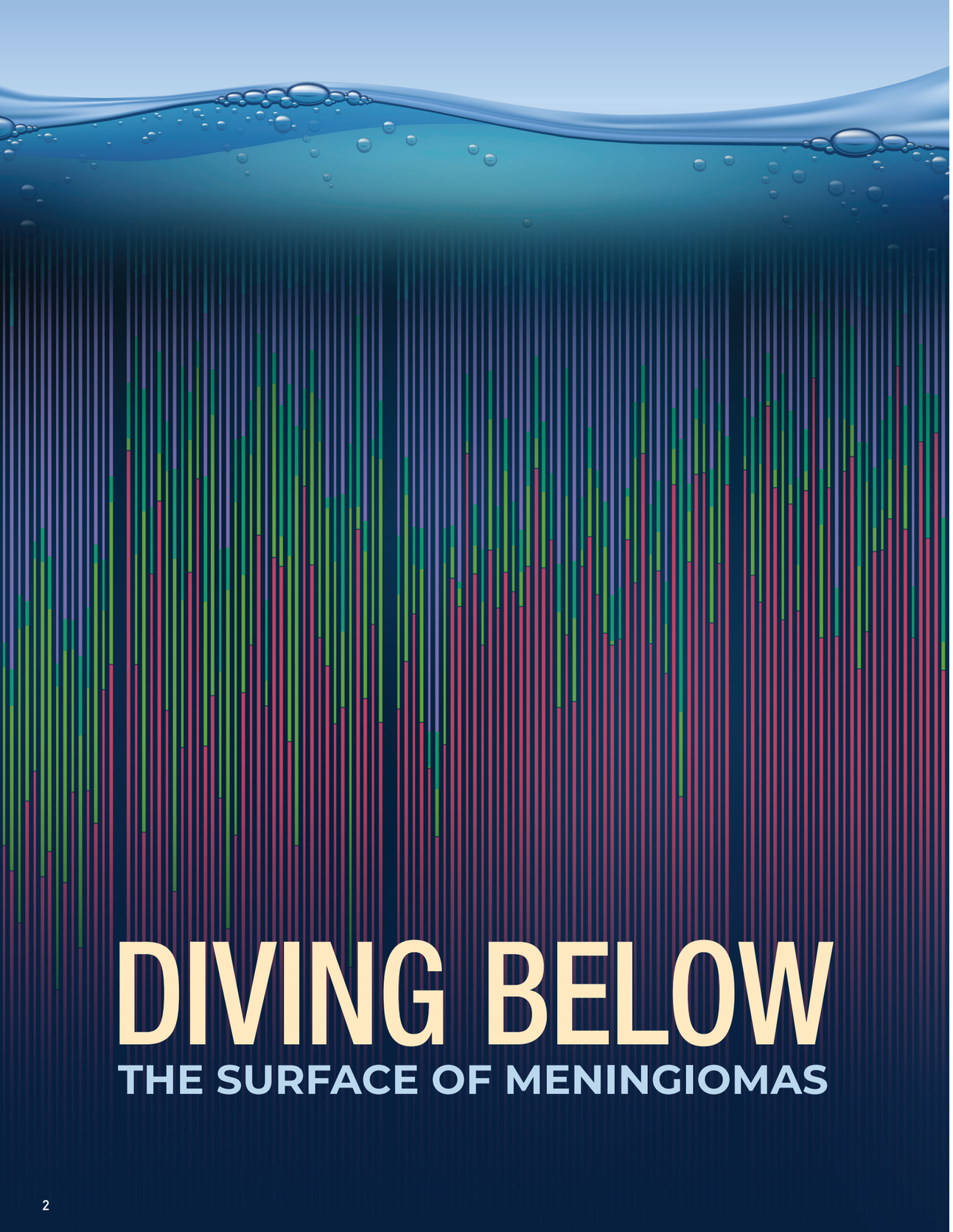
These advances address many of the most pressing challenges in cancer research. CCR scientists have identified novel biomarkers that predict a patient's immunotherapy outcomes or that are associated with higher risk of cancer in specific ethnic groups. We have contributed to the most detailed classification systems of brain tumors based on molecular markers and to powerful new tools to predict the treatment response of immunotherapy and to tailor patient-specific treatments using advanced computational methods and transcriptomics.

A striking example of the importance of precision in medicine is the demonstration of high treatment efficiency in a subgroup of lymphoma patients but not in the general population. Conversely, our scientists are also developing simplified immunotherapy approaches for use in low-resource settings.

Other advances contribute more indirectly to the development of new cancer treatments by uncovering the fundamentals of cancer biology. We harnessed artificial intelligence to generate the most comprehensive characterization of molecular features of T-cell activation, and we discovered the molecular fingerprint of the most effective T cells for use in cell-based immunotherapy approaches. We developed advanced imaging techniques to visualize the atomic structure of cancer signaling molecules and we observed cancer stem cells in action using live cell microscopy.

Much of what we do in CCR is about opening doors. We are fascinated by the unknown that lies beyond them and we are motivated by the new opportunities we will find. Some doors open to new discoveries, some unlock new treatments, but all offer a vista of progress and hope for every cancer patient.

Tom Misteli
Director
NCI Center for Cancer Research



A detailed molecular analysis reveals four subtypes of a common brain cancer.

Kenneth Aldape, M.D.
Chief
Laboratory of Pathology

Meningiomas are relatively common tumors that form in the membrane lining the brain. Although most of the time these tumors are not aggressive and can be treated with surgery, there are limited treatment options for more aggressive cases.

To better understand the biology of this cancer and identify new therapies for it, a multi-national consortium co-led by Senior Investigator **Kenneth Aldape, M.D.**, conducted a thorough molecular analysis of meningiomas, identifying four subtypes of the disease, as well as one potential treatment for a particularly aggressive subtype. The results were published in *Nature*.

"Even if most meningiomas are benign, the brain tumor can affect the person's life in important ways in terms of neurological deficits, and can be lethal in some cases," explains Aldape, noting that there are currently no drugs approved by the U.S. Food and Drug Administration (FDA) to treat meningiomas.

This prompted Aldape and his CCR colleagues to partner with researchers at the University of Toronto and the International Consortium on Meningiomas to conduct a large-scale analysis of meningiomas. Specifically, they analyzed DNA copy numbers, gene mutations and RNA expression, as well as DNA methylation, which influences DNA expression. "We wanted to define robust subtypes and the only way to do that would be to get this composite of molecular data," explains Aldape.

The team then applied a machine learning algorithm to the data to identify four previously unknown molecular subtypes of meningioma. The subtypes differ in their immunogenic features, genetic mutations, metabolism and aggressiveness.

Next, the researchers cross-referenced the gene activity patterns of the meningiomas to a database of FDA-approved drugs, exploring whether any existing therapies could be suitable candidates for treating each subtype. These results suggested that the drug vorinostat may be effective against MG4, one of the more aggressive subtypes. Vorinostat binds to the active site of enzymes known as histone deacetylases, which alter chemical modifications of major DNA-binding proteins.

In follow-up experiments, the researchers showed that vorinostat in fact can impair the viability of MG4 cancer cells in a petri dish and can limit tumor growth and improve survival in mice with MG4 tumors.

Aldape notes that this study will advance research on meningiomas in several ways, including the development of better animal models to study the various subtypes of meningioma and the development of new targeted therapies.

"Further work will examine whether specific drugs will work against the different subtypes of these tumors," says Aldape, noting it's exciting to be learning new insights into this understudied type of brain cancer.

Nassiri, F. et al. *Nature*. 2021 Aug 25;597(7874):119-125.

A deeper look at the molecular makeup of meningiomas revealed four distinct subtypes of the common brain tumor. These bars — shown here below the surface of water — illustrate how the proportions of T cells (blue), macrophages (purple), endothelial cells (dark green), fibroblasts (light green) and neoplastic cells (red) vary in tumor samples from patients with the four subtypes. These variations helped to define the four subtypes, separated here by thick dark bars. Identifying and describing the subtypes will help researchers better predict the aggressiveness of patients' tumors and select better treatment options. Credit: Nassiri, F. et al. Nature*; SPGM, FNL, NCI, NIH; iStock*

PHOENIX RISES

A second look reveals a highly effective lymphoma treatment.

Louis M. Staudt, M.D., Ph.D.
Chief
Lymphoid Malignancies Branch

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

Senior Investigators **Louis Staudt, M.D., Ph.D.**, and **Wyndham Wilson, M.D., Ph.D.**, have been working together at CCR for decades to develop targeted therapies for patients with diffuse large B-cell lymphoma (DLBCL). While Staudt conducts the basic science experiments, Wilson leads the clinical work. Their expectations were high when one of those therapies was tested in a large, international trial called PHOENIX. On paper, it should have been an effective anti-cancer treatment, yet when all data was analyzed, the trial fell short of its expectations and was deemed unsuccessful.

However, digging just a little deeper, Staudt and Wilson conducted an analysis of a subset of the PHOENIX data. They report in a study published in *Cancer Cell* that the drug being investigated, a cell signaling inhibitor called ibrutinib, in combination with standard chemotherapy, was highly effective in patients under the age of 60 with some subtypes of lymphoma — resulting in 100% event-free survival and 100% overall survival after three years.

"The results were the most amazingly perfect example of precision medicine that you would ever want to see," says Staudt. "We had preliminary reasons to think that people with certain subtypes of DLBCL should respond to ibrutinib, which were supported beautifully by the trial results."

In earlier pioneering work, Staudt had identified genetically unique subtypes of DLBCL, including some subtypes that rely on B cell receptor (BCR) signaling to survive. Subsequently, ibrutinib was developed as an anti-cancer drug to block this mechanism. The first analysis of the PHOENIX study data, however, did not show a large enough improvement in outcomes for all patients for the U.S. Food and Drug Administration to approve ibrutinib for this indication. "We thought not approving ibrutinib was basically throwing the baby out with the bath water, if you will," says Wilson.

Motivated by their extensive understanding of the molecular features of various DLBCL subtypes, Staudt and Wilson decided to revisit the data. In their re-analysis of the PHOENIX outcomes, every person under the age of 60 with DLBCL subtypes called MCD or N1 who was given ibrutinib in combination with chemotherapy was still alive after three years. Those with the MCD or N1 subtypes who received only chemotherapy had survival rates of 70% and 50%, respectively. For people over the age of 60, the combination of ibrutinib with chemotherapy was associated with too many severe side effects, which made the use of the drug impractical for them, hence the initially unsatisfactory results.

Staudt and Wilson note that their unique position at CCR — where they can conduct a follow-up study without needing to apply for a grant — was critical for confirming ibrutinib's potential as a targeted therapy. Their partnership, as well, where basic science and clinical data are used in tandem to advance science, has been key to their success, they say.

Wilson, W.H., et al. *Cancer Cell*. 2021 Dec 13;39(12)1643-1653.e3.

A second look at data from the PHOENIX trial yielded amazing results and appropriately generated new life for the aptly named study. Most patients enrolled in the large, international trial to test the combination of a new targeted drug, ibrutinib, and chemotherapy for diffuse large B-cell lymphoma (DLBCL) did not benefit enough from the treatment, but a well-defined subset of patients did. Here, the mythical phoenix bird rises from the ashes to new life. Credit: Elina He, NIH Medical Arts

THE KISS OF THE MACROPHAGE

Breast cancer cells undergo dangerous reprogramming within passageways that connect tumors to the bloodstream.

Lalage M. Wakefield, D.Phil.
Senior Investigator
Laboratory of Cancer Biology and Genetics

Cancer's excessive, uncontrolled growth is its most malicious trait. But there is reason to believe that only a tiny and elusive subset of cancer cells truly drive a tumor's growth: the so-called cancer stem cells. These cells' unusual resilience and ability to divide in stressful settings may also make them efficient instigators of metastasis, which occurs when cells break off from a primary tumor and make their way to other locations in a patient's body, often via blood vessels.

Senior Investigator **Lalage Wakefield, D.Phil.**, and her colleagues watched cancer cells as they began their metastatic journey in mice using a microscopy technique developed by collaborators Maja H. Oktay, M.D., and John Condeelis, Ph.D., at Albert Einstein College of Medicine, New York. Working with a biosensor developed in Wakefield's lab, they found that many of those cells took on properties of cancer stem cells the moment they broke free of a tumor.

Because the biosensor lights up when cancer cells take on stem cell properties, Wakefield and her team could watch in real time as human breast cancer cells left tumors and entered the bloodstream in living mice. They were able to capture a movie of this transformation and their observations were reported in *Nature Communications*.

To access the bloodstream, breast cancer cells must pass through specific portals that connect the tumor surface to a blood vessel's outer wall. Three different types of cells come together to form these portals, and it was one of these — the macrophages — that the researchers found triggered migrating cancer cells to take on the properties of cancer stem cells. Macrophages are a type of white blood cell, some of which can support tumor growth and metastasis.

"We observed a number of instances where, when a non-stem cancer cell came into close proximity with the macrophage, the macrophage turned it into a cancer stem cell. That interaction — a cellular 'kiss' — essentially gave your standard tumor cell the superpowers of a cancer stem cell," Wakefield says. Following the transformation, she says, cancer cells would have heightened abilities to disseminate through the body, invade tissues and resist most types of cancer therapy.

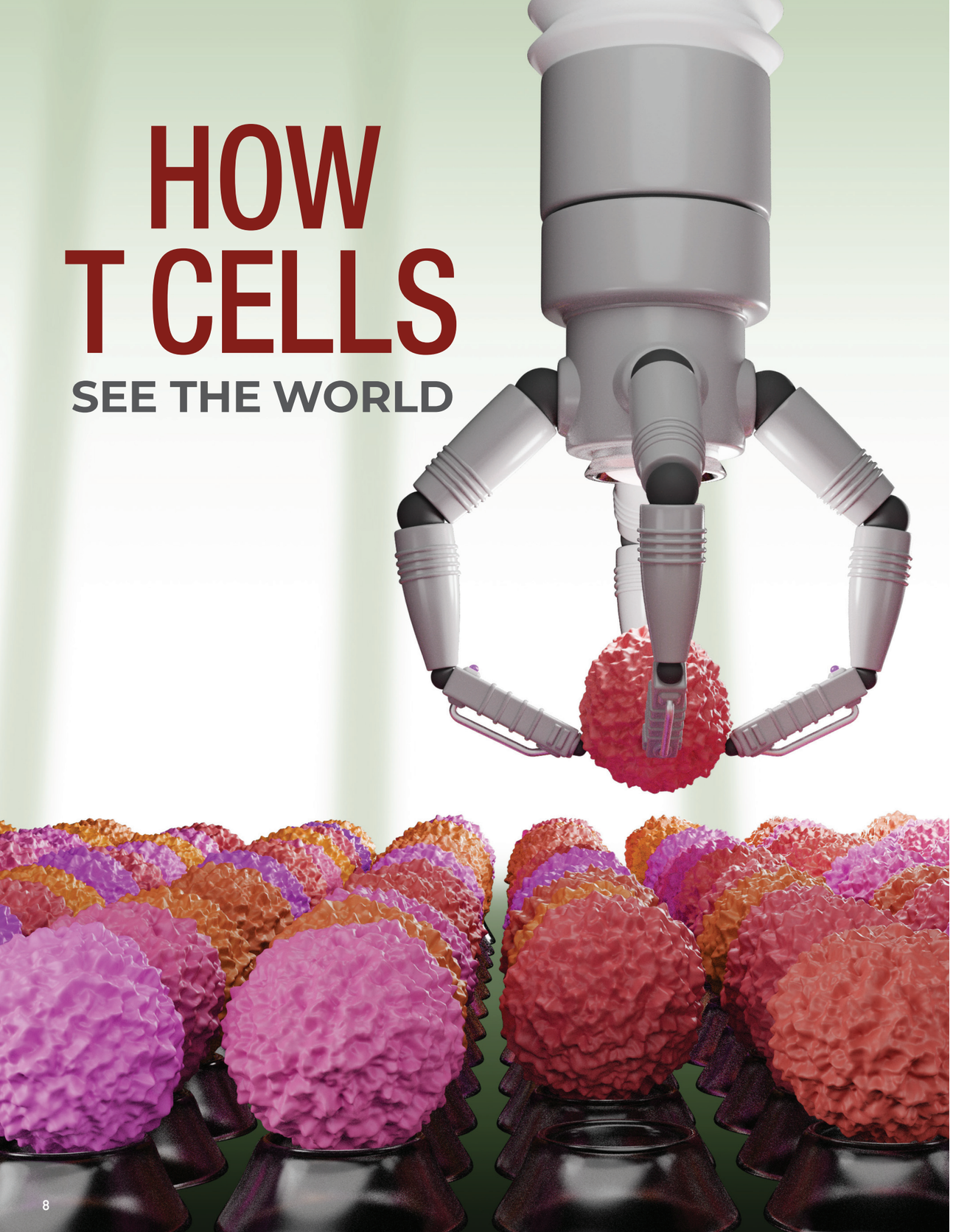
Since every cancer cell that passes through a portal into a blood vessel must squeeze past a macrophage, these interactions happened over and over again. While only about 1% of the cells in the primary breast tumors they studied were cancer stem cells, Wakefield and her colleagues found that more than 60% of tumor cells had taken on that more aggressive identity by the time they entered the bloodstream.

Incidentally, in patients with breast cancer, high densities of tumor-to-blood-vessel portals are associated with an increased risk of metastasis. Wakefield's team has identified the signal that macrophages use to trigger tumor cells' transformation to cancer stem cells. The next step? They think it may be possible to block the dangerous reprogramming that goes on within these cellular passageways.

Sharma, V.P., et al. *Nat. Commun.* 2021 Dec 15;12(1):7300.

To access the bloodstream and travel to other parts of the body, cancer cells must pass through a portal made up of three cells. In transit, the cancer cell is "kissed" by one of these three — a macrophage — and the cancer cell takes on new stem cell-like properties. Using a biosensor that lit up when the cell took on these new attributes, CCR researchers and colleagues at the Albert Einstein College of Medicine were able to record this transformation. Stills from the video of the "macrophage kiss" can be seen here. A better understanding of this process may help researchers prevent cancer from spreading. Credit: Ved P. Sharma, Albert Einstein College of Medicine; SPGM, FNL, NCI, NIH; iStock

HOW T CELLS SEE THE WORLD



Artificial intelligence untangles the cellular signals that matter for anticancer immunity.

Grégoire Altan-Bonnet, Ph.D.
Senior Investigator
Laboratory of Integrative Cancer Immunology

T cells are the immune system's anticancer warriors. When they come across a cancerous cell, T cells can go on the attack. But not every tumor triggers a robust immune response, and even when the immune system does recognize a threat, not every T cell engages in the fight.

Senior Investigator **Grégoire Altan-Bonnet, Ph.D.**, and his colleagues have turned to artificial intelligence to make sense of the complex cellular communications that determine the outcome of a T cell's interaction with a tumor. In a study reported in *Science*, they developed a model to predict how T cells will respond to specific immune-stimulating molecules called antigens, including those found on the surface of tumor cells. To obtain the necessary data for the model, Altan-Bonnet's team designed and built a robotic platform that can carry out thousands of experiments at the same time. The model, Altan-Bonnet says, will aid in the development of more effective cancer immunotherapies.

The goal of cancer immunotherapy is to help a patient's immune system find and destroy cancer cells, but the treatments available today do not always work. Altan-Bonnet says part of the challenge in making immunotherapy effective for more patients is the overwhelming complexity of T cells' antigen responses.

"T cells do many different things when they get activated, and we don't know what to look at to predict what matters in terms of cancer immunotherapy," he says. "We know a lot about the way these T cells are wired, but we can't take a T cell and predict whether it's going to be a good T cell, which can go and fight, or whether it's a T cell that is not going to be very responsive against the tumor."

To make better predictions about how T cells will respond to tumors, Altan-Bonnet and collaborator Paul François, Ph.D., at McGill University in Montreal, knew they needed a comprehensive catalog of how various antigens impact T-cell signaling.

With the help of their custom-built robot, they used their system to measure seven key immune signals, monitoring how each signaling molecule rose and fell in the hours and days after T cells were exposed to various antigens. After generating an enormous volume of data, they used artificial intelligence to find patterns within it and make predictions about T cell behavior. Their model, which was built using data from mouse T cells, accurately predicts how human T cells respond to tumor antigens. It can also predict the behavior of engineered T cells, such as the CAR (chimeric antigen receptor) T cells used in some cell-based cancer immunotherapies.

The new model doesn't just predict T cell behavior. It exposes the underlying biology of the system, helping to reveal how T cells make the decisions that shape their behavior. "We've learned the rules of the way T cells see the world," says Altan-Bonnet.

Achar, S.R., Bourassa, F.X.P., Rademaker, T.J., et al. *Science*. 2022 May 20;376(6595):880-884.

This image is a reimagination of the custom robot that CCR researchers developed to investigate how T cells react to seven different stimuli. The robot is capable of conducting thousands of experiments at the same time and gathering an enormous amount of data. Researchers applied artificial intelligence to this data to predict how T cells will behave in response to proteins on tumor cells. These insights could help improve immunotherapy responses in the future. Credit: Joseph Meyer, SPGM, FNL, NCI, NIH; Grégoire Altan-Bonnet, CCR, NCI, NIH; DALL•E AI Art Generator

A RED FLAG FOR IMMUNOTHERAPY

A potential new marker for immunotherapy response could help guide treatment decisions.

Mary N. Carrington, Ph.D.
Senior Investigator
Laboratory of Integrative Cancer Immunology

James L. Gulley, M.D., Ph.D.
Co-Director
Center for Immuno-Oncology

Immune checkpoint inhibitors and other cancer immunotherapies can empower the body's immune system to fight tumors so effectively that they sometimes bring advanced cancers into long-lasting remission. But it's hard to predict which patients will have lasting results.

As patients and their doctors consider whether to try immunotherapy treatments, a discovery from CCR scientists reported in *The Lancet Oncology* could help inform their decision. Researchers led by Senior Investigators **Mary Carrington, Ph.D.**, and **James Gulley, M.D., Ph.D.**, have found that people with a genetic marker called *HLA-A*03* may be less likely than others to respond to immune checkpoint inhibitors. Up to 16 percent of people in the United States carry *HLA-A*03*.

"The incredible thing about immune checkpoint inhibitors is you get rapid, deep and durable responses in patients — but it's only a subset of patients, and it does come with a potential cost of side effects," Gulley says. "If there are patients that are less likely to benefit, that would be good to know up front."

Immune checkpoint inhibitors work by releasing a natural brake on cancer-fighting immune cells. But for the treatment to shrink tumors, the immune system must be able to find its targets. That recognition depends in part on proteins called human leukocyte antigens (HLAs), which help alert the immune system when cells become infected or cancerous. There are thousands of different versions of HLA proteins. Every person carries the genes that encode three to six distinct versions of class I HLA molecules, and their particular set of HLAs helps shape how their immune system responds to specific threats.

"These genes are so central to the immune response," Carrington says. "They are hugely polymorphic [meaning they come in different forms] and those polymorphisms determine how we respond to this virus or against this tumor." It seemed likely, she says, that some *HLA* genes could either help or hinder the body's response to immune checkpoint inhibitors. So, she teamed up with Gulley to find out.

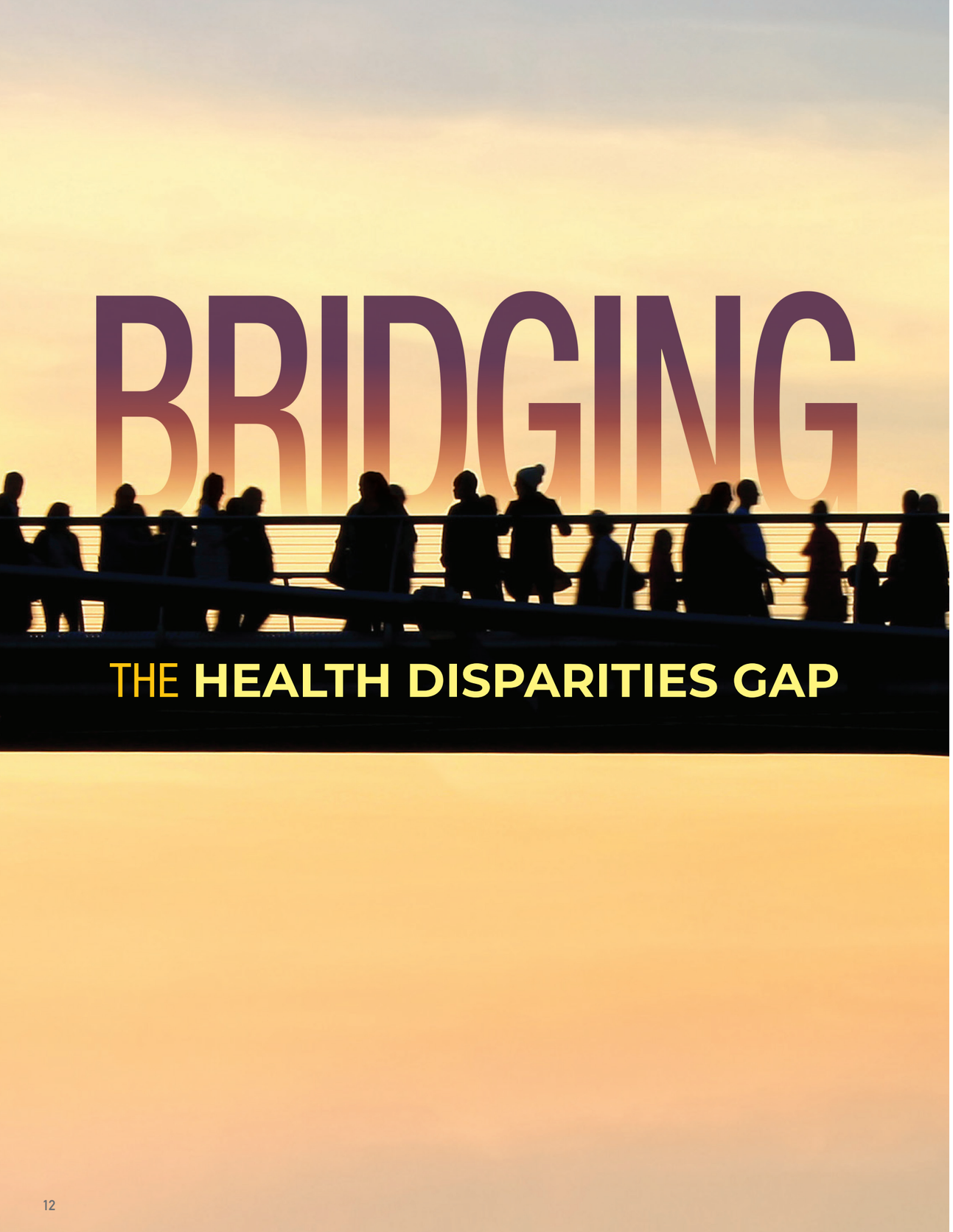
After analyzing data from thousands of patients, they found that regardless of which type of cancer a patient had or which checkpoint inhibitor they had received, most people with the HLA known as *HLA-A*03* benefitted less from the immunotherapy than people without *HLA-A*03*. Compared to other patients who received the same treatment, their survival after diagnosis was shorter and they saw their cancer return more quickly.

In one group of patients with kidney cancer, the team found that among patients with *HLA-A*03*, outcomes tended to be no better for people treated with immune checkpoint inhibitors than they were for people who received standard chemotherapy — even though the study had found that overall, immunotherapy was associated with longer survival times than chemotherapy. The researchers found no evidence linking *HLA-A*03* to a poor response to chemotherapy.

While *HLA-A*03* was associated with worse outcomes after immune checkpoint inhibitors overall, not every person with *HLA-A*03* included in the analysis responded poorly to those drugs. Additional data from past and ongoing clinical studies will help researchers further assess *HLA-A*03*'s relationship to immunotherapy outcomes. Gulley and Carrington say that if the marker is validated as a reliable predictor of patient response, it could give patients and their doctors important information to consider alongside other predictive factors as they decide whether to choose an immune checkpoint inhibitor to treat their cancer.

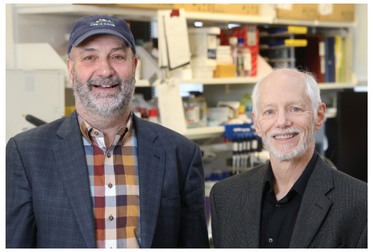
Naranbhai, V., Viard, M. et al. *Lancet Oncol*. 2022 Jan;23(1):172-184.

*CCR researchers found that people with the protein HLA-A*03 on their cells benefited less, as a group, when treated with immune checkpoint inhibitors compared to those with other HLA types. The presence of* HLA-A*03 *in patients beginning immunotherapy could raise an important red flag. The next course of action is to determine the biological mechanism that explains this observation. Credit: iStock*



BRIDGING THE HEALTH DISPARITIES GAP

Aggressive breast and prostate cancers in African Americans have distinct molecular features.



Stefan Ambs, Ph.D., M.P.H.
Senior Investigator
Laboratory of Human Carcinogenesis

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

Many health disparities across ethnic groups are predominantly caused by socioeconomic and environmental factors. But biological factors can also play a role. CCR researchers have identified several molecular features associated with aggressive and lethal prostate and breast cancers in African Americans — potentially creating opportunities for more targeted therapies and reduced health disparities.

One study, led by Senior Investigator **Stefan Ambs, Ph.D., M.P.H.**, sought to better understand why African Americans disproportionately develop aggressive prostate cancer and are more likely to die from the disease compared to European Americans. To do so, Ambs and his team analyzed a large dataset that includes about 2,000 African American and European American men recruited primarily in and around Baltimore, Maryland, as well as a group of African men in Ghana. Whereas previous similar studies typically focused on analyzing tumor cells, Ambs' team chose to analyze cancer-related immune signatures in the blood.

The results, published in *Nature Communications*, show a clear trend. Certain immune signatures associated with suppressed tumor immunity and more metastatic and lethal prostate cancers were found more frequently in Ghanaian and African American men compared to European American men. In particular, in African American men, two biomarkers, pleiotrophin, a pro-metastatic factor that regulates blood flow to tumors, and TNFRSF9, which regulates T cells, predicted poor disease survival among patients.

Ambs says these results suggest that African American men with suppressed systemic anti-tumor immunity might respond better to certain therapies that boost the immune system, and notes that other recent studies support this theory.

"We, as health disparity researchers, have really done something here in terms of helping clinicians tailor how they treat patients," Ambs emphasizes. "Based on whether their patients have these biomarkers, clinicians might be able to decide if immunotherapy should be given or not."

Several years ago, Ambs uncovered another health disparities pattern when he was sifting through a different dataset — this time related to breast cancer in African American women. He noticed increased RNA expression of a ubiquitin ligase, gp78, which helps to degrade proteins, in this population. To follow up on this finding, he alerted a CCR colleague, Senior Investigator **Allan Weissman, M.D.**

Weissman has spent more than 20 years studying ubiquitin ligases and had previously shown that increased expression of gp78 promotes the formation of metastases in sarcoma. Weissman in turn teamed up with collaborator Kevin Gardner, M.D., Ph.D., now at Columbia University, New York, who had been diligently collecting tumor samples from more than 500 breast cancer patients in North Carolina.

Their analysis, published in *JCI Insight*, showed that increased protein expression of gp78 is independently associated with more aggressive disease and poor breast cancer survival in African American women.

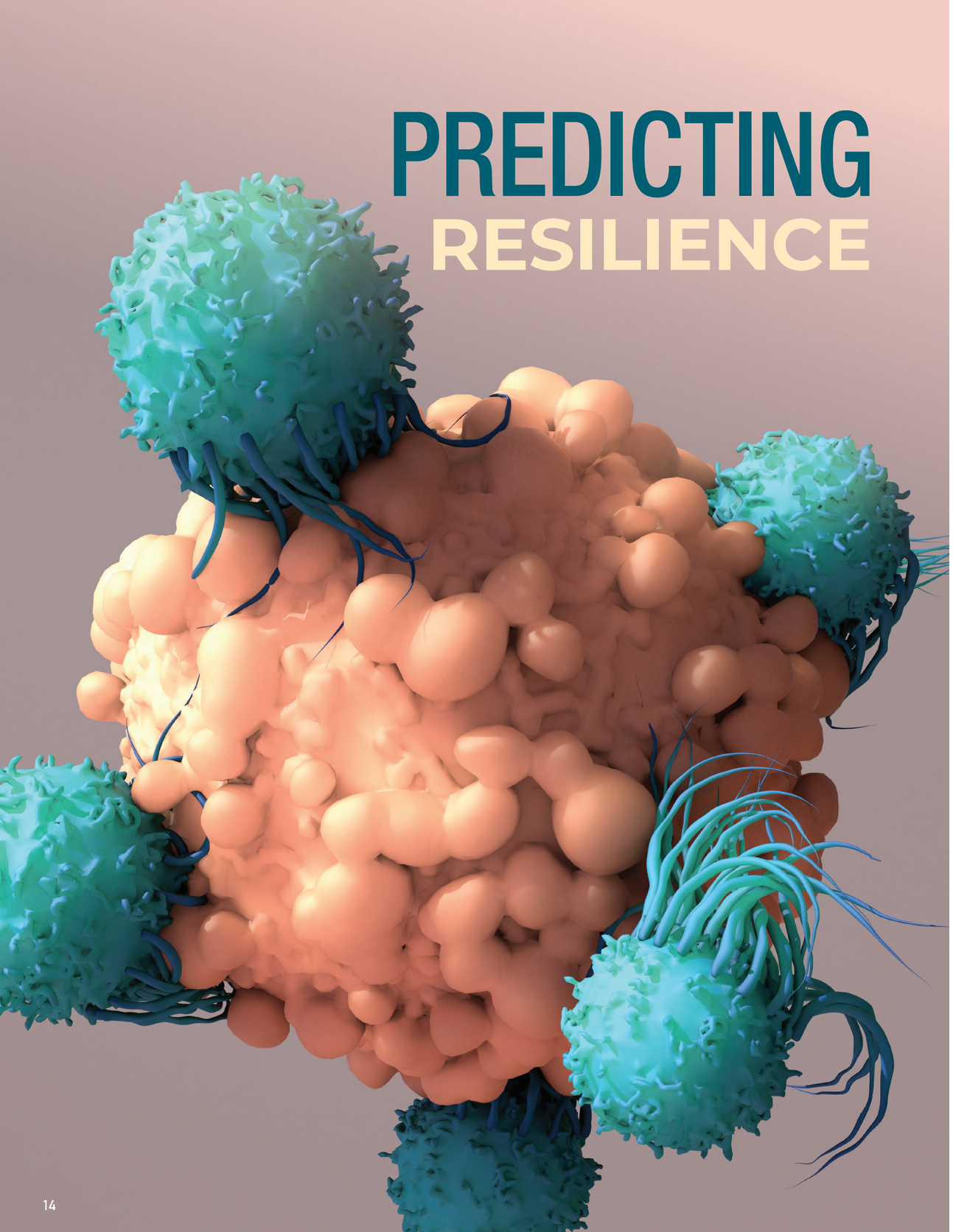
Weissman says this finding could help clinicians better predict their patients' prognoses, but also has broader therapeutic implications. "Knowing so much about the protein from our previous basic research provides opportunities to develop new strategies for more precise patient-specific breast cancer treatments."

Health disparities research involves multi-faceted challenges and requires multi-faceted solutions. These studies are important first steps for understanding the molecular differences in tumor biology across diverse populations to help develop new therapies to close the health disparities gap.

Minas, T.Z., Candia, J., et al. *Nat Commun*. 2022 Apr 1;13(1)1759.
Singhal, S.K., et al. *JCI Insight*. 2022 May 31;7(13)e157465.

These two studies found molecular differences in prostate and breast cancers for people with African ancestry. Understanding these differences may help clinicians develop new treatments to bridge health disparity gaps for these two cancers, illustrated by the suspension bridge in this image. Credit: iStock

PREDICTING RESILIENCE



To fight cancer, T cells must first overcome a tumor's hostile environment to reach their target.

Peng Jiang, Ph.D.
Stadtman Investigator
Cancer Data Science Laboratory

Many cancer immunotherapies work by bolstering a patient's T cells. However, in solid tumors, the tumor microenvironment that surrounds the cancer cells can be treacherous, and not all T cells are well equipped to survive it. If one could predict the resilience of a patient's T cells in this hostile environment, more effective immune-directed treatments could be developed.

A team of CCR researchers, led by Stadtman Tenure-Track Investigator **Peng Jiang, Ph.D.**, has created a computational tool called *Tres* (tumor-resilient T cell model) that analyzes gene activity in T cells to determine their resilience in a tumor environment. The tool will help researchers better evaluate an individual's treatment options and find the best possible treatment. The team's findings were published in *Nature Medicine*.

"One common approach in our work as a data science lab is to develop computational models that can repurpose large amounts of existing data to reveal new findings," Jiang says. For example, cells have a lot of information in their transcriptomes, which are catalogs of expressed genes that characterize a cell's unique profile and how it functions.

To build the *Tres* model, Trang Vu, Ph.D., a postdoctoral fellow in Jiang's lab, and Yu Zhang, M.D., Ph.D., a visiting graduate student, used existing patient single-cell RNA molecule transcriptomes to identify T cells that have gene signatures that allow them to proliferate even when exposed to a highly immunosuppressive tumor environment.

Applying this model to T cells from patients with melanoma, breast, lung or blood cancers, Vu and Zhang calculated resilience scores to predict how well the cells survived in the tumor environment. They found that patients with the most resilient T cells were more likely to respond well to immunotherapy and the resilience scores accurately predicted outcomes for patients that underwent various types of immunotherapies.

In addition to predicting patient response, Jiang found that *Tres* can also be used to discover new T-cell regulators that can be targeted to enhance T-cell function. As proof of principle, Jiang's team linked the activity of a gene called *FIBP* to T-cell resilience and discovered that turning it off boosted the ability of T cells to kill cancer cells in cultured cells and in mice. "This finding highlights *FIBP* as a potentially important drug target," Jiang says. "The gene may serve as a metabolic switch that can make the T cells more effective."

Tres is freely available online for public use. "Our tool can be used by anyone in the cancer research community to uncover new biomarkers," says Jiang. "We hope it will provide useful insights to improve current immunotherapies and develop new treatment options as well."

Zhang, Y., Vu, T., Palmer, D.C., et al. *Nat Med*. 2022 May;28(7):1421-1431.

T cells, shown here as smaller blue cells attacking a larger cancer cell, are a crucial part of the immune system's fight against cancer. But many cannot survive in the often-hostile environment that surrounds the cancer cells. A new tool will help identify the biomarkers of T cells that mark them as resilient to this harsh environment and allow them to persist in their pursuit to destroy cancer cells. Credit: iStock

NARROWING THE SEARCH

Elusive tumor-targeting T cells share a telltale gene activity signature.

Steven A. Rosenberg, M.D., Ph.D.
Chief
Surgery Branch

When standard cancer treatments fail to keep cancer in check, cell-based immunotherapies can bolster the body's own anticancer defenses. These highly customized and sophisticated treatments are created from a patient's own immune cells and are either selected or engineered to be able to specifically recognize the patient's tumor as a target.

In an advance that could accelerate the development of more effective immunotherapy treatments, researchers in the lab of Senior Investigator **Steven Rosenberg, M.D., Ph.D.**, have made tumor-targeting immune cells much easier to find. As reported in *Science* and *Cancer Cell*, they have identified patterns of gene activity shared by tumor-reactive T cells.

Usually, one finds tumor-reactive T cells inside a tumor itself. They recognize their targets based on markers on cancer cells. But tumor-reactive T cells make up only a tiny fraction of a person's army of immune cells. Even inside tumors, they are outnumbered by T cells of other types, so finding them can be challenging.

In meticulous, cell-by-cell analyses of tumor-reactive T cells taken from patient tumors, Research Biologist Frank Lowery, Ph.D., Research Fellow Sri Krishna, Ph.D., and Staff Scientist Ken-ichi Hanada, M.D., Ph.D., found that tumor-reactive T cells shared a characteristic pattern of gene activity. Guided by this gene activity signature, researchers can more easily find T cells that respond to a specific tumor.

Even once located, the tumor-reactive cells may not be strong enough to mount an effective attack. Rosenberg explains that while the T cells isolated from patient tumors are often tumor-reactive, they may also be exhausted and ineffective.

However, researchers can still learn from them how to equip other more vigorous immune cells with receptor molecules so that they can home in on the cancer. "Once we can identify the T cells, we can identify the T-cell receptors and put them into a patient's normal cells that we can then grow and use for treatment," Rosenberg says.

Rosenberg's lab pioneered the use of tumor-infiltrating T cells as cancer immunotherapy decades ago. The approach has been most successful in treating melanoma — sometimes with long-lasting results. Rosenberg and his colleagues have also found that this type of immunotherapy can shrink other types of solid tumors, including colon, liver and cervical cancers.

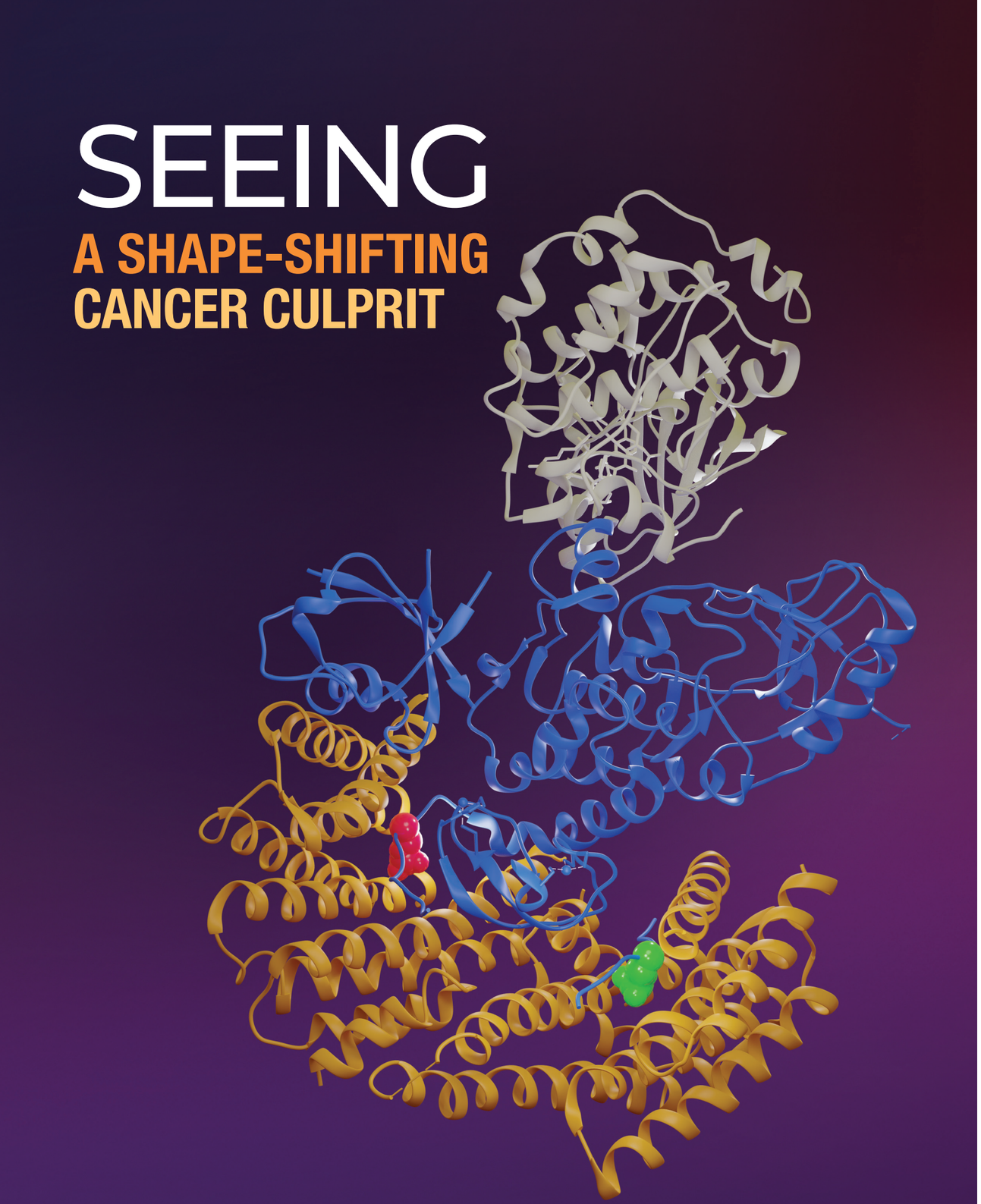
In 2022, they reported on successes in treating advanced breast cancer in the *Journal of Clinical Oncology*. They found tumor-reactive T cells in the majority of tumor samples they examined, and three women whose disease had failed to respond to other forms of therapy saw their tumors shrink dramatically following treatment with tumor-targeting T cells and a short course of the immunotherapy drug pembrolizumab. One saw her cancer disappear completely and remains cancer-free years after the treatment.

Still, many patients who receive cell-based immunotherapies do not benefit. Rosenberg and his colleagues want to know what happens when things go right so they can develop treatments that work for more people. "We're chipping away at this mystery of how to get the immune system to work against the cancer and provide improved treatments for patients," he says.

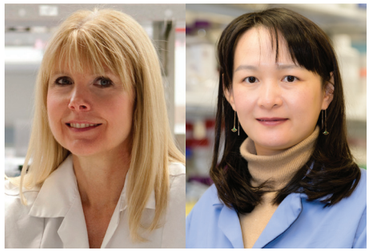
Lowery, F.J., Krishna, S., et al. *Science.* 2022 Feb 25;375(6583):877-884.
Hanada, K.I., et al. *Cancer Cell.* 2022 May 9;40(5):479-493.e6.
Zacharakis, N., et al. *J Clin Oncol.* 2022 Jun 1;40(16):1741-1754.

T cells that react to a patient's tumor can be used to develop immunotherapy treatments but can be hard to find. Inside of this hourglass, thousands of dots each represent a single T cell from a patient's tumor sample. CCR researchers examined the cells one by one and grouped them by their mRNA and protein expressions. In this analysis, they found that one group, 2.5% of these cells, included tumor-neoantigen reactive cells (red dots). Using this genetic signature to find these elusive tumor-reactive cells faster should also accelerate the process of creating these immunotherapies for cancer patients. (Gray T cells are CD4⁺; blue are CD8⁺ and don't express CXCL13*; red are CD8⁺ and do express* CXCL13.*) Credit: Ken-ichi Hanada, CCR, NCI, NIH; SPGM, FNL, NCI, NIH; iStock*

SEEING
A SHAPE-SHIFTING CANCER CULPRIT



The architectural details of a notorious cancer-promoting protein offer clues about how to keep it safely switched off.



Deborah K. Morrison, Ph.D.
Chief
Laboratory of Cell and Developmental Signaling

Ping Zhang, Ph.D.
Stadtman Investigator
Center for Structural Biology

The growth of many skin cancers is driven by a mutated, overactive version of a protein called BRAF. Even without mutations in the gene, BRAF helps drive excessive growth of cancer cells, because it is an essential partner of another commonly mutated, growth-promoting protein called RAS. The RAS protein is one of the most common drivers of human cancer — but it can only stimulate cell growth with the help of BRAF.

Senior Investigator **Deborah Morrison, Ph.D.**, and Stadtman Investigator **Ping Zhang, Ph.D.**, have now used sophisticated atomic imaging methods to reveal the structure of BRAF in two distinct states: in its active and inactive forms. Those studies, reported in *Nature Communications*, are the first to depict the full BRAF protein at atomic resolution. The data show how the protein dramatically reconfigures itself as it shifts from its inactive to active form — an insight that could help guide the design of a drug that could lock BRAF into its inactive state so that it can no longer drive the growth of cancer cells.

Morrison's team, which has studied BRAF for decades, was able to produce BRAF in animal cells and extract it in association with members of the 14-3-3 protein family. Then Zhang and her team used cryo-electron microscopy to take a series of very high-resolution snapshots, capturing the molecules from all angles.

BRAF molecules work in pairs. When cell growth is not needed, they remain separate, folded up into their inactive form. 14-3-3 proteins act as a molecular clamp that locks each BRAF molecule into this inhibited state. Interaction with RAS disrupts that configuration, freeing the BRAF molecules to pair up and relay growth signals through the cell, and in this way contributes to cancerous cell growth.

With the new electron microscopy images, Zhang and Morrison's teams were able to assemble three-dimensional structures of BRAF in both its solitary, inhibited state and in its active, paired-up form. Those structures reveal some unexpected details about how autoinhibited BRAF transitions into its active state when it interacts with RAS. For example, it appears that RAS may shove the 14-3-3 protein aside, enabling BRAF to unfold into a shape that can grab onto another BRAF molecule.

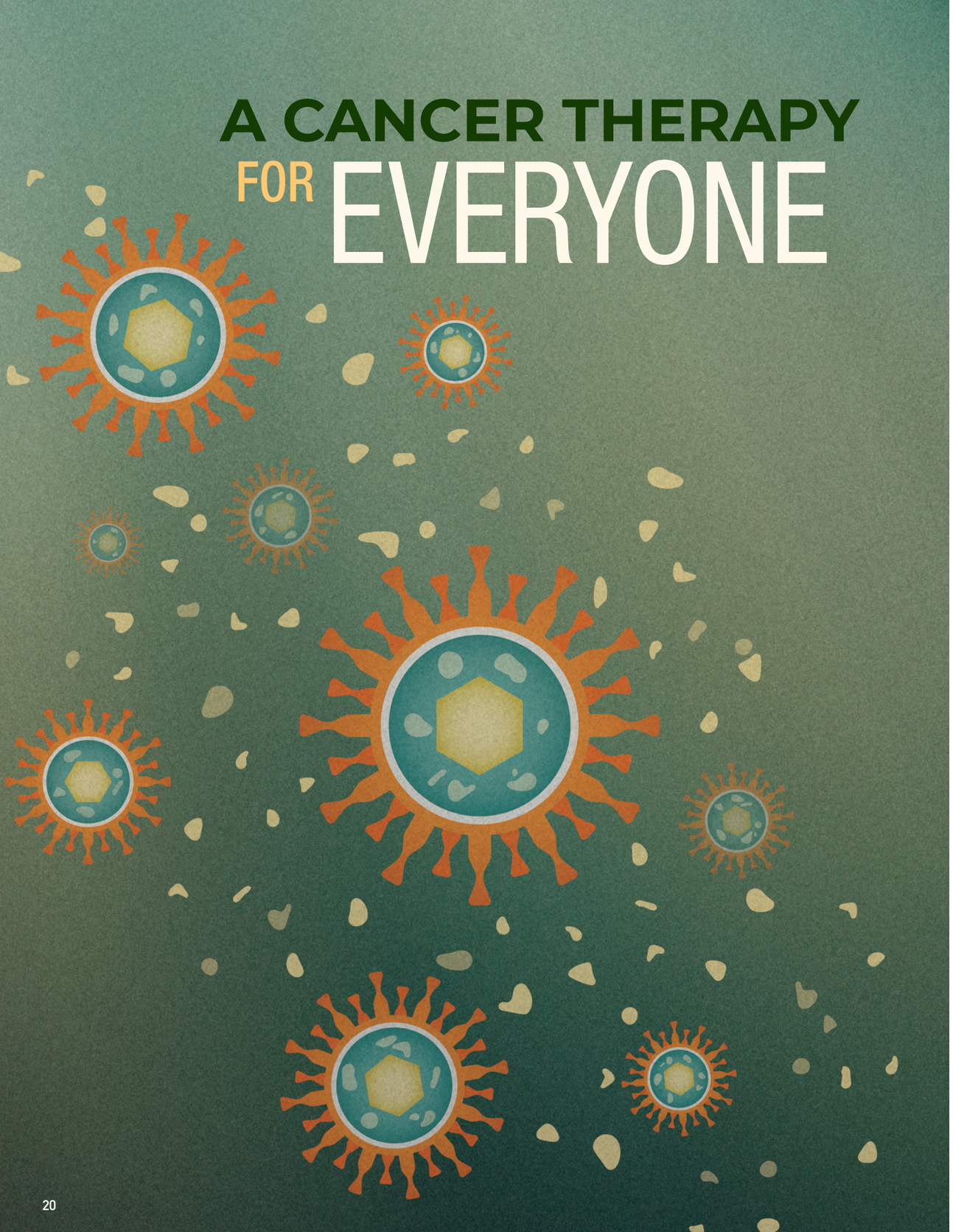
"We have a picture of the starting and end points," says Zhang. "From here we can understand how RAS binds to the autoinhibited BRAF as a whole complex and how that binding can initiate BRAF activation by releasing it from its autoinhibitory state."

Zhang and Morrison are excited about these findings because their new structures could help drug developers figure out how to block the interaction between BRAF and RAS. Knowing the precise configurations of these key cancer players could also suggest ways to halt BRAF's activity so it can no longer trigger cell growth, with or without RAS. "If you could find a way to stabilize the autoinhibited state, that could be useful in drug design," Morrison says.

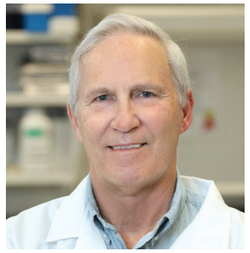
Fiesco, J.A.M., Durrant, D.E., Morrison, D.K., Zhang, P. *Nat Commun.* 2022 Jan 25;13(1):486.

BRAF and other RAS pathway proteins are notorious in cancer development. This 3D structure shows inactive BRAF (blue, middle) bound to MEK (gray, top) and two 14-3-3 proteins (yellow, bottom). The 14-3-3 proteins bind to the pS729 (red) and pS365 (green) sites in the BRAF protein. Knowing how these proteins bind together at such a high resolution may help find ways to stop the BRAF protein from triggering cancerous cell growth. Credit: Juliana A. Martinez Fiesco, David E. Durrant, Deborah K. Morrison and Ping Zhang, CCR, NCI, NIH; Joseph Meyer, SPGM, FNL, NCI, NIH

A CANCER THERAPY FOR EVERYONE



A simple approach using viral peptides shows efficacy against diverse tumor types in mice.



John T. Schiller, Ph.D.
Deputy Chief
Laboratory of Cellular Oncology

Many cancer therapies are becoming increasingly complex and reliant on expensive technologies, which threatens to exclude people in low-resource settings from access to effective treatments. To address this issue, Senior Investigator **John Schiller, Ph.D.**, is searching for approaches that apply to a wider range of patients and that can be easily delivered, no matter where patients are located.

His idea is to harness existing long-term immunity that most people already have against common viruses. In an initial study, published in *PNAS*, Schiller and colleagues provide proof-of-principle for this approach using the cytomegalovirus (CMV), a common virus that has infected an estimated 83 percent of people around the world.

"The overwhelming trend in cancer therapy is to develop things that are highly personalized and complex, and if that trend continues there's no way we're going to reduce health disparities," emphasizes Schiller. "So, we've been trying to develop de-personalized approaches that involve a simple intervention against a broad range of cancers at a relatively low cost."

Through Schiller's pioneering research on human papillomavirus (HPV) vaccines to prevent cervical cancer, it became clear that HPV virus-like particles can bind to and infect cancer cells but not healthy cells in intact tissues. This inspired Schiller and Staff Scientist Nicolas Çuburu, Ph.D., to explore using CMV to target cancer. The investigators speculated that infecting tumors with a few CMV genes would fool the immune system into thinking that the tumor cells are infected with CMV and eliminate them.

Initial experiments introducing CMV genes into the tumors of mice did not yield significant results. But injecting short pieces of viral proteins that could directly bind to the surface of the cancer cells worked like gangbusters, says Schiller.

In mice with lung-, colon- and melanoma-derived tumors, the injection of viral peptides induced a strong response from two powerful cancer-fighting immune cells: $CD4^+$ and $CD8^+$ T cells. As a result, tumor growth was reduced and survival improved, regardless of cancer type.

Importantly, the approach also yielded a long-term anti-tumor response. When the researchers transplanted additional tumors into the mice four months after the initial injection of CMV peptides, the mice still maintained their anti-tumor immunity.

Next, Schiller plans to partner with Senior Scientist Amy LeBlanc, D.V.M., to explore this novel strategy in dogs with naturally occurring cancers. Schiller says he's excited for this next step, because it could help lay the foundation for the research to eventually be translated into humans.

"There's no guarantee it's going to work, but we believe it's worth the effort because the potential for bending the curve of cancer in low-resource settings is a worthwhile goal to have, even if it's difficult," says Schiller.

Çuburu, N., et al. *Proc Natl Acad Sci U S A*. 2022 Jun 28;119(26): e2116738119.

This diagram depicts cytomegalovirus (CMV), a common, usually harmless virus that has infected about 83% of humans around the world. By injecting pieces of proteins from CMV, shown here as pale yellow particles, directly into tumors, CCR researchers were able to activate preexisting anti-CMV T cells and reprogram the tumor microenvironment. This led to slower tumor growth and improved survival in mice with lung-, colon- and melanoma-derived tumors. Credit: Pamela Beltowski, SPGM, FNL, NCI, NIH

New Faculty

Stanley Adoro, Ph.D.

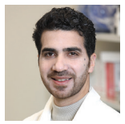
Stanley Adoro, Ph.D., has joined the Experimental Immunology Branch as a Stadtman Tenure-Track Investigator from Case Western Reserve University. Dr. Adoro is an immunologist with an interest in understanding the process of blood cell development.

Mirit I. Aladjem, Ph.D.

Mirit I. Aladjem, Ph.D., has been appointed Deputy Branch Chief of the Developmental Therapeutics Branch. Dr. Aladjem studies cellular signaling pathways that regulate DNA synthesis to help understand cancer biology and elucidate the cellular response to chemotherapeutic drugs.

Clint T. Allen, M.D.

Clint T. Allen, M.D., has joined the Surgical Oncology Program as a Senior Investigator from the National Institute on Deafness and Other Communication Disorders. Dr. Allen's research centers on immunologic aspects of head and neck cancer and neoplasm development, progression and treatment. Dr. Allen leads a program that focuses on developing novel treatment approaches for human papillomavirus (HPV)-positive and -negative head and neck squamous cell carcinoma as well as recurrent respiratory papillomatosis (RRP).



A. Rouf Banday, Ph.D.

A. Rouf Banday, Ph.D., has joined the Genitourinary Malignancies Branch as a Stadtman Tenure-Track Investigator from the NCI Division of Cancer Epidemiology and Genetics. Dr. Banday's research goal is to understand the genomic alterations that govern the development of bladder cancer and confer resistance to therapies.

Lisa D. Boxer, Ph.D.

Lisa D. Boxer, Ph.D., has joined the Laboratory of Genome Integrity as a Stadtman Tenure-Track Investigator from Harvard University. Dr. Boxer's lab studies the role of chromatin regulation in neural development and how mutations in chromatin regulators lead to neurodevelopmental disorders and cancer.

John Brognard, Ph.D.

John Brognard, Ph.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Laboratory of Cell and Developmental Signaling. Dr. Brognard's lab studies cancer-associated kinases using bioinformatics and functional genomic approaches to understand the molecular mechanisms by which these kinases promote tumorigenesis.

Takeo Fujii, M.D., M.P.H.

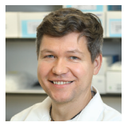
Takeo Fujii, M.D., M.P.H., has joined the Women's Malignancies Branch as a Physician-Scientist Early Investigator from Cold Spring Harbor Laboratory. Dr. Fujii is a medical oncologist whose research focuses on finding novel therapeutic targets for breast cancer brain metastasis by understanding the role of inflammation and immune cells in the tumor microenvironment.

Jennifer A. Kanakry, M.D.

Jennifer A. Kanakry, M.D., has been appointed Senior Clinician and Director of the Hematology/Oncology Fellowship Program in CCR's Office of the Clinical Director. She leads a clinical research program related to allogeneic hematopoietic cell transplantation for patients with hematologic malignancies and inherited and acquired disorders of the immune system.

Alexander E. Kelly, Ph.D.

Alexander E. Kelly, Ph.D., was awarded tenure at NIH and appointed as a Senior Investigator in the Laboratory of Biochemistry and Molecular Biology. His lab seeks to understand how errors in chromosome segregation are prevented and corrected using a combination of biochemical, biophysical and cell biological approaches.

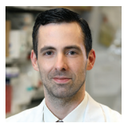


Mardo Kõivomägi, Ph.D.

Mardo Kõivomägi, Ph.D., has joined the Laboratory of Biochemistry and Molecular Biology as a Stadtman Tenure-Track Investigator from Stanford University. Dr. Kõivomägi studies the biochemical mechanisms cyclin-dependent kinase complexes use to control cell division and how to target these mechanisms with novel therapeutics against cancer.

Mikhail Kolmogorov, Ph.D.

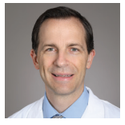
Mikhail Kolmogorov, Ph.D., has joined the Cancer Data Science Laboratory as a Stadtman Tenure-Track Investigator from the University of California, Santa Cruz. The focus of Dr. Kolmogorov's lab research is computational genomics — algorithms, mathematical models and tools aimed at answering fundamental questions about living systems through the analysis of large-scale sequencing data.



Vid Leko, M.D.

Vid Leko, M.D., has joined the Immune Deficiency Cellular Therapy Program as a Physician-Scientist Early Investigator from the CCR Surgery Branch. Dr. Leko's research focuses on developing T cell-based therapies for patients suffering from myelodysplastic syndromes, acute myeloid leukemia and other cancers resistant to current therapies.

New Faculty continued



Nyall R. London Jr., M.D., Ph.D.

Nyall R. London Jr., M.D., Ph.D., has joined the Surgical Oncology Program as a Tenure-Track Investigator from the National Institute on Deafness and Other Communication Disorders. Dr. London is an otolaryngology surgeon-scientist with expertise in disorders and cancers involving the nasal cavity, sinuses and base of the skull.

Lichun Ma, Ph.D.

Lichun Ma, Ph.D., has joined the Cancer Data Science Laboratory as a Stadtman Tenure-Track Investigator from the CCR Laboratory of Human Carcinogenesis. Dr. Ma is a systems biologist with a specific focus on understanding the intrinsic tumor biology of liver cancer using single-cell and spatial approaches.

Yuichi Machida, Ph.D.

Yuichi Machida, Ph.D., has joined the Developmental Therapeutics Branch as a Senior Investigator from the Mayo Clinic. Dr. Machida is a molecular biologist investigating the effects of DNA damage on DNA replication.

Stavroula Mili, Ph.D.

Stavroula Mili, Ph.D., has been awarded tenure at NIH and appointed as a Senior Investigator in the Laboratory of Cellular and Molecular Biology. Dr. Mili's work focuses on the roles of localized RNAs in mammalian physiology.

Senthil K. Muthuswamy, Ph.D.

Senthil K. Muthuswamy, Ph.D., has joined the Laboratory of Cancer Biology and Genetics as Chief and Senior Investigator from Harvard University. Dr. Muthuswamy pioneered the development and use of three-dimensional organoid culture and co-culture methods for mechanistic, translational and co-clinical studies. Research from his laboratory helped define the role cell polarity proteins play in cancer biology and therapy resistance.

Samuel Y. Ng, M.D., Ph.D.

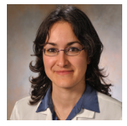
Samuel Y. Ng, M.D., Ph.D., has joined the Lymphoid Malignancies Branch as a Lasker Clinical Research Scholar and a Tenure-Track Investigator from Harvard University. Dr. Ng is studying the molecular mechanisms that underlie mature T-cell malignancies in order to improve the treatment of T-cell non-Hodgkin lymphomas.

Francis J. O'Reilly, Ph.D.

Francis J. O'Reilly, Ph.D., has joined the Center for Structural Biology as a Stadtman Tenure-Track Investigator from the Berlin Institute of Technology. Dr. O'Reilly is a structural biologist who combines structural proteomics, electron microscopy and integrative modeling to discover and structurally characterize protein complexes directly inside cells.

Marta Penas-Prado, M.D., M.Sc.

Marta Penas-Prado, M.D., M.Sc., has been appointed Senior Clinician in the Neuro-Oncology Branch. Dr. Penas-Prado is a neuro-oncologist focused on caring for patients with rare brain and spine tumors. Her clinical research seeks to uncover the molecular underpinnings of rare central nervous system (CNS) tumors.



Vassiliki Saloura, M.D., Ph.D.

Vassiliki Saloura, M.D., Ph.D., has been appointed as a Stadtman Tenure-Track Investigator in the Thoracic and GI Malignancies Branch. Dr. Saloura's laboratory investigates the role of histone and non-histone protein methylation in tumor growth, therapy resistance and immunogenicity in squamous cell carcinoma of the head and neck.

Urbain Weyemi, Ph.D.

Urbain Weyemi, Ph.D., has joined the Developmental Therapeutics Branch as a Stadtman Tenure-Track Investigator from the University of Texas at Austin. Dr. Weyemi is a molecular biologist who investigates the link between genomic instability and metabolism in human diseases using genomics tools and mouse models.

Newly Retired

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

Michael Bustin, Ph.D., Senior Investigator, Laboratory of Metabolism

William L. Dahut, M.D., Scientific Director for Clinical Research, NCI Clinical Director and Senior Investigator, Genitourinary Malignancies Branch

Ronald E. Gress, M.D., Chief/Senior Investigator, Experimental Transplantation and Immunotherapy Branch

Stephen H. Hughes, Ph.D., Chief/Senior Investigator, Host-Virus Interaction Branch and Retroviral Replication Laboratory

Michael Lichten, Ph.D., Deputy Chief/Senior Investigator, Laboratory of Biochemistry and Molecular Biology

Faculty list is for calendar year 2022.

Awards & Honors

Stanley Adoro, Ph.D., received a 2022 NIH Distinguished Scholars Award.

Christina M. Annunziata, M.D., Ph.D., received the distinction of Fellow of the American Society of Clinical Oncology.

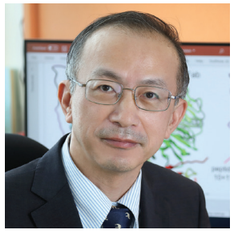
Andrea B. Apolo, M.D., was elected to the American Society for Clinical Investigation.

Mary N. Carrington, Ph.D., was elected to the American Academy of Arts & Sciences Class of 2022.

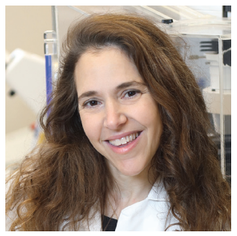
Deborah E. Citrin, M.D., received the designation of Fellow of the American Society for Radiation Oncology.

Mark R. Gilbert, M.D., received the 2022 Joel A. Gringas Jr. Award.

James L. Gulley, M.D., Ph.D., received the National Alliance of State Prostate Cancer Coalitions Award for Outstanding Contributions to the Field of Prostate Cancer.



Mitchell Ho, Ph.D., received the 2022 Dr. Francisco S. Sy Award for Excellence in Mentorship at HHS from the Federal Asian Pacific American Council-NIH Chapter.

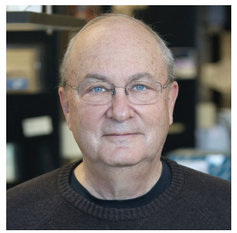


Rosandra N. Kaplan, M.D., was elected to the American Society for Clinical Investigation.

Elaine S. Jaffe, M.D., received the inaugural 2022 American Association for Cancer Research James S. Ewing-Thelma B. Dunn Award for Outstanding Achievement in Pathology and a 2022 Career Achievement Award from the Department of Health and Human Services.

Awards & Honors continued

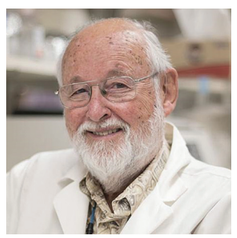
Susan M. Lea, D.Phil., F.Med.Sci., was elected to the 2022 American Academy of Microbiology Fellows and was elected as a Fellow of the Royal Society.



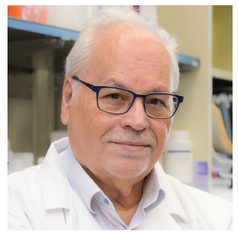
Michael Lichten, Ph.D., was elected to the National Academy of Sciences.

Ravi A. Madan, M.D., received the Veterans Health Administration Office of Research and Development Exemplary Service and Leadership Award.

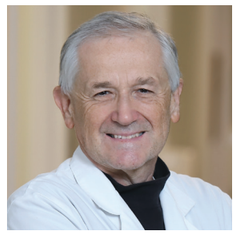
Deborah K. Morrison, Ph.D., was elected to the National Academy of Sciences.



Joost J. Oppenheim, M.D., was elected as a 2022 Distinguished Fellow of the American Association of Immunologists.



George N. Pavlakis, M.D., Ph.D., received the Insignia of the Officer of the Gold Cross of the Order of the Phoenix by the President of the Hellenic Republic.



Steven Z. Pavletic, M.D., M.S., was named a 2022 finalist for the Top 10 Clinical Research Achievement Awards from the Clinical Research Forum.

Nitin Roper, M.D., M.Sc., was recognized in the 2021 40 Under 40 in Cancer class.

Steven A. Rosenberg, M.D., Ph.D., received the 2022 Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research and was selected as an Icon in Surgery from the American College of Surgeons.

Eytan Ruppin, M.D., Ph.D., received the 2023 Delano Award for Computational Biosciences from the American Society for Biochemistry and Molecular Biology.

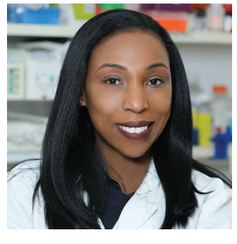
Awards & Honors continued

Lawrence E. Samelson, M.D., was elected as a 2022 Distinguished Fellow of the American Association of Immunologists.

Susan Sharrow, received the Department of Health and Human Services 50 Years of Service Award.

Louis M. Staudt, M.D., Ph.D., received a 2022 Giants of Cancer Care award.

William G. Stetler-Stevenson, M.D., Ph.D., received the 2023 Rous-Whipple Award from the American Society for Investigative Pathology.



Kandice Tanner, Ph.D., received the 2021 Arthur S. Flemming Award from George Washington University and was elected to the 2022 class of fellows of the American Society for Cell Biology.

Anish Thomas, MBBS, M.D., was elected to the American Society for Clinical Investigation.

Urbain Weyemi, Ph.D., received a 2022 NIH Distinguished Scholars award.

Giorgio Trinchieri, M.D., was elected to the 2022 class of fellows of the Society for Immunotherapy of Cancer.

Ying E. Zhang, Ph.D., was elected as a fellow of the American Association for the Advancement of Science.

Awards & Honors continued

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:

Yihan Wan, Ph.D., Laboratory of Receptor Biology and Gene Expression

Scott Wilkinson, Ph.D., Laboratory of Genitourinary Cancer Pathogenesis

CCR Outstanding Ph.D. Student Award

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

Laura Chopp, University of Pennsylvania Graduate Partnership Program, Laboratory of Immune Cell Biology

Farid Rashidi Mehrabadi, Indiana University Graduate Partnership Program, Cancer Data Science Laboratory

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:

Amiran K. Dzutsev, M.D., Ph.D., Laboratory of Integrative Cancer Immunology

Staff Scientist/Staff Clinician Leadership Merit Award

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

Pamela L. Wolters, Ph.D., Pediatric Oncology Branch

Marta Penas-Prado, M.D., M.Sc., Neuro-Oncology Branch

Staff Scientist/Staff Clinician Outstanding Mentor Award

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

Orieta Celiku, Ph.D., Neuro-Oncology Branch

CCR by the Numbers

346 Open Clinical Trials

42 New Clinical Trials

1,496 New Patients

245 Principal Investigators

18 New Faculty Recruits*

3 Newly Tenured Investigators*

281/70 Staff Scientists/ Staff Clinicians

~500 Technical Lab Staff

697/118 Postdoctoral/ Clinical Fellows

338/72 Postbaccalaureate/ Predoctoral Students

162 Summer Students

>1,100 Articles in Peer-Reviewed Journals

64 Technology Facilities and Platforms

Numbers are for FY22 unless otherwise marked.

**Numbers are for calendar year 2022.*

Technology Transfer Activities

63 New Employee Invention Reports

42 Issued U.S. Patents

29 New Cooperative Research and Development Agreements (CRADAs)

184 Active CRADAs

85 Clinical CRADAs

7 Umbrella CRADAs

12 New Clinical Trial Agreements (CTAs)

113 Active CTAs

120 New Licenses for CCR Technologies

668 Active Licenses

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, 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**).

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

Cancer Immunology and Immunotherapy at CCR
https://ccr.cancer.gov/research/immunology-and-immunotherapy

NCI CCR Prostate Cancer Multidisciplinary Clinic
https://ccr.cancer.gov/clinical-trials/prostate-cancer-clinic

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Center for Cancer Research

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