JILL BIDEN SIGNALS WHITE HOUSE RESOLVE ON CANCER RESEARCH: “THIS IS THE FIGHT OF OUR LIVES”

Jill Biden stopped by at NCI earlier this week to reaffirm the Bidens’ pledge to “fight cancer as we know it”—an early signal that cancer research is near the top of the national agenda at the Biden-Harris White House.

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Research Executive Officer

SWOG Cancer Research Network, a member of the National Cancer Institute's (NCI) National Clinical Trials Network (NCTN), seeks an executive officer to lead its clinical trials in lung and breast cancers, a substantial part of the group's research portfolio.

DESCRIPTION:

**SWOG Cancer Research Network** seeks a dynamic individual who brings scientific vision, inclusive leadership, and an innovative spirit to a leading member of the nation's oldest and largest publicly-funded cancer clinical trials network to serve as executive officer for breast and lung cancer research.

The **SWOG breast and lung committees** create, implement, and execute publicly-funded clinical trials that improve medicine through the prevention, detection, and treatment of cancer, and by improving quality of life for cancer survivors. SWOG lung and breast trials can involve translational science, biomarker assessment, and multi-modal treatment areas such as surgery and radiation. Executive officers routinely work with SWOG partners in the National Clinical Trials Network, funded and managed by the National Cancer Institute, as well as pharmaceutical partners. They also play a key role in reinforcing the group's culture of patient-centricity, continuous improvement, inclusion, and collaboration.

**SWOG executive officers** are the scientific and managerial leaders of their committees. They oversee the science and protocol-building process in their committees; encourage innovative trial strategies; coach committee leaders and members to high performance; share and promote best practices in clinical cancer research; and promote diversity, equity, and inclusion. Executive officers play a critical role in advancing SWOG's mission of lengthening and improving lives by removing barriers to committee success, stewarding the timely development of trials, advising the group chair, and identifying and mentoring exceptional young investigators.

**SWOG seeks a candidate** with nationally-recognized expertise in breast or lung research and in planning and conducting high-impact clinical trials. Experience with the NCTN or another similarly complex, multi-institutional setting or consortium is essential.

Executive officers may serve up to three consecutive five-year terms, or a maximum of 15 years. Performance is measured each year in a review conducted by the group chair, who also conducts a mid-term 360-degree evaluation.

**Location:** Applicants will be accepted from any U.S. region or territory. They must be willing to travel twice a year to group meetings, and travel to attend other SWOG and NCI leadership meetings as necessary.

**Salary:** Effort is budgeted at 20 percent and will be compensated in keeping with scaling set by the National Institutes of Health (NIH).

**Contact:** To apply, submit a CV or NIH biosketch and a one-page statement of vision and intent to lesliew@ohsu.edu no later than close of business on Feb. 15, 2021.
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JILL BIDEN SIGNALS WHITE HOUSE RESOLVE ON CANCER RESEARCH: “THIS IS THE FIGHT OF OUR LIVES”

By Matthew Bin Han Ong

Jill Biden stopped by at NCI earlier this week to reaffirm the Bidens’ pledge to “fight cancer as we know it”—an early signal that cancer research is near the top of the national agenda at the Biden-Harris White House.
I want you to know, I want to just say it again, the president and I stand with you," the first lady said in a Feb. 3 live-streamed Zoom call. "This is the fight of our lives, and we will never stop working to end this disease. And together, I know that we're going to go farther than ever before."

The virtual visit showed no signs of being a political afterthought. It looked like the real thing.

Jill Biden's White House page highlights three areas of advocacy:

"As First Lady, Dr. Biden continues her work for education, military families, and fighting cancer."

Cancer researchers and advocates, already enthused by the prospect of a pro-science Biden presidency, expressed pleasant surprise at Jill Biden's NCI visit, a mere two weeks after the inauguration.

NCI leaders are palpably delighted by the speed at which the White House is engaging the subject matter—a declaration of purpose that many in oncology didn't anticipate for at least a few months as the new administration deals with a maelstrom of urgent foreign and domestic issues (The Cancer Letter, Jan. 22, 2021).

In a Feb. 4 email to his colleagues titled "A historic week for NCI!" Director Ned Sharpless gushed:

“What a wonderful week for NCI! Yesterday, we had the distinct honor of a truly inspiring virtual visit from First Lady, Dr. Jill Biden. It is difficult to overstate the significance of this event; just two weeks after the Inauguration, the Vice President and the First Lady have both visited the NIH and addressed staff. Their message of support for our work is clear, and the nation is counting on us."

The first lady's visit comes at a time when NCI is in dire need of help. In the past, including the time of the doubling of NIH's budget, advocacy for NCI was at the forefront in driving the increases. However, those increases were distributed proportionally across NIH institutes and centers.

Now, NCI is facing a budgetary crunch. Over the past five years, a tsunami of grant applications has been forcing down the NCI payline.

This leaves the institute's leadership with a challenge other NIH institutes
don’t have—the gap is so large that re-distribution of funds can’t fix it.

If not dealt with, paylines could drop to the point where investigators would consider it pointless to apply for an NCI grant.

The problem can only be solved through legislative intervention and a bolus of funds, NCI officials, advisors, and advocates say (The Cancer Letter, June 14, Feb. 15, Jan. 25, 2019).

At the virtual event, Sharpless introduced three women researchers at the institute, inviting them to present their work to the first lady:

- **Worta McCaskill-Stevens**, a medical oncologist, chief of the Community Oncology and Prevention Trials Research Group, and director of the NCI Community Oncology Research Program,

- **Stephanie Goff**, an associate research physician in the Surgery Branch of the Center for Cancer Research and a member of the senior staff of Steven Rosenberg’s team, and

- **Ligia Pinto**, director of the Vaccine, Immunity and Cancer Program at the Frederick National Laboratory for Cancer Research.

“To give you a flavor of some of the great work that goes on at the NCI, we have three of our researchers here to tell you about their areas of cancer investigation,” Sharpless said in his remarks to the first lady.

Now that the White House is officially engaged with NCI, Sharpless is taking a cue from Jill Biden’s visit to push up plans for its campaign to mark the 50th anniversary of the National Cancer Act:

“Next week, we will officially kick off our commemoration activities for the 50th anniversary of the National Cancer Act of 1971,” Sharpless wrote in the Feb. 4 email to NCI staff. “The community’s theme for this milestone is ‘Nothing will stop us,’ because nothing will. As the past year has shown, unforeseen challenges can and do emerge, but our commitment, dedication, and resilience help us face and overcome them and drive our focus on our mission.”

If you’re interested in joining more than 600 individuals and organizations in commemorating the 50th anniversary of the National Cancer Act, contact Sona Thakkar [thakkars@mail.nih.gov] at the NCI.

As a partner organization, The Cancer Letter has launched the Cancer History Project, an open-access historical resource curated by experts that is designed to grow in perpetuity.

After four years of sporadic engagement—or non-engagement—from the White House, the Bidens’ statement of commitment to NCI and the cancer research enterprise is as welcome as it is expected.

“The first time I heard the diagnosis for someone I loved, I was in my early 40s and the year it happened, not one, but actually four of my friends found out that they had breast cancer,” Jill Biden said in her virtual visit to NCI. “And cancer took the life of both my parents. My sister had to have an auto-stem cell transplant and then, there was our son, Beau, as you referred to. Cancer touches us all and because of that, your work touches us all.

“You’ve brought the Cancer Moonshot to where it is today.”

The National Cancer Act of 1971 gives NCI authorities unique in the U.S. government. The NCI director is the only presidential appointee who does not need to be confirmed by the U.S. Senate. Also, the NCI director has the capacity to communicate directly with The White House, bypassing NIH and HHS, on matter that involve opportunities in cancer research.

In 2016, then-Vice President Joe Biden advocated for a doubling of the rate of progress in cancer research—often accompanied by speeches from Jill at public events—which resulted in the Beau Biden Cancer Moonshot. The measure, which was folded into the 21st Century Cures Act, designated NCI as the steward of the unprecedented $1.8 billion in federal funds (The Cancer Letter, Nov. 13, 2020; To the Moon, 2016-2017).

“The NCI staff here today, took that vision and ran with it, bringing together stakeholders across the research community to work towards the goals he set for us,” Sharpless said at the virtual visit.

“To date, this has led to the launching of more than 240 exciting new programs and initiatives aimed at the laudable goal of rapidly accelerating cancer progress. It includes things like expanding our ability to treat cancer by awakening the immune system.”

If Jill Biden is to lead the White House charge against cancer this time, she may well reprise the role her husband played in the Obama administration—as Cancer Wonk-In-Chief.

The NCI visit wasn’t her first cancer gig since Joe settled into the Oval Office.


During the in-person visit, she talked about cancer screening in the COVID-19
era, patient navigation, and mental health with WWH CEO Naseema Shafi and Kim Thiboldeaux, executive chair of the Cancer Support Community, both of whom led a tour of the federally-qualified health center’s 14th St NW facility.

“You know we’re in your corner,” the first lady said at the Jan. 22 visit. “The first thing we have to do is address this pandemic and get everybody vaccinated and back to work and back to their schools, and get things back to the new normal. So, it’s going to be critical, I think, during this time period.

“The pandemic is [Joe Biden’s] number one priority at this moment, and if we can just come together as a nation and say, ‘Okay, maybe I don’t believe in wearing a mask, but I’m going to wear it for my neighbor who is a cancer survivor and is immunocompromised.’”

In her closing remarks to NCI at the virtual visit, Jill Biden reiterated the administration’s commitment to accelerate cancer research:

“I hope that you know of our commitment—of Joe’s commitment and my commitment—to carry on that work and to really be a partner with you and everybody at NIH, NCI, because we’ve got to work to fight cancer as we know it. And we know what it takes for family and friends to support their loved ones, to hold their hand while they get their chemotherapy or sit with them after surgery.

On this World Cancer Day, I want every family facing this fight to know this: there is hope. On the strength of dedicated scientists and researchers, tireless health care workers, and brave families like yours, we are going to win this fight once and for all.

Excerpted remarks from Jill Biden’s NCI visit follow:

“...I want to begin by thanking Dr. Biden for joining us today. It’s great to have the first lady visit the NCI.

We all need this morale boost: 2020 has been a pretty rough year. This global tragedy of the public health has been hard on an agency whose mission is devoted to advancing the public health, so we really appreciate your interest and I want to express our heartfelt thanks.

Despite the challenges of the last year, it has been a remarkably pro-
productive time for cancer research and a remarkably productive time at the NCI. We are seeing progress against cancer at a faster rate than at any time in human history:

- Lots of new great scientific advances that translate into new ways to diagnose, prevent, and treat cancer,
- Important advances in cancer screening and prevention, and improvements in how we do clinical trials,
- Record numbers of FDA approvals for new drugs and devices for cancer, and, importantly,
- A steadily dropping annual cancer mortality.

Cancer mortality in the U.S. has been declining since the early 1990’s, but in the last few years the pace of that progress has sharply accelerated, with the largest year-over-year declines in cancer mortality in the history of our statistics occurring in the last two years in a row!

As you know, Feb. 4 is World Cancer Day, which focuses on Intl Progress Against Cancer. NCI is proud to work with many international partners throughout the world to address cancer on a global scale and that work is coordinated by our outstanding Center for Global Health.

In 2021, the National Cancer Institute is partnering with others across the community to commemorate the 50th anniversary of the National Cancer Act, legislation that established some of the programs that form the backbone of today’s cancer research enterprise. So, it’s really a good time to reflect on what’s been accomplished and how much work remains.

It’s all too clear that despite this progress I mentioned, this has not been good enough. We still have too many Americans dying of cancer, and we have too little progress against certain types of cancer like pancreatic cancer and glioblastoma. And even when we have treatments for these cancers that are able to cure some of these patients, often these treatments are really toxic and leave patients with lifelong survivorship challenges.

And now we have this new problem against that backdrop of the pandemic’s effect on cancer diagnosis and cancer care. The pandemic has closed hospitals and clinics throughout the country. And because of this, there have been many delays in screenings, diagnosis, and treatments, and we believe these delays incurred may translate into worse outcomes for people with cancer over the next decade.

So, a main challenge right now for the NCI is to get over the disruption caused by the pandemic and to get back on that great pace of progress in cancer research. We will face this challenge and declare together that nothing will stop us, nothing will stop us in our work on behalf of people with cancer.

And I know that Dr. Biden is very much with us in this challenge. The first lady, as everyone knows, has been a longtime advocate for cancer research and for people with cancer. Her interest in the topic began in the 1990s when friends were diagnosed with breast cancer. And I think we are all aware of Beau Biden’s battle with glioblastoma, succumbing to that disease in 2015 and the impact this has had on the president and first lady.

In fact, I think it was this private tragedy of the Biden family that led to a really great public act, the Beau Biden Cancer Moonshot, which came about under the leadership of then-Vice President Biden. The NCI staff here today, took that vision and ran with it, bringing together stakeholders across the research community to work towards the goals he set for us.

To date, this has led to the launching of more than 240 exciting new programs and initiatives aimed at the laudable goal of rapidly accelerating cancer progress. It includes things like expanding our ability to treat cancer by awakening the immune system.

The Moonshot has worked on new approaches to fight childhood cancer. And there are Moonshot initiatives aimed at improving cancer care and underserved populations so that all patients can benefit from cancer progress and this is really just scratching the surface. There are many more great programs in the Moonshot. It is our fervent hope and belief at the NCI that this remarkable effort to improve the lives of all people with cancer will live up to Beau’s memory. So Dr. Biden, thank you again for coming today and we were so eager to hear your remarks.

Jill Biden: Thank you, Dr. Sharpless, and your remarks are so heartwarming to me. Ned, we’re so grateful to have an accomplished researcher, academic inventor, physician, and author at the head of our nation’s premier cancer research institution. So, thank you for your leadership.

And Dr. Collins, thank you for joining us today as well and for your years of service at NIH in three administrations now. On behalf of both the president and me, I also want to thank you and the NIH for helping to create the vaccines and the treatments that are going to save so many lives and help our
nation recover. And we're just so lucky to have you.

So, it's a pleasure to visit the National Cancer Institute virtually today. And I'm grateful to be coming to you from the White House today as your first lady. It's the honor of a lifetime, but I know that even more than that, it's a responsibility to serve the American people.

And from coast to coast, we face so many diverse and complicated challenges and yet when I was second lady and in my travels across the country over the last few years, I've seen again and again, that there is one challenge that unites us all, one thread of pain that runs through every community, North and South, rich and poor, in the best of times, the depths of this pandemic—and that's cancer.

The first time I heard the diagnosis for someone I loved, I was in my early 40s and the year it happened, not one, but actually four of my friends found out that they had breast cancer. And cancer took the life of both my parents. My sister had to have an auto-stem cell transplant and then, there was our son, Beau, as you referred to. Cancer touches us all and because of that, your work touches us all.

You've brought the Cancer Moonshot to where it is today. You've dedicated years to studying our immune systems and supporting clinical trials. You've lifted up community-based clinics and treatment research. You've led breakthroughs and discovered new ways to test.

And though this last year has been so difficult, NCI has risen to meet the challenge, uncovering how this pandemic has affected rates and figuring out how to continue this work, your work, because cancer doesn't stop for COVID. For more than 50 years, this organization, your organization has pioneered this frontier. Thanks to you, countless lives have been saved, countless families are whole, and there is more hope than ever for every person who is touched by this disease.

So, on behalf of the president and me, thank you, on behalf of every family who has faced cancer and a very grateful nation, thank you. We are so proud of everything that you're doing here, and now I'm more excited to learn about the work that you're doing, so let me pass it back to Ned.

Sharpless: Thank you. To give you a flavor of some of the great work that goes on at the NCI, we have three of our researchers here to tell you about their areas of cancer investigation.

The first is Dr. Worta McCaskill-Stevens. Worta is a medical oncologist and chief of our Community Oncology and Prevention Trials Research Group. And then we'll hear from Dr. Stephanie Goff, who is a surgical oncologist at the National Cancer Institute. And then finally, from Dr. Ligia Pinto, who's a scientist at NCI's Frederick National Lab.

I thought we'd start by hearing about patient outreach and engagement, and this is getting patients from underserved populations into clinical trials. For example, as you can imagine, a big problem in cancer research is translating these exciting new advances in cancer therapy and cancer prevention into real-world progress for all patients. This means reaching cancer patients in rural communities and underserved populations. And it's really critical that we figure out how to do this.

And so, I've asked Dr. McCaskill-Stevens here to come to tell you about the NCORP Network. Worta, will you take it over?

Worta McCaskill-Stevens: Thank you, Dr. Biden and welcome to the National Cancer Institute. Thank you, Ned.

Clinical trials provide the scientific pathway to treatment. However, clinical trials are much more than science. They are about science helping people. Through clinical trials, our aim is to enable the advances in cancer research and to make sure that they're applied as broadly as possible. We won't have done our job if the outstanding research that we conduct is only enjoyed by a few.

“
You’ve brought the Cancer Moonshot to where it is today. You’ve dedicated years to studying our immune systems and supporting clinical trials. You’ve lifted up community-based clinics and treatment research. You’ve led breakthroughs and discovered new ways to test.

– Jill Biden”
But it all begins by improving access and diligently seeking ways in which we can increase participation in clinical trials. One way that we do this is to take the trials where the people are, and this brings me to the NCI Community Oncology Research Program, which provides access to clinical trials in communities where adults and children with cancer and those who are at risk of cancer live.

The NCI NCORP program is an academic and community partnership in which clinical trials related to the management of symptoms, prevention, screening, the delivery of care, quality of life and disparities and treatment are conducted.

NCORP has 46 community sites, 14 of these sites are focused in areas throughout the country that have large areas of rural patients and racial and ethnic minorities. Over 4,000 physicians participate in this network at over 1,000 sites that reflect very diverse oncology practices.

Enrollment into NCORP traverses over 43 states and includes Puerto Rico in Guam. Enrollment from the NCORP is almost one half of the enrollment in the NCI National Clinical Trials Network, which enrolls over 20,000 patients per year. Enrollment at the local NCORP sites allows those sites to be up-to-date on research tools and for their staff to contribute to the progress against cancer.

We've learned a lot from the community sites. This has led us to great insights about the importance, for example, of understanding chronic diseases, diabetes, and hypertension, which is so prevalent in underserved communities. Also, to appreciate interactions of socioeconomic factors of social injustice when enrolling, and to have us consider these factors in our trial designs. Allow me to share with you an example of a recent trial that has been practice-changing.

This is the TAILORx trial. This is the trial that assigned individualized options for treatment. This was the first and the largest of NCI's precision cancer trials. It enrolled over 2,000 woman, 16% of which were minors and most of these women came from rural areas and community settings. This trial showed us that only about 20% of the women with early-stage breast cancer benefited from chemotherapy after surgery. These data affect and apply to 50% of breast cancer in the United States.

This trial, due to its size, the duration, and the fact that it had hypothesis testing, the fact that women may receive less therapy, could only have been conducted within the NCI. We now know using a molecular test that we can identify those women who only need endocrine therapy to reduce their risks of recurrence. These women now don't have to have chemotherapy side effects such as nausea, fatigue, risk of infection, or hair loss. These women can be cured and go back to their families and to their work.

So, that woman in rural America doesn't have to drive many miles to have the chemotherapy. Access to this and other very important clinical trials, we think, is a very important step in the direction of health in cancer therapy. Thank you.

Biden: Well, I've seen a lot of the need for the information to get out to the rural communities. Where I've traveled around this country. And really one of the major places that I actually saw a need for—and you're saying, the chemotherapy center—was the Navajo nation and how they had no chemotherapy center. And they were traveling two hours to go get chemotherapy and then to travel home.

So, I think we just have to do a better job disseminating information out to communities about what's available to help people, because I think people are desperate for information on people who have cancer. Thank you for all that you're doing. I really appreciate it.

Sharpless: The dissemination of information about clinical trials is a real challenge because it's often hard to find patients to the right trial and it's something we've really worked on very hard. And having the ability to enroll patients at 1,100 sites nationally has, I think, made that somewhat easier, but there's still challenges that exist. Thanks, Worta.

McCaskill-Stevens: Well, this is actually a network and one of the unique things about the NCORP is that they really connect with their communities. When they come in they bring the specific demographics and understand their patients. They have connections within the community so that the referral patterns come to them.

The NCI also does a great job of providing information to the public about clinical trials. Information comes from our societal meetings, and because it's an academic-community partnership, much information is shared at those meetings and those direct contacts with those individuals, those organizations.
science on how to treat cancer. This involves this topic of cellular immunotherapy, which sounds like science fiction, but the idea is you use a patient's own T cells to sweep them up, in a way, and give them back to the patients, re-infuse them to treat their cancer, and this technology really was pioneered at the National Cancer Institute. And so I'd like to invite Dr. Stephanie Goff to tell you about her exciting work in this area, Stephanie?

Stephanie Goff: Thank you, Dr. Sharpless, and thank you, Dr. Biden. As the daughter of a teacher, it’s a real honor for me to be able to present my work to you, and a virtual welcome to building 10. Dr. Collins refers to the NIH as the National Institutes of Hope and every place like that needs a house and so this is the house of hope here in Bethesda, where we’re able to take care of the patients that enroll in all of the clinical trials, across the institutes and centers.

We practice the medicine of tomorrow here and we take that responsibility very seriously. There are approximately 1,600 different clinical trials happening at the clinical center right now. And even in this challenging pandemic year that we just finished, 45 new clinical trials were started by investigators in the NCI and we were able to see over 1,500 new patients from all 50 states and territories.

And the work that we do here is the work that we refer to as "first-in-humans." So, it’s really after those long hours and nights in the lab, it’s when those moments that a theory becomes a reality when you’re able to see it work for the first time in a patient and those moments are magical.

I was fortunate enough to train here and now have been able to come back and work side-by-side with my mentor, Dr. Steven Rosenberg, who has been pursuing this concept of immunotherapy quite literally my entire life. And what he’s been pursuing is, can we get the immune cells of our body to learn how to see cancer? And because of the pandemic, so many people now understand a little bit about how T cells see things, particularly viruses.

We have a lot of amateur immunologists blooming these days, but can we get T cells to see a patient’s cancer? And if they can do that, can they make it go away? His career has been one built on bench-to-bedside. That cycle of learning that we all do. When we take something from the lab, we try it in patients once it’s safe. And then we see if we can get it to work. We learn from the successes, we learn from the failures, and then we go back and we try again.

He started that work in patients with metastatic melanoma, a very rare disease, but a very deadly one. And he learned that by stimulating all the T cells in the body with a drug called interleukin-2, which was one of the first immunotherapies to be approved, that he could make people’s tumors go away.

And it wasn’t just away for a little while, it was away forever. There was a small portion of patients, maybe 4-5%, but they would live the rest of their lives cancer-free, normal lives, no more chemotherapy, no more additional drugs.

And so, as our tools got better, as Dr. Collins and the work that he did on the human genome became possible, we became able to see tumors much more clearly in a way that we couldn’t do before, because the problem is that our immune systems are actually designed to ignore our bodies.

We don’t want them attacking all the tissues that we have, not to attack our breast or our thigh or our pancreas.

But when that tissue starts to go bad, when it becomes a cancer, what is it that makes it switch? How can we get the immune system to engage? And it turns out when you look down at the very, very fundamental level, at the DNA, when that change is enough to make that cell no longer look like the person that it lives in, that’s when the immune system can kick in.

So, if we can find those cells, what can we learn from them? And how can we give them back to patients? Because if we can harness that, then we can just set the body on top of itself. The Achilles heel of that cancer is that it has changed and made itself visible.

I was teaching a course in basic immunology and cancer immunology to a group of breast cancer advocates, when a woman who was suffering from widespread metastatic cancer caught me and said that she wanted to join us as a patient volunteer.

And we did some stuff first to make sure that we weren’t going to be wasting her time, because time is such a valuable and precious commodity. And once it became clear that she was eligible, I took her to the operating room, I took a small tumor off her chest wall, and we were able to study that tumor in a number of ways.

We were able to look at the DNA changes in her tumor and we were able to test the T cells that lived there. And it turns out that takes us some time and her cancer was worsening, she was having to increase her pain medication, the lymph nodes in her armpit had started to press on her nerves, such that she couldn’t use her arm.
And we finally had the cells ready. She came to us in Bethesda, she was here with us for about three weeks and she was convinced the treatment was working even while she was here. Now, I’m a little bit more suspect than that and I wanted to watch and wait and see, but it turns out she was right.

Five years later, she’s disease-free. She has taken up ocean kayaking. So she’s using that arm with no problems and she hasn’t had to have another single treatment for her cancer since then. She teases me though that I won’t say that she’s cured. I’ll continue to say though, that she has no evidence of disease.

I could tell you a handful of stories like that, but the reality is there are far more families, as you well know, that don’t have happy endings. And I, and so many of us carry those stories with us during the late nights and weekends in the lab and on the ward, because the NCI gives us the space and time to create tomorrow’s medicine and that’s really what we’re all here for. So, thank you for paying attention to the work that’s going on at the NCI. And on behalf of all my colleagues here in Bethesda, welcome.

Biden: Having lived through cancer with so many members of my family and Beau, it’s just amazing what you’re doing and the hope that you’re giving to families. Because I know with Beau’s cancer, I mean, we tried everything and it’s just, like you’re saying, you’re trying all different things and you’re giving families hope, and you have no idea how much that means. Thanks.

Sharpless: Thank you, Stephanie. That was terrific. I thought next I’d like you to hear, Dr. Biden, a little bit about our work we’re doing related to SARS-CoV-2, to the coronavirus pandemic. It may not be obvious why the National Cancer Institute would work on coronavirus, but about 30% of cancers worldwide are caused by viruses. And so, there’s been a long interest in virology at the NCI.

HIV, the virus that causes AIDS was co-discovered at the National Cancer Institute as was the first effective therapeutic for HIV. And then, John Schiller and Doug Lowy, who are still quite active NCI researchers invented the vaccine against Human Papillomavirus, which shows the significant expertise of the NCI in vaccinology.

Importantly, relevant to SARS-CoV-2, we have this really great serology lab, which studies antibody levels in the blood, run by Dr. Pinto at Frederick National Lab, which had been working on HPV serology with the WHO. Frederick International Lab is the largest federal biomedical research facility, run by the NCI.

And so, when the pandemic began, it was relatively straightforward for the NCI to pivot that serology lab on HPV to SARS-CoV-2 and this is how I think we played a crucial role in the fight against COVID. So, let me get Ligia to tell you about what her team has been doing as part of the coronavirus research effort.

Ligia Pinto: Thank you, Dr. Sharpless, Dr. Biden. I’d like to share with you some of the key highlights of the exciting work on COVID-19 serology that we have been doing at the Frederick National Laboratory and the NCI. Frederick National Lab is a Federally Funded Research and Development Center with the infrastructure and the expertise to rapidly respond to public health crisis, such as the COVID-19 pandemic.

First, I’d like to tell you a little bit about myself. I’m originally from Portugal and I came to the NCI to do my PhD in immunology almost 30 years ago. My initial plan was to return to Portugal, but I decided to stay because of the incredible research opportunities at the NCI and in the United States in general. Our group works on serology. Let me tell you why we think it’s important and why this work is being done by cancer researchers.

Serology is the measurement of antibodies in blood predicting response to infection or vaccination. For COVID-19, serology tests are a critical public health tool for identifying individuals who were previously infected with SARS-CoV-2 or were vaccinated, and therefore maybe protected against the new infection. In order to inform public health decisions, antibody tests need to be reliable and highly accurate.

My laboratory at the Frederick National Lab has leveraged our expertise in studying immune responses to Human Papillomavirus infection and cervical cancer vaccines to develop serology tests and standards that are relevant to understanding SARS-CoV-2 infection and immune responses to the virus.

Because of this expertise at the beginning of the pandemic in April, when many serology tests were being developed, the FDA asked us to assist in evaluation of commercially available antibody tests for SARS-CoV-2, leading to evaluating more than 100 of these tests for the FDA. We have been able to do this thanks to a fantastic trans-governmental collaboration.

It has included several government agencies and academic medical centers. The FDA has used our perfor-
So, the poet, Gwendolyn Brooks, another life lost to cancer, wrote:

_We are each other’s harvest:_
_We are each other’s business:_
_We are each other’s magnitude and bond._

And cancer, as you all know better than anybody, can be such a lonely journey for patients and the people who care for them and love them, but they aren’t alone.

And you’re fighting for them every single day, all the hundreds and hundreds of people who work with you and you’re making our world a better, brighter, healthier place and your legacy is the lives you save and the families you protect—because we are each other’s harvest, each other’s magnitude and bond.

So, I want you to know, I want to just say it again, the president and I stand with you. This is the fight of our lives, and we will never stop working to end this disease. And together, I know that we’re going to go farther than ever before. So, thank you for the hope that you are giving millions of Americans. Thank you.

Sharpless: Thank you so much on behalf of the NCI.

Biden: Thank you.

Sharpless: Well, so that’s a sort of brief couple of snapshots of what’s going on at the National Cancer Institute. There’s so much more work in both our intramural funded program and our extramural funded portfolio that we’d love to tell you about, and we hope we get a chance to have you back sometime to talk more, but we really, really, really appreciate your doing this. It means so much to the National Cancer Institute to have you come and visit, and it’s so exciting for everyone at the NCI and we very much appreciate it.

_Biden:_ Oh gosh. Thank you, Ned. And thank you to everyone who shared their stories today and what you’ve been doing. It’s just incredible and I have to agree that you are the Institute of Hope, because so many people in this country are patients of cancer or have someone they love that’s dealing with cancer, and Joe and I have worked in this space for a long time. I have personally worked with families and caregivers.

One thing I think that we found in the Obama-Biden administration was the benefit of collaboration and how much that meant, whether it was through all the agencies of the government just working together.

And so, I hope that you know of our commitment—of Joe’s commitment and my commitment—to carry on that work and to really be a partner with you and everybody at NIH, NCI, because we’ve got to work to fight cancer as we know it. I mean, we have to, because it’s not a red issue, a blue issue. It’s a human issue, it affects all Americans.

So, I want you to know, I want to just say it again, the president and I stand with you. This is the fight of our lives, and we will never stop working to end this disease. And together, I know that we’re going to go farther than ever before. So, thank you for the hope that you are giving millions of Americans. Thank you.
It started a half of century of significant progress in research and outcomes that continues through today.

The recent statistics released by the American Cancer Society illustrate the fruits of that labor. Just before the pandemic started, the United States saw the single largest drop—2.4%—in the rate of cancer deaths on record. This is mainly attributable to efforts in lung cancer, including both prevention (e.g., innovation around smoking cessation) as well as new immunotherapies and genomically targeted therapies capitalizing on decades of basic science.

In January, after tumultuous weeks filled with unprecedented political tension and rising COVID-19 infections across the nation, thrilling news arrived quietly in my email inbox: official notice of the Abramson Cancer Center’s five-year, $45 million Cancer Center Support Grant award from the National Cancer Institute, which had bestowed us with a merit rating of “Exceptional” Comprehensive Cancer Center last year.

The news capped off a two-year grant renewal effort at the Abramson Cancer Center of the University of Pennsylvania, one accomplished through a virtual site visit in May amidst the early days of the COVID-19 pandemic and against the backdrop of this human tragedy.

That required complete reorganization of cancer research and care here and at cancer centers across the country and throughout the world.

Now, after a year of keeping our heads down to address the challenges from the pandemic, that email served as an important reminder to me to look up and embrace our many decade gains against cancer—and confidently reassert our focus for the years ahead.

It’s a time to feel energized.

2021 marks the 50th anniversary of the National Cancer Act that brought together scientists, physicians, government, and industry to combat cancer. It started a half of century of significant progress in research and outcomes that continues through today.

The recent statistics released by the American Cancer Society illustrate the fruits of that labor. Just before the pandemic started, the United States saw the single largest drop—2.4%—in the rate of cancer deaths on record.

This is mainly attributable to efforts in lung cancer, including both prevention (e.g., innovation around smoking cessation) as well as new immunotherapies and genomically targeted therapies capitalizing on decades of basic science.
In Philadelphia, we are hopeful about signs of progress. Statistics released in 2020 show that the incidence of cancer has fallen since 2000, with incidence among Non-Hispanic Black men now nearly the same as non-Hispanic white men. Overall cancer mortality is also declining, although sadly, remains higher among Black patients.

More than 80% of all women in Philadelphia, Black or white, aged 50 to 74, have had a mammogram in the last two years. More than 80% of teenage girls in Philadelphia have also been vaccinated against human papillomavirus, or HPV—among the highest rate in the country.

These data give us fresh hope as our organization, like so many others, puts community outreach, health equity, and racial justice at the top of our agenda to build healthier communities.

Also this January, we celebrate the five-year anniversary of the launch of the Cancer Moonshot. Then-Vice President Joe Biden visited Penn and Abramson Cancer Center, met our team, and made the announcement. It was a needed shot to the cancer research community’s arm, infusing an additional $1.8 billion into our work, thanks to the 21st Century Cures Act passed by Congress later that year. So far, 240 research projects across more than 70 initiatives have been supported by Moonshot funding, with more to come for this seven-year initiative.

Now with the Biden administration taking office, a strong focus on cancer research and care will no doubt press on. “My commitment is not for the next 12 months,” Biden told the Penn crowd that day as he launched the Moonshot. “I plan on doing this the rest of my life.”

I remember the Moonshot kicking off, as my colleagues and I provided the vice president a tour of our brand-new Center for Advanced Cellular Therapeutics and gathered to discuss treatments in the pipeline that we believed were bound to make a difference in patients’ lives. Already, so many have.

In all, far more than 100 cancer drug approvals from the U.S. Food and Drug Administration have materialized in the last five years. Thirteen new FDA oncology approvals were based on studies led or co-led by investigators at Penn, including the first cellular therapy, Kymriah, to treat pediatric and adult patients with a form of acute lymphoblastic leukemia.

I remember Tom Whitehead—father of Emily Whitehead, the first pediatric patient to receive that therapy in the early days of clinical trials —at that event, advising Mr. Biden about the Cancer Moonshot, “Be sure you include the kids.” Tom’s vision paved a path to a major national initiative in pediatric cancer research.

We are proud that a recent FDA approval, for crizotinib, was for childhood anaplastic large cell lymphoma, based on 15 years of basic and clinical work from labs and investigators at Children’s Hospital of Philadelphia and the Abramson Cancer Center.

Progress goes beyond “miracle” treatments. Moonshot projects tackle prevention, such as cutting-edge smoking cessation programs, germline genetic testing, behavioral economics, and implementation science to help provide higher-value care that will also lead to improved patient outcomes. The hunt for new targets for immunotherapy continues. Finding ways to overcome treatment resistance remains critically important, as does improving engagement with patients to increase clinical trials and improve design.

It is fitting to have renewed our NCI core grant in January, too, as we find our way out of a difficult year. Across NCI designated cancer centers, the process of review and renewal validates our science-driven and hard-earned progress, and also prompts rethinking and reformulation of new plans to keep this momentum going.

Ideas once on the horizon are rapidly coming into focus: CRISPR-based therapeutics for patients with advanced disease, novel metabolic imaging technologies, multiplex and routine immune health profiling, and hyper-energized FLASH radiation delivered in less than a second, to name a few.

These data give us fresh hope as our organization, like so many others, puts community outreach, health equity, and racial justice at the top of our agenda to build healthier communities.

Beyond the funding—whether from the CCSG or the Cancer Moonshot—these programs raise and support our ambitions. They embolden the scientific community to capitalize on and accelerate new discoveries that will bring even better treatments to our patients and lead to continued declines in cancer mortality.

The email news of the “NOGA” is not the end; it’s the start. United with our patients, families, and communities we serve, let’s strengthen our resolve for 50 more years and beyond to improve the lives of cancer patients and those at risk.
Storytelling is a part of J Freireich’s legacy

By Paul Goldberg

J enjoyed explaining that the letter J in his name appeared in his birth certificate.

He had no idea why his mother, an immigrant seamstress at a Chicago sweatshop, put it there, but it was certainly not an abbreviation for an actual name, Jacob, for example.

J’s J was its own thing. No period was to be used.

Great stories beautifully told are a part of J’s legacy. He spoke with reporters and historians, leaving behind more primary source material than your average Joe.

Emil J Freireich died Feb. 1, aged 93, at MD Anderson Cancer Center.

Here are J’s stories in his own words:

- Freireich’s conversation with Daniel Hayes, a breast cancer expert at the University of Michigan and former president of the American Society of Clinical Oncology, is particularly entertaining.
- There is also a beautifully annotated, three-session, seven-hour oral history done by MD Anderson.
- NIH historians, too, sat down with Freireich. The interview appears here.
- Another fine resource is a book by John Laszlo, “The Cure of Childhood Leukemia: Into the Age of Miracles.” Laszlo, both a participant and a historian of these events, records a lengthy conversation with Freireich and makes it a part of the narrative.

In this issue, we supplement J’s storytelling with an obituary by MD Anderson, and appreciations by Hagop Kantarjian, Moshe Talpaz, and Otis Brawley.

Photo courtesy of MD Anderson Cancer Center
Esteemed faculty member at MD Anderson passes away:

**OBITUARY**

**Legendary MD Anderson faculty member Emil J Freireich dies at 93**

*By MD Anderson Cancer Center staff*

Emil J Freireich, MD, a trailblazing oncologist who developed groundbreaking therapies for childhood leukemia and came to be recognized as a founding father of modern clinical cancer research, passed away peacefully in Houston at his beloved institution, The University of Texas MD Anderson Cancer Center, on Feb. 1. He was 93.

Known for his confidence, passion and occasional ferocity, Freireich was a faculty member of MD Anderson for 50 years, from 1965 to 2015. He led the Leukemia Research Program for decades, training hundreds of physicians and scientists who carried on his commitment to conquering cancer. His protocols helped establish the groundwork for randomized clinical trials, and he instituted many teaching programs for graduate students, fellows and faculty to drive progress in cancer research and treatment.

“Dr. Freireich was a giant of modern medicine whose impact on the field of cancer is beyond compare. His passing will be felt around the world and within the MD Anderson community,” said Peter WT Pisters, MD, president of MD Anderson. “For more than 60 years, he pushed boundaries and devoted himself to saving young lives and relieving suffering. Dr. Freireich’s compassion and empathy, with a focus on the holistic needs of individual patients, was fused with scientific creativity and perseverance. This rare blend of exceptional qualities has created a lasting legacy that will forever be part of the history of cancer research and that of MD Anderson.”

Early in his career, Freireich helped introduce the idea of treating childhood leukemia with combination chemotherapy, in which cancer drugs are given simultaneously rather than singly. Prior to this, Freireich had determined that leukemia patients frequently bled to death because of insufficient platelets, a finding that led to the development of the first continuous-flow blood cell separator, for which he holds the patent.

“He truly is the father of modern leukemia therapy, being the first to test leukemia drugs and to drive innovation in a disease that no one else had the courage to confront with his force,” said Hagop Kantarjian, MD, chair of Leukemia, who met Freireich in 1978 as a fourth-year medical student and eventually joined him on staff. “He encouraged us to dare and challenge existing dogmas in cancer research. He inspired my passion to work toward cures for patients and to change the face of this disease.”

The son of Hungarian immigrants, Freireich was born in 1927 and grew up poor in inner-city Chicago during the Great Depression. The death of his father at age two had a dramatic impact on him, and the loss of other loved ones was prominent in his formative years. Best-selling author Malcolm Gladwell, in “David and Goliath: Underdogs, Misfits, and the Art of Battling Giants” (2013), cast Freireich as a “David,” observing that those early hardscrabble years...
Freireich shared his idea for an automatic blood separating machine with IBM engineer George Judson, who built some rudimentary models with parts from a hardware store. Freireich then managed to persuade doubting NCI colleagues to sign an agreement to build the first continuous-flow blood cell separator, which allowed platelets and white blood cells to be extracted correctly. He was also correct in suspecting that platelets were useless unless obtained from fresh blood.

"Platelets in donated blood last only 48 hours," he said. "Because blood bank protocol demanded that the oldest blood be used first, the children all along had been getting blood that was too dated to contain platelets."

Freireich and Kathryn Boyer, a physician assistant. Photo courtesy of MD Anderson Cancer Center

gave him the will to push himself and his patients particularly hard in order to achieve dramatic results.

A high school physics teacher encouraged Freireich to enter the University of Illinois in Champaign at age 16. He waited tables and did other odd jobs to help pay for his education. By the time he completed his bachelor's degree, he was working on his medical degree, which he received in 1949 from the University of Illinois College of Medicine at age 22.

After an internship and residency in internal medicine at two Chicago hospitals, Freireich accepted a fellowship in hematology at Massachusetts Memorial Hospital in Boston, where he conducted and published an original study about anemia and met his future wife, Haroldine Lee Cunningham, a beautiful nurse. She started to call him "Jay," after his solitary middle initial, and friends and colleagues followed suit.

In 1955, Freireich was hired at the fledgling National Cancer Institute (NCI) in Bethesda, Md., the first full-time, patient-oriented clinical research center in the world. On his first day, he was assigned to care for children in the leukemia ward.

"Leukemia at that time was a horrible illness—a death sentence," Freireich said in a 2015 interview. "Most children lived only eight weeks after being diagnosed."

His priority was halting the nonstop bleeding that is the hallmark of leukemia. Early chemotherapy drugs were available, but patients bled to death before they could undergo treatment. Freireich believed the bleeding was caused by insufficient platelets, the colorless discs in circulating blood that are necessary for clotting. Indeed, medical research had already revealed that the platelets of World War II atom bomb victims had been wiped out by radiation and that the victims had died of hemorrhaging. Freireich's hunch proved to be correct.
are considered crazy when initially presented to the scientific community. These “crazy” ideas are the ones that often evolve into revolutionary medical and scientific advances.”

In 1965, Freireich and Frei were recruited by MD Anderson to launch a chemotherapy program. The doctors formed the Department of Developmental Therapeutics and hired scientists to develop drug combinations that cured various cancers based on the same methods used to treat childhood leukemia. Freireich’s unbounded enthusiasm for clinical research to develop and evaluate anti-cancer agents helped recruit experienced physicians and scientists, galvanizing a new generation of hematologists and oncologists to improve from the whole blood of donors and then transfused to leukemia patients.

In the late 1950s, Freireich and Emil “Tom” Frei III, MD, James F. Holland, MD, and Charles Gordon Zubrod, MD, began investigating the treatment of childhood leukemia using drugs in combination. Tuberculosis had been cured that way, and they hoped to employ some of the same strategies.

“We knew that three drugs controlled tuberculosis, but you had to administer them all at once,” Freireich said. “If given separately, they didn’t work.”

The team started administering two highly toxic drugs to young leukemia patients. Then three drugs. When Freireich added a fourth drug in a 1961 trial, the medical establishment spoke out, fearing the children would perish.

“Instead, 90 percent of them went into remission,” Freireich said. “It was magical.”

Today, the five-year survival rate for children with acute lymphocytic leukemia, the most common childhood leukemia, is about 90% overall, according to the American Cancer Society.

“Dr. Freireich’s creative passion and fierce determination to break medical barriers led to lifesaving treatments for his young leukemia patients,” said Jordan Gutterman, MD, professor of Leukemia. “Most breakthrough ideas

[Photo of Freireich working with a blood cell separator centrifuge at MD Anderson Hospital. Photo courtesy of G. Terry Sharrer, PhD, National Museum Of American History.]
chemotherapy and supportive treatments for multiple types of cancer.

Freireich helped pioneer the application of cytogenetics and molecular genetics to patient care and to the evaluation of the effects of therapy, including detection of minimal residual disease. He had a joint appointment as a professor of Laboratory Medicine, and for many years held the Ruth Harriet Ainsworth Research Chair in Developmental Therapeutics.

Over the course of his career, Freireich contributed to more than 600 scientific papers and more than 100 books. He was recognized with numerous honors for his role in developing modern clinical cancer research, including the Albert Lasker Clinical Medical Research Award, the Charles F. Kettering Prize from the General Motors Cancer Research Foundation, the first National Institutes of Health Distinguished Alumnus Award, the David A. Karnofsky Memorial Award from the American Society of Clinical Oncology, the Robert Roesler de Villiers Award from the Leukemia Society of America and the Medicus Hippocraticus Award presented at the First International Medical Olympiad in Greece. Both the European Society of Haemapheresis and the World Apheresis Association gave Freireich major awards for developing blood component technology.

MD Anderson also created the Emil J. Freireich Award for Excellence in Education in his honor, emphasizing his commitment to education and recognizing the excellence in educational contributions of the core teaching faculty.

“Dr. Freireich had a major influence on my personal and professional decisions. His advice always proved to be the very best,” said Zeev Estrov, MD, professor of Leukemia. “He inspired and encouraged me to follow my instincts and my curiosity. I frequently approached him to hear his opinion; which he delivered with scalpel sharp logic and high intellect. No gloves. No sugar coating. The naked truth — Freireich’s way. I appreciated him for that.”

Dr. Freireich’s creative passion and fierce determination to break medical barriers led to lifesaving treatments for his young leukemia patients. Most breakthrough ideas are considered crazy when initially presented to the scientific community. These “crazy” ideas are the ones that often evolve into revolutionary medical and scientific advances

— Jordan Gutterman

In 2005, Freireich was honored for his teaching contributions as a founding member of The University of Texas Academy of Health Science Education. He initiated an innovative core curriculum required by Graduate Medical Education (GME) governing bodies and granting agencies, and he chaired MD Anderson’s GME Committee for years. He also was the long-time leader of Institutional Grand Rounds held on Fridays for faculty members to share their research with colleagues and trainees.

Late in his career, Freireich inspired the formation of the Association for Patient-Oriented Research, which elected him president. In 2014, he was honored a fellow of AACR Academy, the American Association for Cancer Research. In 2019, he received presidential recognition during a Fourth of July celebration on the mall in Washington, D.C. That same year, the American Association for Cancer Research honored him with the AACR Award for Lifetime Achievement in Cancer Research during its annual meeting.

Even after retiring in 2015, Freireich made regular visits to the MD Anderson campus in Houston to teach and consult.

“We mourn his passing, but his legacy will live forever,” Pisters said. “How fortunate are we to have had Dr. Freireich as part of our MD Anderson family for five decades. His wisdom, passion and exacting standards set a bar for all of us to emulate in our ongoing efforts to end cancer.”

Emil J. Freireich, MD, is survived by his wife, Haroldine Lee Cunningham, and his children Debra Ann Freireich-Bier (Ralph Bier); David Alan Freireich (Susan Morgan); Lindsay Gail Freireich; and Thomas Jon Freireich (Kelly Freireich). He will also be remembered by his grandchildren Emily, Ellen, Chris, T.J., Sam and Macy, and his great-grandchildren Wyatt, Lyla and Myles. Services will be held virtually; details are still being set. In lieu of flowers, the family would appreciate donation to MD Anderson via http://mdacc.convio.net/goto/Freireich.
Dr. Emil J Freireich gave me hope—just as he did for millions of patients, loved ones, physicians and researchers. He brought me from Lebanon to the United States and provided me with endless opportunities to develop as a leukemia researcher and as a human being.

Not only was he my mentor, I considered him my third parent. After losing both my parents, in 2000 and 2001—my mother being the most intelligent person I have ever known and my father being the hardest-working person I have ever met—I realized that the people I loved most outside my immediate family were those in my professional one.

Foremost among them was Freireich.

When I started my career as a medical student at the American University of Beirut in 1972, I had decided I wanted to “cure cancer” (like millions of others). I told my father, but he said, “There is no such specialty. Don’t waste your time.”

This was somewhat true considering that the field of cancer research and care was in its infancy. When Freireich joined the National Institutes of Health in 1955, he was among the first generation of cancer doctors, perhaps a dozen, that included Gordon Zubrod, James Holland, Emil Frei, and others—today’s pioneering giants in cancer.

He was the “inaugural” leukemia expert, and soon enough demonstrated that leukemia was the first cancer that could be cured with drugs. Before him, M.C. Li had shown that choriocarcinomas could be cured with methotrexate (1955), but a common belief then was that this was a tumor of the fetus, thus foreign or “allogeneic,” but that “syngeneic” tumors were incurable. But I digress...

Despite my father’s objections, I was reading the 1970’s literature, and the name of Freireich and his colleagues from MD Anderson came up over and over in many of the innovative cancer discoveries and papers: Gerald Bodey, Edmond Gehan, Michael Keating, Kenneth McCreedie, Evan Hersh, Jordan Guterman (the list goes on and on).

Memorial Sloan Kettering was then the only other fully dedicated cancer research center. So, in 1978, as a fourth-year medical student, I applied to both Memorial Sloan Kettering and MD Anderson for a four-month elective rotation.

Memorial rejected me immediately. Freireich—who led the “Developmental Therapeutics” department at MD Anderson—accepted me immediately, “sans voir” (as they say in poker). I thought it was because I was so great,
but I realized later that Freireich’s motto was similar to a line in Georges Brassens’s poetry: “Embrasse-les tous, Dieu reconnaîtra le sien” (Embrace them all, God will sort his own).

He accepted us all, the geniuses and the less so, the hardest working and the lesser ones, and molded us over time into the best cancer researchers we could be. And perhaps because of Freireich’s massive magnetic personality, his dashing expansive charisma, his unlimited innovative capacities, his larger-than-life figure, and his infinite optimism, he attracted a certain breed of physicians, students, cancer researchers and followers destined to remain in cancer research and transformed them into the cancer researchers he wanted them to become.

And he attracted then from the four corners of the world. Fernando Cabanillas tells this story:

“When Freireich welcomed the new fellows in July 1974, in his welcome speech he said that all of us in the room had been selected because we were geniuses. I was so naive that I believed him. I did not consider myself a genius, and was even worried that I had been accepted at MD Anderson through a bureaucratic error, and that I would eventually be discovered. Nevertheless, I started believing him, and he made us all feel important and capable of anything, which I obviously think was what he wanted.”

When Freireich came with Frei to MD Anderson in 1965, the institution was barely on the map. Freireich was tasked with starting a cancer research program for developmental therapeutics, or DT.

Ten years later, DT became the largest cancer research program in the world, with more than 100 experts drawn from over 60 countries: New Zealand (Kenneth McCredie), Australia (Michael Keating, Andrew Burgess, Gary Spitzer, John Seymour), Japan (Ryuzo Ohno), Sweden (Borje Andersson), Czechoslovakia (Miloslav Beran), Germany (Bart Barlogie and Axel Zander), Hungary via Colombia (Gabriel Hortobagyi), Canada (Razelle Kurzrock), Holland (Karl Diekie, Lejda Vellekoop), India (Sewa Legha, Sunda Jagannath, Varsha Gandhi), Israel (Giora Mavligit, Moshe Talpaz, Zeev Estrov, Meir Wetzler), Lebanon (Elias Anaissie, Issam Raad, Fadlo Khuri, Philip Salem), Mexico (Jorge Quesada, Jorge Cortes), Panama (Adan Rios), Puerto Rico (Fernando Cabanillas), Peru (Manuel Valdivieso, Carlos Vallejos, who later became minister of health in Peru), and on and on.

There were even Americans: Gerald Bodey, Edmond Gehan, Evan Hersh, William Plunkett, Walter Hittleman, Susan O’Brien, Jeanne Hester, Jordan Guterman, Robert Benjamin, Elihu Estey, etc...

The 1974-75 fellowship class included the “four bearded ones”: Keating, Hortobagyi, Cabanillas, Barlogie. Each became one of the most prominent cancer researchers in his field (leukemia, breast, lymphoma, myeloma, respectively). The Department of Developmental Therapeutics was not only the largest, but also the most diverse in the world, akin to the Tower of Babel.

Before meeting Freireich, I was very much a person who followed established medical traditions and textbooks. I accepted medical standards and norms without questioning and believed everything that was in the books—unchallenged. At the American University of Beirut as in many other places in the world, knowledge is acquired by absorption of existing facts and information.

Freireich emphasized that all knowledge is contemporary and transient, that medical knowledge doubles every two years, and that 90% of what we hold as true in cancer research and care will be obsolete in 10 years. He taught me to think outside of the box, to always challenge concepts of leukemia care and research.
When I first arrived at MD Anderson in 1978, I started going to the DT meetings, attended by over 40-50 of the then best known cancer researchers in the world, the ones whose work and research I was reading in numerous publications (Bodey, Hersh, Guttermans, Benjamin, Hortobagyi, Keating, McCredie, Barlogie, Cabanillas, Legha, etc.).

I was still a 24-year-old who accepted established authorities, but I realized that this was Texas, the Wild West, a true Babel of cacophonies and opposing views espoused by brilliant researchers with big egos, brought together to advance the cancer cause.

Meetings would get tense, as many opinions were shared, sometimes even shouted. I would leave that dangerous environment four months later to return home to the safety of the civil war in Lebanon.

But I was already infected by the Freireich bug and returned to MD Anderson in 1981 to join his fellowship program. In 1983, I became an associate faculty member in the Leukemia Department and spent the next three to four years rounding with Freireich, McCredie, Keating and Estey almost every other month.

Each was a great teacher, and all had a great sense of humor. For me, these were the happiest, most fun memories. Freireich was a great raconteur, and I learned much through his humor.

The so called “Freireich’s Laws” were often funny, and he delivered them, as he did many of his conversations, with the perfect pitch and timing of a great comedian, while they still carried an unparalleled depth of wisdom and knowledge.

Discussing a famous statement attributed to Hippocrates, “First do no harm,” Freireich pointed out in his Karnofsky lecture that *Primum non nocere* fails to do the possible and the necessary (Law number 5; physician’s creed).

“Certainly, any lay person is qualified to ‘do no harm.’ The physician’s admonition must clearly be—do what can possibly be done and, perhaps more important, do that which is necessary.”

Law number 1 (clinical investigator’s creed): “The primary beneficiary of clinical research is the patient participating in that research.”
Freireich loomed over our lives. On our best days, we could only wish to be what Freireich was on any one of his average days.

Still, because of his dominating personality, strong opinions and unfiltered counsel, the world of Freireich was divided into two kinds of people: Those who loved him unconditionally and those who resented him unconditionally. Yet, even in their resentment, they admired him, respected him and continued to follow his research.

Still, because of the clashes with the cancer establishment, he never received his full due. He was the first leukemia researcher ever and the first to cure leukemia, yet he never received any of the American Society of Hematology awards. He was never awarded the Nobel Prize in Medicine, but then, greatness is not measured in awards.

Georges Brassens and Jacques Brel, the two greatest French poets ever, and Van Morrison were never awarded the Nobel Prize in literature (although Bob Dylan finally was). And neither were Philip Roth or Salman Rushdie (yet).

But as controversial as Freireich was in leukemia and cancer, he was extremely respectful of the opinions of individuals he loved.

As an example, he and I were on far opposite ends of the political spectrum—I'll let you guess which ends—but we never had a cross word about this.

Yes, he was larger than life, bombastic, abrasive, and politically incorrect at times. He was good at ruffling feathers, but he also had a sense of humor in abundance and a magnetism so irresistible that he made everyone who worked with him feel like they were the most important and favorite person to him.

If you asked the hundreds of researchers who worked with Freireich, each would categorically state that they were his favorite and they are carrying the torch of his legacy. And we all are.

Freireich always said, “We are going to cure all the leukemias in my lifetime.”

Initially, it was thought of as a pipe dream. When he started, none of the leukemias were curable. When I joined the MD Anderson faculty in 1981, only 20% of acute leukemias were cured, but none of the chronic leukemia were.

By 2018, all the chronic leukemias—CML and CLL—had become functionally or molecularly curable, and the cure rate of acute leukemia had reached more than 60-70%. We started to think his prophecy might actually be realized in his lifetime.

When I last saw him, in January 2021, over a span of a 30-minute conversation, he asked me three times, “Are you happy?” I replied each time in the affirmative.

Of course, I was sad in the moment, but to have spent 40 years with Freireich has made my life on this Earth very much worthwhile. I am the happiest person here because of him. Rest in peace, dearest friend of mine and of many others.

Your prophecy will come true very soon.

The author is professor and chairman, Department of Leukemia, Samsung Distinguished University Chair in Cancer Medicine, MD Anderson Cancer Center
In the departmental clinical research meetings, the fellows were sitting in the back and observed Dr. Freireich leading the meeting expecting accurate presentation and criticizing the most senior faculty, if needed.

People argued loudly in disagreement, only to be friendly to each other once the meeting was over. I learned soon that for J Freireich, scientific accuracy and knowledge were more important than seniority.

He never let any one of us get away with sloppy, inaccurate presentation.

Over the years I have learned about his multiple scientific accomplishments that significantly impacted the life of cancer patients. I was duly impressed.

However, I was much more impressed with his personality as a leader.

He was a man of principles, and he never caved to pressure from administrators. He was always willing to give up political capital if it required compromising his scientific principles.

He was perceived by some as a controversial figure, at times upholding controversial concepts. Nonetheless, he defended his views rationally and with conviction.

Dr. Freireich was among those who pioneered clinical research in oncology as a structured, scientifically-supported discipline. He was among those who developed the therapeutic principles of chemotherapy in cancer.

At the same time, he also understood the changes in the fields and the value of therapeutic disciplines, such as biologic therapies, targeted therapies, and immunotherapies. Even in his later years, he was quick to grasp new concepts, remaining a sharp observer and critic when appropriate.

I see myself among many others who are Dr. Freireich's proud students, who feel blessed to have had the opportunity to have him as a mentor who had considerable impact on their careers and lives.

The author is a professor at the Department of Internal Medicine, University of Michigan.
J Freireich was one of the few oncologists to have developed a cancer cure

By Otis W. Brawley, MD

Emil J Freireich was a big man in stature, with a booming voice. He was one of the last of the 60 original members of the American Society of Clinical Oncology.

He would go on to impact the profession for nearly seven decades. In the process, he trained hundreds of oncologists and influenced thousands.

He was friendly, often confrontational, but always supportive of young talent. Perhaps it came from his childhood in Chicago. He lived in poverty. He went to the University of Illinois by train, and personally persuaded someone in the admissions office to admit him. He worked as a waiter in a sorority to pay the tuition.

He went on to the University of Illinois for medical school and did residency at Cook County Hospital. He was outraged that they gave up
on the cancer patients and put them in “the corner room” to die.

In the 1950s, this fellow from humble beginnings would work with several men who would become giants of oncology: Gordon Zubrod, James Holland and Emil Frei. Together, they made up a large part of the National Cancer Institute Clinical Program.

People called him “J” to distinguish him from the other fellow who by coincidence had an almost identical name.

J would become one of the originators of the concept of combination chemotherapy, platelet transfusions, and establish many of the rules of cancer treatment used to this day. Later in life, he would give a talk entitled “How we cured childhood leukemia.”

There are very few of us in oncology who could give a talk entitled “How we cured anything.”

J was always controversial. I got to know him when he was sent on sabbatical to the NCI from MD Anderson to write a paper on the training of young oncologists. I learned that he was quick to tell you he disagreed with you.

Even though he disagreed with a young oncologist, he would still support them and even occasionally point out a fact that suggested his point of view was wrong, sometimes asking, “Why didn’t you see that?”

In a long lunchtime conversation, he and I disagreed once on the value of phase III clinical trials. J felt that it is obvious if a drug works, and phase III clinical trials are an attempt to market something that does not work.

He rather loudly asked me if there had ever been a phase III trial of cisplatin in testicular cancer. I said no.

Realizing others in the lunchroom were listening and he had an audience, he came up with one of his famous lines: Phase III studies are only for product promotion, and the only reasonable phase III trial was a comparison of Coke versus Pepsi.

He was fair and open-minded and ahead of his time. He trained and mentored people from many backgrounds and multiple countries. It would not unusual for Freireich to have someone from Israel working with someone from Lebanon.

He was quick to point out that no race and no country has a monopoly on good talent.

Recently, I was talking to another of the greats of oncology and the subject of J came up. We both remembered the ASCO meeting of 2000 in New Orleans.

The president’s reception was in the then relatively new World War II Museum. Emil Frei was then wheelchair-bound due to Parkinson’s.

Freireich pushed Frei around in the wheelchair all night. To those of us who appreciate the field, there was something special about two men who had done so much for oncology and really liked and admired each other.

The author is Bloomberg Distinguished Professor of Oncology and Epidemiology, Johns Hopkins University
Co-editor, Cancer History Project
Rosen spoke with Paul Goldberg, editor and publisher of The Cancer Letter.
For those watching *The Crown*: Remember when Princess Diana raised money for Northwestern Cancer Center?

“

They had decided that they were going to close the hospice unit for financial reasons. Then, Diana decided she wanted to visit the hospice unit. Not only didn’t they close it, but they refurbished it.

— Steven Rosen

Princess Diana visiting the Robert H. Lurie Cancer Center at Northwestern University in June 1996, pictured here with then-Director Steven Rosen.
Twenty-five years ago, The Cancer Letter missed a big story.

On June 4, 1996, Diana, Princess of Wales, swept into Chicago for a 48-hour visit to raise money for Northwestern University, Gilda’s Club, and the Royal Marsden Hospital, and all we did was run a paltry item in the “In Brief” section:

PRINCESS DIANA made opening remarks at a breast cancer symposium conducted by the Robert H. Lurie Cancer Center at Northwestern University on June 5. Her 48-hour visit to Chicago was expected to help raise more than $1 million for cancer research through ticket sales to a lunch and black-tie dinner. The funds are to be shared equally by the Lurie Center, the Royal Marsden Hospital of London, and Gilda’s Club, a New York-based ovarian cancer support group named for the late actress Gilda Radner.

It wasn’t even the lead brief.

A tidbit about the National Surgical Adjuvant Breast and Bowel Project’s successful re-competition of NCI grants for the chemoprevention and therapy was deemed more important and ran above it.

Yes, Norman Wolmark, chairman of NSABP, was prioritized above Diana, Princess of Wales. Of course, the Diana story was thoroughly covered by celebrity-oriented outlets, and all Norman had was The Cancer Letter.

To plot Diana’s Chicago visit on the timeline—for those watching the Netflix series The Crown—at the time the People’s Princess was separated from Prince Charles, but not yet divorced. She died in an automobile accident not quite a year and two months later, on Aug. 31, 1997.

One reminder of the 1996 visit is the Diana, Princess of Wales Professorship at Northwestern.

The chair was first held by Craig Jordan, whose research led to widespread utilization of tamoxifen for the treatment and reduction of risk of breast cancer.

In August 1998, days before the FDA Oncologic Drugs Advisory Committee vote that resulted in approval of the risk reduction indication for tamoxifen, Jordan reflected on Diana’s visit:

“Diana being British, me being British, tamoxifen being a British drug; it’s the symmetry. [It was] like the planets aligned,” Jordan said to Chicago Tribune.

The Princess Diana chair at Northwestern is now held by Daniela E Matei, chief of reproductive science in medicine in the Department of Obstetrics and Gynecology at Northwestern.

In 2016, at Matei’s investiture as the Diana, Princess of Wales professor, Ann Lurie, president of Ann and Robert H. Lurie Foundation and Lurie Holdings Inc. recalled the day Diana came to town, inspiring her to establish the professorship.

“Back in 1996, I remember that Diana urged cancer researchers at Northwestern to avoid the other ‘c’ word—complacency—in their work. Today, we have adopted ‘urgency’ in its place,” Lurie said. “I am happy that through this professorship that exists in perpetuity I could help to leverage the recruitment of someone like Dr. Matei.”

I might as well just say it: I was the guy who screwed up by failing to do a proper story 25 years ago.

Accepting full responsibility for this failure of news judgment, I called Steven Rosen, former director of Northwestern University Lurie Cancer Center, who is now the provost and chief scientific officer at City of Hope and director of Beckman Research Institute.

Paul Goldberg: Like everyone else, I was watching The Crown, and then I thought, “Wait, wait, wait. Princess Diana did something at Northwestern.” And then I thought, “Why don’t I give Steve Rosen a call and ask about it.” So, how did this come about?

Steven Rosen: She was going through her marital issues, and she was tied to People magazine. Every time she was featured, they had more sales than ever before.

They had a unique relationship, and there was someone from People magazine who knew her. She felt like she had to leave London for a period of time, just to clear her head. The only way she could leave was to be involved in some sort of philanthropic activity.

And it was decided that it would be appropriate to come to the United States. Fergie had been to Chicago—I don’t know if they had dialogue, for a fundraising event for ALS prior to that.

What I heard from People magazine was their feeling was that New York would be too much pressure, Washington was too quiet, and Chicago would be ideal.

There was a connection between the editor of People magazine, who had been at Princeton University at some point and Henry Bienen, the president of Northwestern, who had been at Princeton.

Everything led to a discussion with People magazine of bringing her to Chicago for a fundraising event that would benefit her charity, which was the Roy-
SR: It was magical. She had a great sense of humor. She was very down to earth. She had a natural kindness to her. And then that evening, there was a gala in her honor at the Field Museum, and Tony Bennett performed.

There were a number of celebrities there. She danced with [talk show host] Phil Donahue. And even Michael Jordan’s mother came before one of his basketball games, which happened to be that evening, and brought some souvenirs. And I can’t recall the exact order, but there was also the symposium, which was quite remarkable.

There was initial dialogue.

There was about six months of planning, and she, I believe, came in June for several days in 1996—25 years ago.

The first night, she came to President Bienen’s home in Evanston, at the university. And there were three separate rooms. One was for donors. One was for university officials. And the third was for those of us that were clinician-scientists that were going to participate in the internationally broadcast symposium focused on breast cancer.

I took her on a personal tour of our hospice unit, and she was just very gracious. There was no media involved. She and I just walked from room to room, and she spent as much time as the families wanted, just meeting with her.

al Marsden and the People magazine’s charity, which was Gilda’s Club, which had been started not long before the visit. And then the Lurie Cancer Center would be the third component. And so, there was initial dialogue.

What was that like?
The symposium was in the law school’s auditorium, and the room was filled to capacity. It was the hardest ticket to get. Many of the governors’ wives from around the country came.

They were invited by Governor [Jim] Edgar. At the time, he was the governor of Illinois. And I was the moderator of the program.

I know Craig Jordan participated. Nancy Brinker was part of it. Karen Antman was part of it.

And the most memorable part for me, obviously, I was a little nervous, but I was fine once I got on the stage, knowing the audience and the fact that it was being broadcast everywhere.

But when I sat down next to her, right before she was going to speak, her hands were trembling. And so, I just gently put my hand on her arm, and she sort of smiled. And then she got up and spoke more eloquently than anyone I’d ever seen in any program.

[Diana’s remarks, first published here, follow:]

I would like to begin by expressing my sincere thanks for the invitation to attend this symposium here in Chicago. It is a great privilege to be amongst some of the world’s most eminent specialists in the field of cancer and to share in this conference with you—and I can only repeat my thanks for the invitation.

Today is an important opportunity to draw the world’s attention to the disease, because there are few subjects which are more likely to raise anxiety and fear than cancer—for some it remains the dreaded “C” word. Most of us have known people who have suffered terribly at
the hands of this disease. It seems to strike out of nowhere, destroying lives almost at will, leaving devastation in its wake. Amongst all the diseases cancer has, justifiably, the very worst reputation.

And yet in the midst of such negative circumstances there is, today, an amazing amount of hope; yes, hope. Ladies and gentlemen, that hope is seated before our very eyes this morning. In so many of the seats before me I see specialists who bring hope, pioneers whose work will soon transform the lives of countless individuals bringing hope to those who might describe themselves as hopeless today.

The advances that have been made are quite staggering and, as we know, research and development continue apace. As president of The Royal Marsden Hospital and of its Cancer Fund, I have witnessed at first hand significant progress in the diagnosis, treatment, and management of patients which the hospital, in collaboration with colleagues here, has achieved through the exchange of scientific knowledge and advances in the care and support of cancer patients.

But our work is not yet finished. And so I would suggest that now might be a good time to consider another “C” word which may threaten us. It is the word complacency! And that is why this symposium is of such importance.

Whilst few of us may be able to pioneer a new form of surgery or test a new drug, we can support those who do. We can raise money for research and work in other ways to ensure that the fight against this disease continues to press ahead. A few years ago I read an article in which the writer suggested that working in the field of cancer might be a very depressing task, since it mostly remains a terminal illness and continues to take the lives of millions of people. At the time I could see the logic of that writer’s viewpoint. And yet he may have missed the point.

It may not always be possible to provide the complete solution to a patient’s predicament—but does that mean we should give up? Sometimes we may only be able to provide support and counsel—does that mean we have failed? I think not.

A letter from Princess Diana to Steven Rosen.
In just a few weeks’ time this nation will be hosting the Olympic games. Almost 90 years ago perhaps the most famous Olympian, Pierre de Coubertin, said these words in a speech in London. We might ponder them as we consider the subject of cancer.

He said: “The most important thing in life is not the victory but the contest; the essential thing is not to have won but to have fought well.”

I wish you all the strength to continue in your most important work and promise that we will continue to support you. Thank you.

And she sat down, and there was, obviously, thunderous applause.

And then she whispered in my ear, “How did I do?’’

I was thinking, “My God. You own the world. You own the planet.” And I didn’t appreciate prior to her visit, her… I knew very little about her and her celebrity status. I mean, obviously, I knew she was, but I wasn’t following the royal family very much.

We underestimated completely how much money we could raise. I think we raised about $1.5 million in a millisecond, but if we had recognized the power of her celebrity, we could have raised at least ten times that amount, if not more.

The last day, there was a luncheon at the Drake, where there were also featured speakers. It was quite a whirlwind three days that I’ll never forget. And then, obviously, the tragedy that followed—I think about six or nine months later, when she was in an auto accident and died.

I can still remember that like yesterday. I was sitting in Michigan and watching TV when the news came on.

The funny part about the visit was there were probably a thousand photographs taken.

This is pre-cellphone, and every photograph she looked perfect, but no one could find that picture they liked of themselves. It was really very cute.

And then she wrote me that beautiful letter, as you saw.

I remember running into you at ASCO after that. I’m pretty sure it was Chicago, and I said, “Hey, I’m really sorry to hear about this.” And you said, “Here we are. We got the comprehensive designation, and she wasn’t there to share the good news with.” Because you did get the comprehensive designation in that interim period. Right?

SR: Right. The core grant. We had gotten the core grant the cycle before. In those days, when you got the first grant, it was for three years, and then you went for renewal, and when we renewed it, we got comprehensive status.

I thought that during the visit you got to dance with her at one point. Did you?

SR: Actually, the funny part, or the embarrassment for me, they said that she couldn’t dance with anybody who was under five-ten, and I’m five-nine-and-a-half. So, they actually said on national TV that she won’t be dancing with me.

Was there any other highlight from her visits with patients? Anything that comes to mind?

SR: Just her sincerity and the fact that she was able to dialogue so effectively with people from every walk of life. There was a mixture. The other part that’s probably the most profound, the hospice unit at Northwestern, one of the first in the nation—ASCO’s Jamie Von Roenn was the inaugural director.

They had decided that they were going to close the hospice unit for financial reasons. Then, Diana decided she wanted to visit the hospice unit. Not only didn’t they close it, but they refurbished it.

Any other thoughts?

SR: Just that we need more Princess Dianas.

We need people who have that celebrity status, that power. They are capable of doing so much if they direct it in a meaningful way as she did.

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BEATING CANCER WITH LEADING-EDGE RESEARCH.

Cancer hits hard in Kentucky. That’s why, every day, the team at Markey steps up, with research projects that include decoding an enzyme that may be behind some resistant strains of prostate cancer. Because we’re not just treating cancer today. We’re working hard to beat it once and for all.

See how at ukhealthcare.com/beatingcancer
Black History Month, the National Cancer Act—and opening up the archives

As the Cancer History Project gets underway, our archives are growing. Now featuring past issues of The Cancer Letter from 1973-2014 and The Clinical Cancer Letter from 1977-2014, the database is becoming a fun place to explore. Go ahead, do a search for your mentors, and unearth lost quotes from times passed.

This new column in The Cancer Letter will feature the latest posts to the Cancer History Project by our growing list of contributors.

Notably, the NCI Library is uploading a treasure trove of primary source materials, AACR and ASCO have uploaded their annual reports, and MUSC Hollings Cancer Center and St. Jude Children’s Research Hospital are posting stories, videos, and images.

The Cancer History Project is a free, web-based, collaborative resource intended to mark the 50th anniversary of the National Cancer Act and designed to continue in perpetuity. The objective is to assemble a robust collection of historical documents and make them freely available.

Quote of the week

"Society can’t afford two classes of citizens, one which can be used in research and one which can’t."

– Charles Gordon Zubrod


Black History Month

The Cancer History Project has invited contributors this month to highlight the achievements and contributions by Black oncologists, researchers, and advocates, as well as any content focusing on health disparities.

The National Cancer Act of 1971

By NCI, Jan. 27, 2021

Video: Paying Tribute to ASCO Founder Jane C. Wright, MD

By ASCO, Feb. 3, 2021

Video: Remembering Ida J. Spruill: A pioneer in cancer health disparities research

By MUSC Hollings Cancer Center, Feb. 1, 2021

A growing collection of posts celebrating the impact on oncology by Black, Indigenous, and People of Color oncologists, researchers, and advocates will continue to be available under the tag “BIPOC Impact.”
**Primary Sources**

**Conquest of Cancer Act. 92nd Congress, 1st Session, S. 1828, June 29 (legislative day of June 28), 1971**
By NCI, Feb. 4, 2021

**Weekly Compilation of Presidential Documents, December 27, 1971**
By NCI, Jan. 27, 2021
Read the remarks by President Nixon on the signing of the National Cancer Act of 1971.

**Statement of Sen. Edward M. Kennedy, Senate Labor and Human Resources Committee Hearing, 20th Anniversary of the NCA**
By NCI, Jan. 28, 2021

**Opening Statement of Senator Edward Kennedy, Subcommittee on Investigations, National Cancer Institute, May 21, 1981**
By NCI, Jan. 28, 2021

**Semicentennial Celebration of the National Cancer Institute, May 26, 1987**
By NCI, Jan. 28, 2021

**Oversight of the National Cancer Program, 97th Congress, 1st Session, May 21, 1981**
By NCI, Jan. 28, 2021

**National Cancer Act Amendments of 1974, 93rd Congress, July 23, 1974**
By NCI, Jan. 27, 2021

By National Cancer Institute, Jan. 28, 2021

**National Cancer Act Amendments of 1974, 93rd Congress, 2nd Session. Report No. 93-954, March 27, 1974**
By NCI, Jan. 27, 2021

**National Cancer Act of 1974, 93rd Congress, 2nd Session (S.2893), January 30, 1974**
By NCI, Jan. 27, 2021

**Conquest of Cancer, White House Fact Sheet, August 17, 1973**
By NCI, Jan. 27, 2021

**The National Cancer Act of 1971, White House Fact Sheet, December 23, 1971**
By NCI, Jan. 27, 2021

**Introduction of the Conquest of Cancer Act, Congressional Record, January 25, 1971**
By NCI, Jan. 27, 2021

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**Recent contributions**

**Archival Photos:** Joseph V. Simone: archival photos from St. Jude Children’s Research Hospital
By St. Jude, Jan. 29, 2021

**Book:** Simone’s Maxims: Understanding Today’s Academic Medical Centers
By Cancer History Project, Jan. 29, 2021

**Book:** Stairway of Surprise: A Biography of Kay and Gordon Zubrod
By Cancer History Project, Jan. 15, 2021

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**Obituary:** Hollings leaves important legacy at namesake cancer center and beyond
By MUSC Hollings Cancer Center, Feb. 1, 2021

**Archival Photos:** Senator Ernest “Fritz” Hollings, namesake of MUSC Hollings Cancer Center
By MUSC Hollings Cancer Center, Feb. 2, 2021

MUSC Hollings Cancer Center awarded NCI designation, February 2009
By MUSC Hollings Cancer Center, Feb. 1, 2021

**History of the AACR**
By AACR, Jan. 27, 2021

**Presidents of the AACR**
By AACR, Jan. 21, 2021

**The Founders of the American Society of Clinical Oncology**
By ASCO, Jan. 28, 2021

**Research Milestones:** Cancer Progress Timeline
By ASCO, Jan. 8, 2021
Jeremy Rich was named deputy director of research at UPMC Hillman Cancer Center.

Rich will also serve as the Pittsburgh Foundation Chair in Personalized Cancer Therapy and a professor of neurology at the University of Pittsburgh School of Medicine. Rich will help oversee Hillman’s strategic cancer research efforts.

Rich is a board-certified neuro-oncologist and physician-scientist specializing in diagnosing and treating brain tumors, with a focus on brain metastases. He is also a brain tumor biology researcher, studying cancer stem cell clinical relevance and how they interact with the tumor microenvironment to help the cancers grow and resist current treatments.

Previously, Rich was a professor of medicine, director of the Brain Tumor Institute and co-director of the Solid Tumor Therapeutics Program at the University of California San Diego. Before that, he was chair of the Department of Stem Cell Biology and Regenerative Medicine at Cleveland Clinic.

Yen-Michael Hsu was named director of the Immunologic Monitoring and Cellular Therapeutics Laboratory at the UPMC Hillman Cancer Center.

Hsu was also named associate professor of hematology and oncology in the Department of Medicine, University of Pittsburgh School of Medicine. He was awarded a Hillman Fellowship for Innovative Cancer Research to support his research.

Hsu, a board-certified pathologist specialized in laboratory medicine, assumes his role from Theresa Whiteside, who directed the IMCPL for nearly three decades.

The IMCPL is responsible for the generation of therapeutic cellular products, or living drugs, to treat cancer and other diseases, monitoring immune function in patients treated with these therapies, and banking patient tissues for basic and clinical research. The IMCPL is also part of Pitt and UPMC’s COVID-19 research efforts, manufacturing the PittCoVacc delivered through a finger-
tip-sized patch, and has shown promise in animal models.

UPMC Hillman plans a significant expansion to the IMCPL to support a steadily increasing demand for cell therapies. The facility will manufacture cell therapies for cancer and other diseases.

Hsu will help translate science into cellular therapies to benefit patients. A trained immunologist, he will also focus on research to optimize or develop new protocols to improve the cellular manufacturing process.

Prior to his appointment at Hillman, Hsu was the founding medical director of the first cGMP cellular therapy laboratory at Weill Cornell Medicine for six years, and led the successful certification effort to make New York-Presbyterian Hospital/Weill Cornell Medical Center an early treatment center for the first CAR T therapies developed by Novartis and Kite.

Jeffrey Bradley named interim chair of Emory Department of Radiation Oncology

Jeffrey Bradley was named interim chairman of the Emory University Department of Radiation Oncology.

Bradley, previously the executive vice chairman of the department, succeeds former Winship Cancer Institute Executive Director Walter J. Curran, Jr., who announced in October 2020 that he would be stepping down from his role as chair (The Cancer Letter, Jan 22, 2021).

Bradley joined Winship in 2019 from Washington University School of Medicine in St. Louis where he was the S. Lee Kling Endowed Professor of Radiation Oncology and clinical director of the Kling Proton Center.

Bradley led the effort to open the world’s first single-room proton center at Washington University’s Barnes-Jewish Hospital. He is a founding member of the Particle Therapy Oncology Group of North America and the chairman of the NRG Oncology Lung Cancer Committee.

Since joining Winship, Bradley has been appointed the James W. Keller, MD Distinguished Professorship in Radiation Oncology in support of his research in innovative radiation therapy technologies such as proton beam therapy and stereotactic body radiation therapy.

Curran was chairman of the Department of Radiation Oncology for 13 years. He led efforts to open the Emory Proton Therapy Center, exclusively operated by department faculty and staff, which treated over 400 patients in its first year, and expanded basic, translational, and clinical research during his tenure.

In mid-January, the Department of Radiation Oncology appointed Curran as professor emeritus.

ASCO 2021 annual meeting to be virtual

The 2021 ASCO Annual Meeting will be an online only experience, June 4-8, 2021.

“We had hoped for a return to an in-person meeting as we all miss the opportunity to see and engage with our colleagues,” ASCO said in a statement. “While that will not be possible, due to continuing COVID-19 concerns, ASCO remains committed to delivering the latest groundbreaking science in oncology and timely information on clinical application and treatment.”

ASCO’s scientific and education programs will be held simultaneously June 4-8. The meeting platform will provide attendees with live and on-demand access to presentations and slides. The online meeting will also offer opportunities to engage with oncology thought leaders, including interactivity and live question and answer in key sessions.

Registration for the meeting launched Feb. 3.

Roswell Park, BMS Foundation create $3.3 million program to address cancer burden for native and rural communities

Roswell Park Comprehensive Cancer Center and the Bristol Myers Squibb Foundation have established a $3.3 million program to address the cancer burden in rural areas and Native Nations across New York State, with an emphasis on the Western New York region.

The grant from the Bristol Myers Squibb Foundation supports a service collaboration between Roswell Park, the Indian Health Service and geographically matched rural federally qualified health centers across New York.

It will allow Roswell Park to provide on-site and virtual patient navigation consisting of cancer prevention, screen-
ing, treatment and education as well as available education on clinical trials, palliative care and survivorship. The primary focus will be on breast cancer and prostate cancer and secondarily on co-occurring conditions that have high rates in these communities.

Six full-time patient navigators in the high-need communities as well as two virtual navigators will be created through the grant. The funding will support:

- Mobilization of a network of patient navigators in collaboration with IHS health centers and adjacent FQHCs that serve Native American and rural community members to provide a tailored program to improve screening and co-occurring disease management.

- Administration of in-person, phone-based and virtual web-based navigation systems for tribal and FQHC communities.

- Work by patient navigators with healthcare staff and participating clinics to provide education on breast and prostate cancer screening guidelines, cancer care continuum and management of co-occurring conditions.

The initiative was designed to incorporate the Two Row Wampum philosophy developed by the Haudenosaunee and based on the Two Row Wampum Belt and the Covenant Chain of Friendship.

Historically, this Wampum agreement was used as a guideline between Native Americans and the Dutch, French, British and Canada. Like the Two Row Wampum, this patient navigation collaboration will provide a bridge between two health delivery systems that are functioning in parallel, like two boats in the same river.

“This work allows us to expand efforts with federally qualified health centers and move into more rural and remote areas, strengthening our established relationships to reshape and refocus our breast and prostate cancer screening,” Kate Glaser, assistant professor of oncology in Roswell Park’s Department of Cancer Prevention and Control, said in a statement. “With limited navigation in IHS sites or rural health centers focused on addressing cancer disparities, this service is providing a unique opportunity to improve cancer screening and cancer care in this population.”

“The initiative does align with the IHS vision of healthy communities and quality health care systems through strong partnerships and culturally responsive practices by creating a Native American patient navigator team focusing on breast and prostate cancer and co-occurring conditions,” Rear Admiral Michael Toedt, chief medical officer of the Indian Health Service, said in a statement.

The grant will serve residents in Erie, Chautauqua, Cattaraugus, Allegheny, Niagara and Oneida counties and further north into the St. Regis Mohawk territory, Tuscarora and Tonawanda Band of Senecas through Indian Health Services–Lockport, as well as the Allegany and Cattaraugus Territories of the Seneca Nation. Recruitment for the navigator positions is underway in partnership with tribal partners, IHS clinics, IHS regional offices and our partnering FQHCs to ensure that the hiring reflects the unique perspectives of the area.

Over the three-year project, it is expected that 3,200 community members will be engaged and educated.
The Delaware experience:
Keeping in contact with those at risk is key to colorectal and breast cancer screening during COVID-19

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COVID-19 continues to ramp on and has affected just about all aspects of the health care system in our country.

This has led to a decrease in cancer diagnosis since the early spring of 2020, when the pandemic started. In general, one would like to see a decrease in cancer diagnosis as a result of a decrease in cancer incidence, but what has happened since the COVID-19 pandemic is that individuals have been staying home and are concerned about contracting the virus by going through standard cancer screening procedures.

This is especially true for colorectal and breast cancer screening with colonoscopy and mammography. This is critical because these cancers can be detected in an early stage, and are potentially curable and preventable.

In 2020, during the early time of the pandemic, the United States Centers for Disease Control and Prevention and several medical professional societies recommended cancer screening be postponed unless the risks outweighed the benefits.

Elective procedures were canceled so health care systems could prepare for the incoming waves of COVID-infected patients. Many hospitals were managing COVID patients by crisis, with a lack of necessary materials and personnel.

During the height of the COVID-19, NCI stated that the pandemic would result in nearly 10,000 additional deaths due to colorectal and breast cancer over the next ten years.

I think we can all imagine that this is probably an underestimate. In view of the fact that we are still learning about the full impact, both short term and long term, of COVID-19 infections, and it will take continued research and experience to better define the impact of this virus on cancer care.

Hence, the pandemic’s global impact on commonly performed cancer prevention and control measures is still unknown.

In Delaware, we have one of the most successful cancer control programs in the United States. In 2016, Delaware ranked 12th highest in the United States for colorectal screenings. In comparing 2001-2005 to 2011-2015, Delaware’s colorectal cancer incidence rate decreased 30% while the national rate decreased 22%. In 2016, Delaware stood 31st and 35th in colorectal cancer incidence and mortality.

It was imperative that despite COVID-19, we needed to find a way to continue the successful colorectal screening program during the pandemic.

Hence, from July 1 to Dec. 31, 2020, a colorectal cancer campaign evolved, which included a colorectal cancer risk assessment through an organic social media campaign from July 27 to Sept. 4, followed by paid digital and social media campaigns from Sept. 14 to Dec. 31, 2020.

Colorectal cancer awareness and risk assessment

During the COVID-19 pandemic, our community outreach team at the Helen F. Graham Cancer Center and Research Institute knew it was important to remind people to still get care including their cancer screenings and in this case colonoscopies.

In partnership with our marketing team, we had recently completed work on a free online colorectal cancer risk assessment. The risk assessment hosted by HealthAware was completed with the assistance of one of the community outreach oncology nurse navigators.

With 15 plus years of experience, the nurse navigator knew that the individuals we were trying to reach about the importance of cancer screenings are impacted by social determinants of health, health literacy, and screening options.

Individuals who committed to screening find it helpful to connect with the navigator to have their questions answered, discuss options and plan next steps.

Others, who are not ready for screening, may contact the navigator in the future when the have decided to take the next steps.

As a result of COVID-19, we found individuals sometimes felt the need to reschedule or change their choice of screening option. The key is to have a reliable contact to help navigate through these COVID times and not stop screening.

Background on the design of the assessment

Knowing the importance of reaching individuals about the risks of colorectal cancer, especially those at high risk who may not know it, we worked on creating a new and free risk assessment.

In late 2019, in collaboration with external affairs and marketing, HealthAware.com and The Helen F. Graham Cancer Center’s nurse navigator, an outdated Colorectal Cancer Risk Assessment was reworked utilizing evidence based references such as the American Cancer Society, National Comprehensive Cancer Network and Christiana Care Genentc Consultation and Risk Assessment Program to create a #12 Screen easy to complete online CRA questionnaire.

Question themes included: age; height/weight; family history of cancer and colon polyps; personal history of cancer,
Although the numbers are small in many areas, the critical outcome of this project was the contacts made to those individuals at risk who will be contacted in the coming months to remind them of the importance of cancer screening and making sure they get scheduled for the screening procedure.

**Next steps:**

- Roll out the campaign again in March 2021 for Colorectal Cancer Awareness Month.
- Included ChristianaCare employees as a target audience through a new Caregiver Connect mobile application.

As we progressed through the pandemic, we realized we still needed to keep in touch with our community about the importance of people getting back to care and getting their screenings.

We did not get discouraged, but sought other ways to move forward and continue our work. In this case, turned to a digital platform. This promotion/push brought great results and touched a good number of our community members.
More than half of cancer survivors have underlying medical conditions associated with severe COVID-19

More than half (56.4%) of cancer survivors in the United States reported having additional underlying medical conditions associated with severe COVID-19 illness. The report appears in *JNCI: The Journal of the National Cancer Institute*, and suggests that prevalence of these conditions among cancer survivors is nearly 40% higher than that in the general population.

Cancer, and other underlying medical conditions, including chronic obstructive pulmonary disease, heart diseases, diabetes, chronic kidney disease, and obesity, are associated with increased risk of severe COVID-19 illness.

For this study, investigators Changchuan (Charles) Jiang, of Roswell Park Comprehensive Cancer Center, Xuesong Han, of American Cancer Society, and colleagues used data from the 2016-2018 National Health Interview Survey, a national cross-sectional survey of the civilian, noninstitutionalized popula-

tion, to examine the prevalence of underlying medical conditions associated with severe COVID-19 illness in adult cancer survivors in the U.S.

“This study investigates the prevalence and factors associated with these underlying medical conditions among cancer survivors in the U.S. We felt it was important to compile and analyze the available data to inform the public and guide the policy makers on opportunities to prevent and control severe COVID-19–associated illness through strategies such as risk-stratified vaccine distribution,” Jiang said in a statement.

Most cancer survivors reported having more than one of the conditions associated with severe COVID-19 illness and nearly one-quarter reported more than two conditions. These conditions were more prevalent in survivors of kidney, liver and uterine cancers, as well as Black survivors, those with low socioeconomic status, and public insurance.

Older age was associated with higher prevalence of medical conditions among cancer survivors and adults without a cancer history. However, even in the youngest age group (18 to 44 years), nearly half of cancer survivors (47.6%) had at least one additional condition associated with severe COVID-19 illness.

In addition to increasing prevalence with age, medical conditions were more prevalent among male survivors (59.9%), those with less than high school completion (68.0%), non-Hispanic Black (67.2%), low income (71.7%), and those living in the South (59.2%).

Gene mutations linked to worse outcomes from leukemia in Hispanic and Latino children

A combination of genetic mutations may explain the higher incidence of and poorer outcomes from pediatric leukemia in Hispanic and Latino children, according to Penn State College of Medicine researchers.

A novel therapeutic drug combination, as well as testing for these mutations, may help address the disparity. The findings were published in *Leukemia*.

Hispanic and Latino children are between 1.2 and 1.75 times more likely to develop B-cell acute lymphoblastic leukemia, the most common childhood cancer, than non-Hispanic and Latino children. They also have a 40% higher death rate than their counterparts after correcting for socioeconomic factors.

Sinisa Dovat, a researcher and pediatric oncologist at Penn State Children’s Hospital and Penn State Cancer Institute, partnered with Dr. Gordana Raca of Children’s Hospital Los Angeles and Kimberly J. Payne of Loma Linda University to understand the biology behind this health disparity after prior research suggested that there may be an increased frequency of a type of genetic mutation in Hispanic and Latino children with B-ALL.

The researchers studied 239 pediatric patients with B-ALL at Children’s Hospital Los Angeles and found two types of genetic mutations—deletion of the IKZF1 gene (IKZF1) which holds instructions for cells to make the IKAROS protein and a rearrangement, or translocation, of the gene with instructions for producing the CRLF2 protein—occurred more frequently in Hispanic and Latino children.

IKZF1 deletion occurred two times more frequently in those children—making it the most frequent genetic alteration that signals poor prognosis of B-ALL. There was a four-fold increased incidence of CRLF2 translocations in Hispanic and Latino children, as compared to non-Hispanic and Latino children.

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“These mutations offer an explanation for the poor prognosis and increased incidence of B-ALL in Hispanic and Latino children and offer us insight into this pediatric cancer health disparity,” Dovat said in a statement.

The researchers found that 11% of Hispanic and Latino children had both mutations compared to 0% of their counterparts. Almost all of the Hispanic and Latino children with B-ALL who had a specific type of CRLF2 translocation also had an IKZF1 deletion, while a large number of them had an IKZF1 deletion without that specific type of CRLF2 translocation. According to Dovat, these results suggest that IKZF1 deletion precedes or predisposes the CRLF2 gene to mutation.

“Sequencing these genes in Hispanic and Latino children with B-ALL is essential to help pediatric oncologists determine a prognosis for these patients and develop appropriate treatment plans,” Dovat said. “Treatments that can restore the function of the IKAROS protein could be an efficient treatment for leukemia.”

In a companion study, also published in Leukemia, Dovat and colleagues outlined a treatment strategy that may be beneficial to patients suffering from this health disparity. It involves targeting a protein, mTOR, that when over produced, can lead to resistance to chemotherapy and poor prognosis.

“The CRLF2 mutation, often found in Hispanic and Latino children with B-ALL, leads to increased activity of mTOR, which has been associated with poor outcomes,” Dovat said. “We proposed that an effective treatment regimen would hinder the activity of the mTOR protein, but also target the gene that carries the instructions for making mTOR by restoring the function of the IKAROS protein.”

The researchers developed a combination therapy, starting with a drug that restores the function of IKAROS by inhibiting another protein called casein kinase 2 (CK2). When CK2 is prevented from carrying out its function, the IKAROS protein can keep mTOR from being produced. The team also used rapamycin to inactivate mTOR proteins already present in cancer cells.

Dovat and his colleagues evaluated this approach in the lab by using the combination, and each drug individually, on cancer cells from Hispanic and Latino patients. They also later tested the approach against each drug individually and in combination in an animal model of leukemia using cancer cells from Hispanic and Latino pediatric B-ALL patients.

They found that in both instances, the combination of two drugs proved more effective against leukemia than either drug individually. These studies laid the groundwork for a phase I clinical trial with this treatment and provided a new paradigm for similar approaches to treat cancer using dual targeted treatments.

Queen’s leading new research aimed at improving outcomes for early-stage bowel cancer

Researchers from the Patrick G Johnston Centre for Cancer Research at Queen’s University Belfast are leading an international consortium that aims to determine better ways to treat patients diagnosed with the earliest stages of bowel cancer.

The consortium is funded by Cancer Research UK.

The consortium includes a multi-disciplinary team of research scientists and clinicians from across the UK and Europe and is led by Philip Dunne, molecular pathologist at the Patrick G Johnston Centre for Cancer Research.

There are approximately 1.4 million cases of bowel cancer diagnosed worldwide every year and the introduction of the bowel cancer screening program for people over the age of 60 has led to a significant increase in the proportion of patients who are diagnosed with early-stage cancers.

Survival rates for patients diagnosed at the earliest stage of bowel cancer are in excess of 95%, but only in a small proportion of cases, screening identifies patients with highly aggressive tumors. This presents a major challenge in the clinic, as current diagnostic techniques are unable to distinguish these aggressive tumors that require more extensive in-patient treatment, from patients with less aggressive tumors that can be treated as outpatients.

“This new project aims to use state of the art molecular technologies to identify for the first time the underlying biology of these aggressive born-to-be-bad tumors,” Dunne said in a statement. “This information can be used to develop clinical biomarkers of aggressive disease that can be used to guide treatment decision making for patients in the future.”

The bowel cancer screening program is freely available to everyone over the age of 60, with a test being sent to your home every two years. The test is designed for people who have no symptoms and can detect very early signs of bowel cancer, sometimes up to 10 years before the development of advanced disease.

In a lot of cases the screening test can identify non-cancerous polyps in the bowel, which, if left unchecked, may become cancerous over time.

“Our consortium aims to improve our understanding of how these tumors grow and develop, with results being used to guide the development of clinical trials in the near future,” Maurice Loughrey, consultant pathologist at the Belfast Health and Social Care Trust and
The initial phase of the Cancer Research UK-funded project will run until 2023, and work has already begun to collect clinical samples from across Europe to be centralised in Belfast for molecular profiling and analysis. Following this initial phase, the teams of scientists will continue to collect and analyse data over the coming years to ensure that clinicians have as much information as possible to inform treatment decisions.

“This work will provide us with the largest known collection of early-stage bowel cancer samples, which will serve as an important resource for scientists worldwide to investigate this disease,” Keara Redmond, researcher from the Patrick G Johnston Centre for Cancer Research at Queen’s, scientific specialist and project manager in Belfast, who will lead the molecular profiling, said in a statement. “This will enable the field to identify changes in tumor DNA, both mutations and gene activation, associated with aggressive disease.”

While the bowel cancer screening program has been significantly affected due to COVID-related delays, it remains an important tool for preventing deaths from bowel cancer.

Yale Cancer Center researchers discover mechanism to overcome drug-resistance in B-ALL

Researchers at Yale Cancer Center have identified how breast cancer cells hide from immune cells to stay alive. The discovery could lead to better immunotherapy treatment for patients.

Xinna Zhang and colleagues found that when breast cancer cells have an increased level of a protein called MAL2 on the cell surface, the cancer cells can evade immune attacks and continue to grow. The findings were published in The Journal of Clinical Investigation.

Researchers noted findings from this study provide new insights into B-cell metabolism as well as B-ALL biology and highlights the significance of glucose and energy supply in leukemic transformation. “From a treatment perspective, the study suggests that the enzyme activity of PON2 can be leveraged to selectively kill B-ALL cells,” Müschen said. “Targeting of PON2 could be developed as a novel therapeutic intervention strategy to overcome drug-resistance in B-ALL.”

IU cancer center researchers discover how breast cancer cells hide from immune attack

Researchers at the Indiana University Melvin and Bren Simon Comprehensive Cancer Center have identified how breast cancer cells hide from immune cells to stay alive. The discovery could lead to better immunotherapy treatment for patients.

“Like other cancer cells, breast cancer cells present tumor-specific antigens on the cell membrane, which immune cells recognize so they can kill the tumor cells,” lead author Zhang said in a statement. “But our study found that MAL2 can reduce the level of these antigens, so these tumor cells are protected and can no longer be recognized as a threat by these immune cells.”

Zhang is a member of the IU Simon Comprehensive Cancer Center and assistant professor of medical and molecular genetics at IU School of Medicine. Understanding how cancer cells avoid immune attacks could offer new ways to improve immunotherapy for patients, Xiongbin Lu, Vera Bradley Foundation Professor of Breast Cancer Innovation and cancer center researcher.

The collaborative research team set out to answer key questions: How do breast cancer cells develop this immune evasion mechanism, and could targeting that action lead to improved immunotherapies?

Zhang and Lu, members of the Vera Bradley Foundation Center for Breast Cancer Research, turned to biomedical data researcher Chi Zhang, assistant professor of medical and molecular genetics at IU School of Medicine. Chi Zhang developed a computational method to analyze data sets from
more than 1,000 breast cancer patients through The Cancer Genome Atlas.

That analysis led researchers to MAL2; it showed that higher levels of MAL2 in breast cancer, and especially in triple-negative breast cancer, was linked to poorer patient survival.

“Chi Zhang used his advanced computational tool to build a bridge that connects cancer genetics and cancer genomics with a clinical outcome,” Lu said in a statement. “We can analyze molecular features from thousands of breast tumor samples to identify potential targets for cancer immunotherapy. From that data, MAL2 was the top-ranked gene that we wanted to study.”

Xinna Zhang took that data to her lab to determine MAL2’s purpose in the cells, how it affects breast cancer cell growth and how it interacts with immune cells. Using breast cancer tissue samples from IU patients, cell models and animal models, she found that breast cancer cells express more MAL2 than normal cells. She also discovered that high levels of MAL2 significantly enhanced tumor growth, while inhibiting the protein can almost completely stop tumor growth.

In Lu’s lab, he used a three-dimensional, patient-derived model called an organoid to better understand how reducing MAL2 could improve patient outcomes.

“Tumor cells can evade immune attacks; with less MAL2, the cancer cells can be recognized and killed by the immune system,” Lu said. “MAL2 is a novel target. By identifying its function in cancer cells and cancer immunology, we now know its potential as a cancer immunology target.”

Lu is co-leading a cancer immunotherapy program for triple negative breast cancer as part of the Indiana University Precision Health Initiative. Both Xinna Zhang and Chi Zhang are also involved in the initiative for developing novel breast cancer immunotherapy.

### Fecal microbiota transplants help patients with advanced melanoma respond to immunotherapy

For patients with cancers that do not respond to immunotherapy drugs, adjusting the composition of the gut microbiome through the use of stool, or fecal, transplants may help some of these individuals respond to the immunotherapy drugs.

Researchers at NCI’s Center for Cancer Research conducted the study in collaboration with investigators from UPMC Hillman Cancer Center at the University of Pittsburgh. The findings were published in *Science*.

In the study, some patients with advanced melanoma who initially did not respond to treatment with an immune checkpoint inhibitor did respond to the drug after receiving a transplant of fecal microbiota from a patient who had responded to the drug.

The results suggest that introducing certain fecal microorganisms into a patient’s colon may help the patient respond to drugs that enhance the immune system’s ability to recognize and kill tumor cells.

“In recent years, immunotherapy drugs called PD-1 and PD-L1 inhibitors have benefited many patients with certain types of cancer, but we need new strategies to help patients whose cancers do not respond,” study co-leader Giorgio Trinchieri, chief of the Laboratory of Integrative Cancer Immunology in NCI’s Center for Cancer Research, said in a statement. “Our study is one of the first to demonstrate in patients that altering the composition of the gut microbiome can improve the response to immunotherapy. The data provide proof of concept that the gut microbiome can be a therapeutic target in cancer.”

Research suggests that communities of bacteria and viruses in the intestines can affect the immune system and its response to chemotherapy and immunotherapy. For example, previous studies have shown that tumor-bearing mice that do not respond to immunotherapy drugs can start to respond if they receive certain gut microorganisms from mice that responded to the drugs.

Changing the gut microbiome may reprogram the microenvironments of tumors that resist immunotherapy drugs, making them more favorable to treatment with these medicines.

To test whether fecal transplants are safe and may help patients with cancer better respond to immunotherapy, Trinchieri and his colleagues developed a small, single-arm clinical trial for patients with advanced melanoma.

The patients’ tumors had not responded to one or more rounds of treatment with the immune checkpoint inhibitors pembrolizumab (Keytruda) or nivolumab (Opdivo), which were administered alone or in combination with other drugs. Immune checkpoint inhibitors release a brake that keeps the immune system from attacking tumor cells.

In the study, the fecal transplants, which were obtained from patients with advanced melanoma who had responded to pembrolizumab, were analyzed to ensure that no infectious agents would be transmitted. After treatment with saline and other solutions, the fecal transplants were delivered to the colons of patients through colonoscopies, and each patient also received pembrolizumab.
The attached miR122 effectively inhibited tumor growth compared to Paclitaxel or miR122 nanoparticles carrying both Paclitaxel and microRNA (miR122) along with HCC targeting ligands. They conjugated 24 molecules of paclitaxel, along with HCC targeting molecules (a derivative of galactosamine) and one microRNA to the multivalent RNA nanoparticle. The sequence for the miRNA extends from one of the RNA strands. The final structure is about 18 nanometers in size.

Targeted RNA nanoparticle shows early promise as liver cancer treatment

A targeted RNA nanoparticle designed to carry a chemotherapy drug along with a therapeutic oligonucleotide against chemical efflux gene might provide an effective treatment for liver cancer, according to a study led by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

The study, published in the Journal of Controlled Release, shows that the RNA nanoparticles efficiently target hepatocellular carcinoma cells and are stable, safe, and effective both in laboratory and animal studies. The findings suggest that the nanoparticles could offer an effective new treatment for HCC.

The RNA nanoparticles carry paclitaxel and display molecules that target HCC cells. They also contain a microRNA that inactivates a chemical efflux pump called p-glycoprotein, which usually pumps out chemotherapeutic drugs from the liver cells, making cancer untreatable.

“Liver cells express drug exporter pumps that are used to remove chemotherapeutic drugs and detoxify the body. This renders the treatment with chemical drugs ineffective, and contributes to drug resistance,” study leader and corresponding author Peixuan Guo, professor at Ohio State’s College of Pharmacy and the Sylvan G. Frank Endowed Chair in Pharmaceutics and Drug Delivery, said in a statement. Guo also is a member of the OSUCCC - James Translational Therapeutics Program. “This could be why liver cancer responds poorly to chemotherapy treatment.”

Earlier work by Guo and his team showed that RNA nanoparticles have rubbery or amoeba-like properties that enable them to stretch, shrink then return to their normal shape.

“We believe that this amoeba and rubber-like property enables RNA nanoparticles to slip through the poorly formed walls of tumor blood vessels and enter the tumor mass,” said Guo, who directs Ohio State’s Center for RNA Nanobiotechnology and Nanomedicine.

“This same rubbery property could allow the kidneys to filter RNA nanoparticles from the blood and excrete them in the urine, thereby eliminating them from the body swiftly,” said Guo. “This, in turn, could reduce retention of anticancer RNA nanoparticles in vital organs, lowering the drug’s toxicity.”

For this study, Guo and his colleagues constructed the RNA nanoparticles using six RNA strands that self-assembled into a globular structure. The nanoparticle served as a cargo system to deliver both Paclitaxel and microRNA (miR122) along with HCC targeting ligands. They conjugated 24 molecules of paclitaxel, along with HCC targeting molecules (a derivative of galactosamine) and one microRNA to the multivalent RNA nanoparticle. The sequence for the miRNA extends from one of the RNA strands. The final structure is about 18 nanometers in size.

The study’s key findings include:

- RNA nanoparticles selectively bind and deliver therapeutic agents into liver cancer cells efficiently.
- The attached miR122 effectively inhibits the liver drug-efflux pump.
- RNA nanoparticles carrying both Paclitaxel and miR122 more effectively inhibited tumor growth compared to Paclitaxel or miR122.
alone; nanoparticles without treatment groups showed no cancer-cell inhibition effects.

- Animal studies showed that the RNA nanoparticle formulation targeted tumor cells effectively and strongly inhibited tumor growth due to the synergistic effect of Paclitaxel and miR122, without affecting healthy organs.

KEYNOTE-598: Keytruda + Yervoy did not improve OS, PFS in Non-Small Cell Lung Cancer

Keytruda (pembrolizumab) in combination with Yervoy (ipilimumab) did not improve overall survival or progression-free survival, and instead added toxicity compared with Keytruda as monotherapy in the phase III KEYNOTE-598 study.

The phase III study evaluates Keytruda in combination with Yervoy compared with Keytruda monotherapy as first-line treatment in metastatic non-small cell lung cancer without EGFR or ALK genomic tumor aberrations and whose tumors express PD-L1 (tumor proportion score [TPS] ≥50%).

Keytruda is sponsored by Merck, and Yervoy is sponsored by Bristol Myers Squibb.

The median OS was 21.4 months for patients randomized to Keytruda in combination with Yervoy versus 21.9 months for those randomized to Keytruda monotherapy (HR=1.08 [95% CI, 0.85-1.37]; p=0.74). Additionally, the median PFS was 8.2 months for patients in the combination arm versus 8.4 months for those in the Keytruda monotherapy arm (HR=1.06 [95% CI, 0.86-1.30]; p=0.72).

“In KEYNOTE-598, the addition of ipilimumab to Keytruda did not improve overall survival or progression-free survival, and patients who received the combination were more likely to experience serious side effects than those who received Keytruda monotherapy,” Michael Boyer, chief clinical officer and conjoint chair of thoracic oncology of Chris O’Brien Lifehouse, Camperdown, NSW, Australia, said in a statement.

These results were presented in the presidential symposium at the IASLC 2020 World Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer on Jan. 29 and published in the Journal of Clinical Oncology.

The study was discontinued due to futility based on the recommendation of an independent data monitoring committee, which determined the benefit/risk profile of KEYTRUDA in combination with Yervoy did not support continuing the trial. The DMC also advised that patients in the study discontinue treatment with Yervoy/placebo.

KEYNOTE-598 (ClinicalTrials.gov, NCT03302234) is a randomized, double-blind, phase 3 trial designed to evaluate Keytruda in combination with Yervoy compared to Keytruda monotherapy as first-line treatment for patients with metastatic NSCLC without EGFR or ALK genomic tumor aberrations and whose tumors express PD-L1 (TPS ≥50%). The dual primary endpoints are OS and PFS. Secondary endpoints include objective response rate, duration of response and safety.

The study enrolled 568 patients who were randomized 1:1 to receive Keytruda (200 mg intravenously [IV] on Day 1 of each three-week cycle for up to 35 cycles) in combination with Yervoy (1 mg/kg IV on Day 1 of each six-week cycle for up to 18 cycles); or Keytruda (200 mg IV on Day 1 of each three-week cycle for up to 35 cycles) as monotherapy. Non-binding futility criteria for the study were based on restricted mean survival time (RMST), an alternative outcome measure estimated as the area under the survival curve through a fixed timepoint.

The pre-specified criteria were differences in RMST for Keytruda in combination with Yervoy and Keytruda monotherapy of ≤0.2 at the maximum observation time and ≤0.1 at 24 months of follow-up.

As of data cut-off, the median study follow-up was 20.6 months. Findings showed the median OS was 21.4 months for patients randomized to Keytruda in combination with Yervoy (n=284) versus 21.9 months for those randomized to Keytruda monotherapy (n=284) (HR=1.08 [95% CI, 0.85-1.37]; p=0.74).

The differences in RMST for Keytruda in combination with Yervoy and Keytruda monotherapy were -0.56 at the maximum observation time and -0.52 at 24 months, meeting the futility criteria for the trial and confirming the benefit/risk profile of the combination did not support continuing the study.

Additionally, the median PFS was 8.2 months for patients randomized to Keytruda in combination with Yervoy versus 8.4 months for those randomized to Keytruda monotherapy (HR=1.06 [95% CI, 0.86-1.30]; p=0.72). In both arms of the study, ORR was 45.4%; the median DOR was 16.1 months for patients randomized to Keytruda in combination with Yervoy versus 17.3 months for those randomized to Keytruda monotherapy.
FDA grants accelerated approval to Tepmetko for metastatic NSCLC

FDA has granted accelerated approval to Tepmetko (tepotinib) for adult patients with metastatic non-small cell lung cancer harboring mesenchymal-epithelial transition exon 14 skipping alterations.

Tepmetko is sponsored by EMD Serono Inc.

Efficacy was demonstrated in the VISION trial (NCT02864992), a multicenter, non-randomized, open-label, multicohort study enrolling 152 patients with advanced or metastatic NSCLC with MET exon 14 skipping alterations. Patients received tepotinib 450 mg orally once daily until disease progression or unacceptable toxicity.

The main efficacy outcome measures were overall response rate determined by a blinded independent review committee using RECIST 1.1 and response duration. Among the 69 treatment naïve patients, the ORR was 43% (95% CI: 32%, 56%) with a median response duration of 10.8 months (95% CI: 6.9, not estimable). Among the 83 previously treated patients, the ORR was 43% (95% CI: 33%, 55%) with a median response duration of 11.1 months (95% CI: 9.5, 18.5).

Keytruda receives positive EU CHMP opinion for expanded approval in some cases of relapsed or refractory classical hodgkin lymphoma

The Committee for Medicinal Products for Human Use of the European Medicines Agency has adopted a positive opinion recommending approval of an expanded label for Keytruda (pembrolizumab).

The opinion is recommending Keytruda as monotherapy for the treatment of adult and pediatric patients aged three years and older with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant or following at least two prior therapies when ASCT is not a treatment option.

Keytruda is sponsored by Merck.

This recommendation is based on results from the pivotal phase III KEYNOTE-204 trial, in which Keytruda monotherapy demonstrated a significant improvement in progression-free survival compared with brentuximab vedotin, a commonly used treatment.

Keytruda reduced the risk of disease progression or death by 35% (HR=0.65 [95% CI: 0.48-0.88]; p=0.00271) and showed a median PFS of 13.2 months versus 8.3 months for patients treated with BV.

The recommendation is also based on supportive data from an updated analysis of the KEYNOTE-087 trial, which supported the European Commission’s approval of KEYTRUDA for the treatment of adult patients with relapsed or refractory cHL who have failed ASCT and BV or who are transplant ineligible and have failed BV.

The CHMP’s recommendation will now be reviewed by the EC for marketing authorization in the European Union, and a final decision is expected in the first quarter of 2021. If approved, this will be the first pediatric indication for Keytruda in the EU.

NCI Trials for February 2021

The National Cancer Institute approved the following clinical research studies last month.

For further information, contact the principal investigator listed.
Phase I - 10355
A Phase I Study of DS-8201a in Combination with Olaparib in HER2-Expressing Malignancies

Dana-Farber - Harvard
Bowers, Daniel Charles
(214) 648-3896

Phase I - A051901
Phase I Trial of Methotrexate, Rituximab, Lenalidomide, and Nivolumab (Nivo-MR2) Induction Followed by Lenalidomide and Nivolumab Maintenance in Primary CNS Lymphoma

Alliance for Clinical Trials in Oncology
Hahn, Olwen Mary
(773) 702-4400

Phase II - EA3191
A Phase II Randomized Trial of Adjuvant Therapy with Pembrolizumab After Resection of Recurrent/Second Primary Head and Neck Squamous Cell Carcinoma with High Risk Features

ECOG-ACRIN Cancer Research Group
Zandberg, Dan Paul
(412) 864-7955

Phase II - PEPN1924
A Phase 2 Study of DS-8201a (NSC# 807708) in Adolescents, or Young Adults with Recurrent HER2+ Osteosarcoma

Pediatric Early Phase Clinical Trial Network
Reed, Damon Russell
(813) 745-3242

Phase III - ACNS1931
A Phase 3 Study of Selumetinib (NSC# 748727) or Selumetinib in Combination with Vinblastine for Non-NF1, Non-TSC Patients with Recurrent or Progressive Low-Grade Gliomas (LGGs) Lacking BRAFV600E or IDH1 Mutations

Children’s Oncology Group
Bowers, Daniel Charles
(214) 648-3896

Phase Other - A152022
Alliance COVID-19 Pandemic Study

Alliance for Clinical Trials in Oncology
Hahn, Olwen Mary
(773) 702-4400

Phase Other - S1912CD
A Randomized Trial Addressing Cancer-Related Financial Hardship Through Delivery of a Proactive Financial Navigation Intervention (CREDIT)

SWOG
Shankaran, Veena
(206) 288-7456

Phase Pilot - PEPN21EHRPBTCCN15
Pilot Study to Enable Electronic Laboratory Data Transfer Into Medidata Rave

Pediatric Early Phase Clinical Trial Network
Miller, Tamara Porter
(404) 727-9268