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Inside information on cancer research and drug development
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THE CANCER HISTORY PROJECT: BUILDING A LIVING RECORD OF PROGRESS AGAINST CANCER—REFLECTING ON OUR IMPACT—AND MOST-READ ARTICLES

Forty-nine years and a few days after the signing of the National Cancer Act of 1971, we launched the Cancer History Project. One year and 11,894 articles later, we have built a shared, collaborative, and unprecedented resource.

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SWOG CANCER RESEARCH NETWORK

Vice Chair for Diversity, Equity, Inclusion, & Professional Integrity

SWOG Cancer Research Network, a member of the National Cancer Institute's (NCI's) National Clinical Trials Network (NCTN), seeks a 0.25-FTE vice chair to lead the group's diversity, equity, and inclusion initiatives and to serve in an ombudsperson role as a neutral and confidential resource for SWOG members.

DESCRIPTION:

SWOG's mission is to significantly improve lives through cancer clinical trials and translational research. SWOG and The Hope Foundation, its charitable arm, are pursuing multi-phased, multi-year initiatives to improve diversity, equity, and inclusion (DEI) in group leadership and membership and in clinical trials. SWOG seeks candidates for a new vice chair position to align its DEI and integrity initiatives.

The vice chair for diversity, equity, inclusion, and professional integrity will provide oversight of DEI initiatives to support SWOG's strategic plan and will hold an ombudsperson position, as a neutral and confidential resource for SWOG members. By integrating these key areas within a single leadership position, SWOG seeks to center diversity, inclusion, and integrity within its operational and scientific infrastructure, supporting a research and work environment in which all have an opportunity to succeed.

The new vice chair will also

- champion the importance and value of a diverse, inclusive working environment and guide the development of a vision and effective strategy to create a culture for DEI and ethical behavior across leadership, including leadership of SWOG committees and subcommittees.
- assess potential barriers and recommend systems change to recruit and retain a diverse SWOG leadership and membership.
- recommend systems change for a neutral, impartial, and confidential pathway to support leaders and members in upholding SWOG's values of integrity and accountability.
- have extensive knowledge in areas of cultural competency, critical race theory, gender differences, dis/ability, sexual harassment, and other topics related to increasing awareness and support of DEI network wide.

SWOG seeks a candidate with a research or health-professional doctoral degree or its equivalent (e.g., MD, PhD, or DO). Experience with faculty-level management is strongly preferred. Experience with the NCTN or another similarly complex, multi-institutional setting or consortium is essential.

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

Salary: Effort is 25 percent, compensated in line with scaling set by the National Institutes of Health (NIH).

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 January 15, 2022.

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EDITORIAL

CANCER HISTORY PROJECT

The Cancer History Project: Building a living record of progress against cancer

Reflecting on our impact—and most-read articles

By Otis W. Brawley and Paul Goldberg

Forty-nine years and a few days after the signing of the National Cancer Act of 1971, we launched the Cancer History Project. One year and 11,894 articles later, we have built a shared, collaborative, and unprecedented resource.

This is only the beginning. The Cancer History Project will continue in perpetuity.

We have demonstrated that we can collaborate with cancer institutions to present a history that has never before existed in one place—a history of an entirely new political and scientific process aimed to control a deadly disease.

A half a century ago, critics belittled the National Cancer Act, calling it a federal boondoggle. This argument is rarely heard today, as effective treatments emerge for cancers that were even recently viewed as incurable and as cancer mortality rates decline. Cancer research has paid dividends in other areas of medicine—including recently in development of vaccines for COVID-19 (*The Cancer Letter*, Feb. 19, 2021).

No other country and no other therapeutic area has a National Cancer Act.

This landmark law launched a government-wide effort, overseen by boards whose members are appointed by the U.S. presidents.

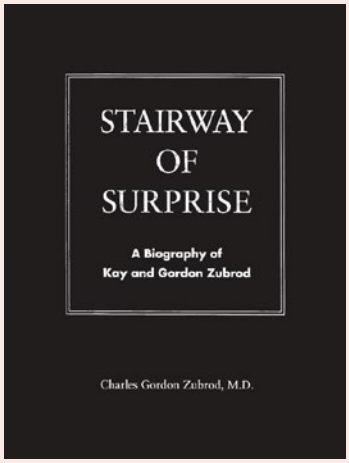
It led to rapid increases in appropriations, creating a funding stream for extramural science, bringing universities into the effort and creating a massive wave of technology transfer to the pharmaceutical and biotechnology industries.

It codified clinical trials cooperative groups as well as a system for gathering cancer statistics, set the goals for cancer prevention and control, and established a nationwide network of cancer centers, describing how they should operate and what they should seek to accomplish. Progress—and politics—can be tracked in the archives of the Cancer History Project.

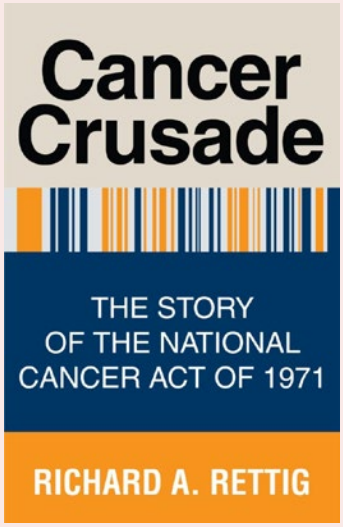
A collection of primary sources discussing the accomplishments of the National Cancer Act is available here.

We opened public access to the archive of *The Cancer Letter*, which has been publishing weekly since 1973. The archive is a detailed, real-time record of the National Cancer Program—and it's searchable.

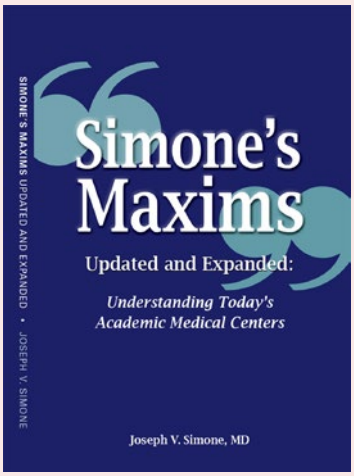
Consider three books that we had the honor to bring to our readers:



- Gordon Zubrod: An argument can be made that the story of the war on cancer begins in 1956, when an infectious disease expert named Gordon Zubrod joins a government research entity nicknamed the National Mouse Cancer Institute. The cancer program without Zubrod is unimaginable, which is why the Cancer History Project began last January with his previously unpublished memoir.



- Richard Rettig: Rettig's authoritative book describes the complex political process that produced the National Cancer Act.



- Joe Simone: Simone's Maxims focuses on the culture of cancer centers and academic medicine. His oft-quoted maxim: "Institutions don't love you back."

Oral histories published in the Cancer History Project paint an even more vivid picture, and podcasts and videos add even more color. We invite you to peruse the NCI Oral History Project, celebrate diversity in our field, and explore the many contributions of women in oncology.

The National Cancer Act was signed into law on Dec. 23, 1971. This was the end of a long political process and the beginning of another. In 1972, the real work began. This anniversary marks the beginning of the 50th year, and the Cancer History Project will continue in our mission to preserve and highlight our shared history.

This week's issue is focused on 1972: the beginning of a new era in cancer research. In addition to our usual news coverage, we invite you to immerse yourself in history:

- Nixon's speeches from the signing are republished in full alongside original footage,
- In The Archives, a weekly column dedicated to cancer history, highlights papers published in *Cancer*, NCI's effort to realize President Joe Biden's promise to end cancer as we know it, and the Richard Nixon Foundation conference that commemorated the National Cancer Act's signing.

This year, we experienced firsthand the urgency of this project. In 2021, we lost Walter Lawrence, Joe Bertino, Joe Simone, Albert de la Chapelle, Emil Freireich, Elihu Estey, Edmund Gehan, David Livingston, Thomas Waldmann, Martin "Mac" Cheever, Franco Muggia, John Potter, and José Baselga. This week's issue features an obituary of Hal E. Broxmeyer.

In 2022, we will continue this work with urgency. We will curate and bring to

your attention more books, more primary sources, more profiles, and more milestones. We will highlight more videos, more podcasts, and more photographs. We will host events and build community around the examination of our history.

To aid us in this mission, we invite you to join us:

- **Become a contributor.** Eligible institutions include cancer centers, advocacy groups, professional societies, pharmaceutical companies, and other groups with a role in shaping or recording the history of oncology. Apply today.
- **Become a sponsor.** The Cancer History Project is funded by sponsorships. Sponsors receive an advertising package commensurate with the sponsorship level, and year-long logo placement on the Cancer History Project. Learn more in *The Cancer Letter*'s media kit.

The Cancer Letter is taking a publication break. We will return on Jan. 7.

Top ten contributors

The following contributors posted the most articles in 2021:

NCCS NATIONAL COALITION FOR CANCER SURVIVORSHIP

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

NIH NATIONAL CANCER INSTITUTE

FOX CHASE CANCER CENTER TEMPLE HEALTH

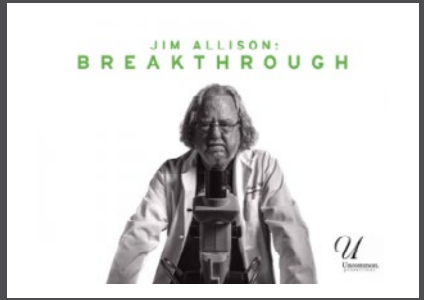
ROSWELL PARK COMPREHENSIVE CANCER CENTER

THE UNIVERSITY OF KANSAS CANCER CENTER

AACR American Association for Cancer Research

RUTGERS Cancer Institute of New Jersey RUTGERS HEALTH RWJBarnabas HEALTH

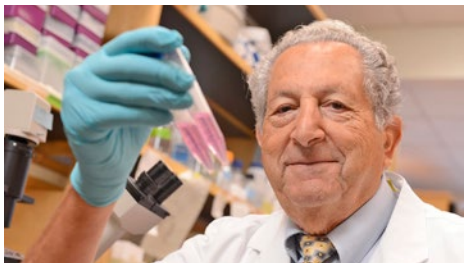
JOHNS HOPKINS MEDICINE THE SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER



Of the Cancer History Project's 11,894 articles, here are the top 25 most-read in 2021:

1. **Video:** Amy Reed, physician and patient who "moved mountains" to end widespread use of power morcellation
   By *The Cancer Letter* | May 26, 2017

2. **Book:** Simone's Maxims: Understanding Today's Academic Medical Centers
   By Joseph V. Simone, made available through his estate | Jan. 29, 2021



3. Joseph R. Bertino: 50 Years of Cancer Research, A "Golden" Opportunity
   By Rutgers Cancer Institute of New Jersey | April 21, 2021

4. Remembering Jane Cooke Wright, a Black woman, who was among seven founders of ASCO
   By Edith Mitchell | Feb. 19, 2021

5. To NCI designation through difficulty: How KU's Roy Jensen made it happen
   By *The Cancer Letter* | July 9, 2021

6. Paul Calabresi: A Founder and Giant in the Field of Medical Oncology
   By Cancer Center at Brown University | May 12, 2021

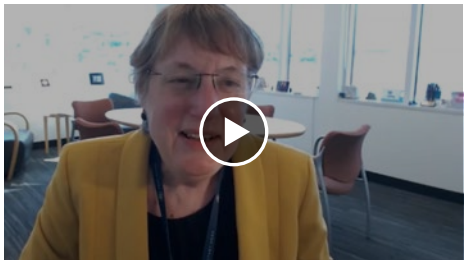
7. **Book:** Gordon Zubrod's panoramic vision shaped modern clinical cancer research
   By Cancer History Project | Jan. 15, 2021

Related: C. Gordon Zubrod, 84, Dies, Led Chemotherapy Research, Built Cooperative Group System
The Cancer Letter archives | Jan. 29, 1999

8. Carol Fabian: A Persistent Pioneer in Breast Cancer Research
   By The University of Kansas Cancer Center | March 2, 2021

9. Fran Visco: How 1960s activism shaped the movement that resulted in the DOD breast cancer program
   By Cancer History Project | Sept. 10, 2021

Related: Susan Love on breast cancer activism in the 1990s
By Cancer History Project | Oct. 22, 2021



10. **Video:** How Fred Hutch, UW and Seattle Children's helped revive NCI-designated consortium cancer centers
By *The Cancer Letter* | July 16, 2021

11. **Video:** NCCN's Bob Carlson talks about the day he stormed out of a meeting with transplanters
By *The Cancer Letter* | March 26, 2021

Related: Bob Young: NCCN is a case study in keeping what works and discarding what doesn't
By *The Cancer Letter* | March 12, 2021

Bill McGivney: How NCCN guidelines came to play a role in payment for cancer therapy
By *The Cancer Letter* | March 19, 2021

12. Dr. Patricia Ganz: Changing the Face of Survivorship
By UCLA Jonsson Comprehensive Cancer Center | March 25, 2021

Related: Patricia Ganz on how survivorship went from being an outlier to the mainstream
By Cancer History Project | Nov. 19, 2021

13. **Video:** Hait and Libutti in conversation; Rutgers Cancer Institute founder and its current director talk history
By Rutgers Cancer Institute of New Jersey | July 30, 2021

14. A Legacy of Hope: Remembering Arti Hurria, M.D.
By City of Hope Comprehensive Cancer Center | Feb. 24, 2021

15. **Video:** Bob Young: The evolution of consortium cancer centers since the signing of the National Cancer Act
By *The Cancer Letter* | July 23, 2021

16. **Podcast:** Cancer Mavericks docu-series explores a history of cancer survivorship
By Cancer History Project | Sept. 24, 2021

17. **Video:** Padmanee Sharma on coming to America and falling in love with science
By Jim Allison: Breakthrough | April 1, 2021

18. Query Theory: A Tribute to Beatrice Mintz, PhD
By Fox Chase Cancer Center | May 4, 2021

19. **Panel:** The three comprehensive cancer centers that set the model for a nation
By Cancer History Project | Aug. 6, 2021

20. Barton Kamen: A "Grand" Illusion
By Rutgers Cancer Institute of New Jersey | June 8, 2021

21. The Story of City of Hope
By City of Hope Comprehensive Cancer Center | Feb. 23, 2021

22. Imagining Roswell Park, the world's first cancer research center
By Roswell Park Comprehensive Cancer Center | March 25, 2021

23. Helen Coley Nauts: The Woman Who Resurrected Cancer Immunotherapy
By Cancer Research Institute | April 1, 2021

24. Legendary MD Anderson faculty member Dr. Emil J Freireich passes away at 93
By MD Anderson Cancer Center | Feb. 3, 2021

25. What the NCI cancer centers program looked like in 1975
By Cancer History Project | Dec. 3, 2021

Related: John Yarbro's "memos for the record" provide a detailed overview of the NCI Cancer Centers Program in 1975
By Cancer History Project | Dec. 3, 2021

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CANCER HISTORY PROJECT

The day the National Cancer Act became law

Speeches, footage, and dispatches from Dec. 23, 1971

Fifty years ago, President Nixon interrupted Christmas festivities to sign the National Cancer Act of 1971 into law. Fifty years later, we invite you to immerse yourself in that day to reflect on how far we've come.

Nixon signing the National Cancer Act.
Photo courtesy of Linda Bartlett, National Cancer Institute

Speaking surrounded by holly and Christmas cheer in the State Dining Room, Nixon declared, "I hope that in the years ahead that we look back on this day and this action shown as being the most significant action taken during this administration."

Patricia Nixon, whose dedication to Christmas established a number of White House traditions still in place today, described her 1971 White House Christmas decor as "a land of enchantment."

"Holly, garlands of evergreens and banks of red poinsettias fill the famous rooms," reported *The New York Times*. "Mrs. Nixon pointed out there is mistletoe, too."

Under the mistletoe, the White House press office readied itself for the signing of landmark legislation. Nixon's statement to the press is imbued with Christmas spirit:

"Hope and comfort, the relief of suffering and the affirmation of life itself—these are qualities which have traditionally been associated with the Christmas season. There could be no more appropriate time than this to sign into law the National Cancer Act of 1971."

Speaking on behalf of the American Cancer Society, then-President Alva Letton said, "We would like to think that this is a wonderful Christmas present in the signing of this bill today for the 52 million people in our country who will develop cancer who are now living."

An in depth analysis of the lead-up to the signing is available in Cancer Crusade: The Story of the National Cancer Act of 1971, the authoritative book by Richard A. Rettig, made available by the Cancer History Project.

We invite you to read Nixon's statements in full below and view the archival footage of the day.

Primary sources provided by NCI:

- The National Cancer Act of 1971
- White House Fact Sheet, Dec. 23, 1971

Statement by the President

Hope and comfort, the relief of suffering and the affirmation of life itself—these are qualities which have traditionally been associated with the Christmas season. There could be no more appropriate time than this to sign into law the National Cancer Act of 1971. For this legislation—perhaps more than any legislation I have signed as President of the United States—can mean new hope and comfort in the years ahead for millions of people in this country and around the world.

The enactment of this legislation culminates a year-long effort to launch an unprecedented attack against cancer. I called for such a program in my State of the Union message in January 1971, and I expanded on that call in my special message to the Congress concerning health on February 18th. Early in May, I submitted to the Congress very specific proposals for a cancer-cure program—proposals which are reflected in all important respects in the legislation I have signed today.

The effort to mobilize a concerted national campaign against cancer has continued to make significant progress since those proposals were submitted. One of the most important steps was the approval by the Congress of the additional $100 million I requested to support an expanded attack on cancer. This additional $100 million, when added to the regular appropriation for this fiscal year, gives the National Cancer Program a current operating level of $337.5 million, compared to only $180 million during the first hall of fiscal year 1972. Another important component in our campaign was put in place in October when I announced that the bacteriological warfare research facilities at Fort Detrick, Maryland would be converted into a leading center for cancer research.

Now this year of preparation for an all-out assault on cancer comes to a climax with the signing of the National Cancer Act. The new organizational structure which this legislation establishes will enable us to mobilize far more effectively both our human and our financial resources in the fight against this dread disease.

I appreciate deeply the months of hard and careful effort which so many members of the Congress gave to this cause. I am especially pleased that the new National Cancer Program incorporates the basic recommendations I made last May. It allows the President to appoint the Director of the National Cancer Institute and provides that the budget of the National Cancer Institute be submitted directly to the President. It creates a 3-member President's Cancer Panel to monitor its development and execution on a regular basis and a 23-member National Cancer Advisory Board to offer general guidance. Both of

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these groups are to be appointed by the President and will report directly to him. The important result of all these provisions is to place the full weight of the Presidency behind the National Cancer Program. As I recommended in May, the President will be able to take personal command of the Federal effort to conquer cancer so that its activities need not be stymied by the familiar dangers of bureaucracy and red tape.

Having asked for this authority—and this responsibility—I now pledge to exercise it to the fullest. Biomedical research is, of course, a notoriously uncertain enterprise and its rate of progress cannot be predicted with confidence. But I can say with the greatest confidence that there will be no uncertainty about the Government's role in this effort. I am determined that the Federal will and Federal resources will be committed as effectively as possible to the campaign against cancer and that nothing will be allowed to compromise that commitment.

I make this statement with even greater confidence knowing that Benno C. Schmidt has accepted my invitation to become the first chairman of the President's Cancer Panel. As Chairman of the National Panel of Consultants on the Conquest of Cancer, Mr. Schmidt has played an active role in the development and enactment of the National Cancer Act. He is an effective leader of men and a dedicated community servant. The Nation is fortunate that he will be heading this important panel in its critical first year.

Even as the plans for our National Cancer Program were being completed in the past few months, other developments have continued to fuel our hopes for further

President Richard Nixon and First Lady Patricia Nixon in front of the White House Christmas tree in the Blue Room, 1971.
Photo courtesy of Richard Nixon Presidential Library and Museum

substantial progress in discovering the causes and cures of cancer. Scientists in all parts of the world have continued to contribute important new findings to the growing pool of knowledge about this disease. There continues to be every reason for believing that cancer research, of all of our research endeavors, may be in the best position to benefit from a new application of human and financial resources.

This is the case, however, only because so many men and women have already given so much to the battle against cancer in the past. Their energies and talents and sacrifices have built the foundations on which all future progress must rest.

As we plan for future progress, we should also remember that the expansion of the Federal campaign against cancer in no way diminishes the continuing importance of private and voluntary activities. It is essential, for example, that an organization such as the American Cancer Society—which has raised so much money for this cause and which has done so much to promote research and education in this field—continue to play its full effective role. The new National Cancer Program must not replace our present efforts to fight cancer; it must supplement them and build on them.

As this year comes to an end, cancer remains one of mankind's deadliest and most elusive enemies. Each year it takes more lives in this country alone than we lost in battle in all of World War II. Its long shadow of fear darkens every corner of the earth. But just as cancer represents a grim threat to men and women and children in all parts of the world, so the launching of our great crusade against cancer should be a cause for new hope among people everywhere.

With the enactment of the National Cancer Act, the major components for our campaign against cancer are

Nixon family and guests enjoy Christmas dinner in the State Dining Room, where a few days prior the National Cancer Act was signed.
Photo courtesy of Richard Nixon Presidential Library and Museum

in place and ready to move forward. I am particularly happy that the year 1971—at the beginning of which I issued my call for a new campaign against cancer—can end with the signing of this landmark legislation.

Remarks of the President at the signing of the Cancer Act of 1971

Members of the Senate, Members of the House, Ladies and Gentlemen:

We are here today for the purpose of signing the Cancer Act of 1971. I hope that in the years ahead that we look back on this day and this action shown as being the most significant action taken during this Administration. It could be, because when we consider what cancer does each year in the United States, we find that more people each year die of cancer in the United States than all the Americans who lost their lives in World War II.

This shows us what is at stake. I sent a message to the Congress the first provided for a national commitment for the conquest of cancer, to attempt to find a cure.

Now, with the cooperation of the Congress, with the cooperation of many of the people in this room, we have set up a procedure for the purpose of making a total national commitment. I am not going to go into the details of that procedure, except to say this: As a result of what has been done, as a result of the action which will come into being, as a result of signing this bill, the Congress is totally committed to provide the funds that are necessary, whatever is necessary, for the conquest of cancer. The President is totally committed—we have a Presidential panel headed by Benno Schmidt, which will report directly to the President so that the President's influence, whenever necessary, can be used to reach this great goal.

And, in addition to that, all of the agencies of government, the National Institutes of Health, HEW, et cetera, are totally committed.

Now, having said that, I have spoken exclusively of government up to this point. In this room are scores of people who have worked voluntarily for this cause for many, many years. The American Cancer Society, of course, is the best known organization, but there are many, many others as well.

In saying that there will be a Presidential commitment, a Congressional commitment and a government commitment, I should emphasize that a total national commitment means more than government. It means all the voluntary activities must also continue. We have to realize that only one-sixth of everything that is produced in America is produced by what government does. Five-sixths of what we do in America is produced by what people do in their voluntary and cooperative capacities.

So, we need the continued cooperation of all the volunteer organizations. You will have, of course, the total commitment of government and that is what the signing of this bill now does.

Finally I should emphasize, as Benno Schmidt mentioned just a moment ago, that we would not want to raise false hopes by simply the signing of an Act, but we can say this: That for those who have cancer, and who are looking for success in this field, they at least can have the assurance that everything that can be done by government, everything that can be done by voluntary agencies in this great, powerful, rich country, now

> But just as cancer represents a grim threat to men and women and children in all parts of the world, so the launching of our great crusade against cancer should be a cause for new hope among people everywhere.
>
> – *Richard Nixon*

will be done and that will give some hope and we hope those hopes will not be disappointed.

(At this point, President Nixon signed the Cancer Act.)

Now, ladies and gentlemen, for those of you who have not participated in signing ceremonies and that, of course, does not include the Members of the House and Senate who are here, I see that many of them have been here previously, the custom is always to sign with the Presidential pen. I will use two pens for the signature, but a souvenir pen will be available to everybody in the audience here. We had to stretch a little to find that many, but we did it.

Incidentally, it is a very good pen, but the box is worth more than the pen.

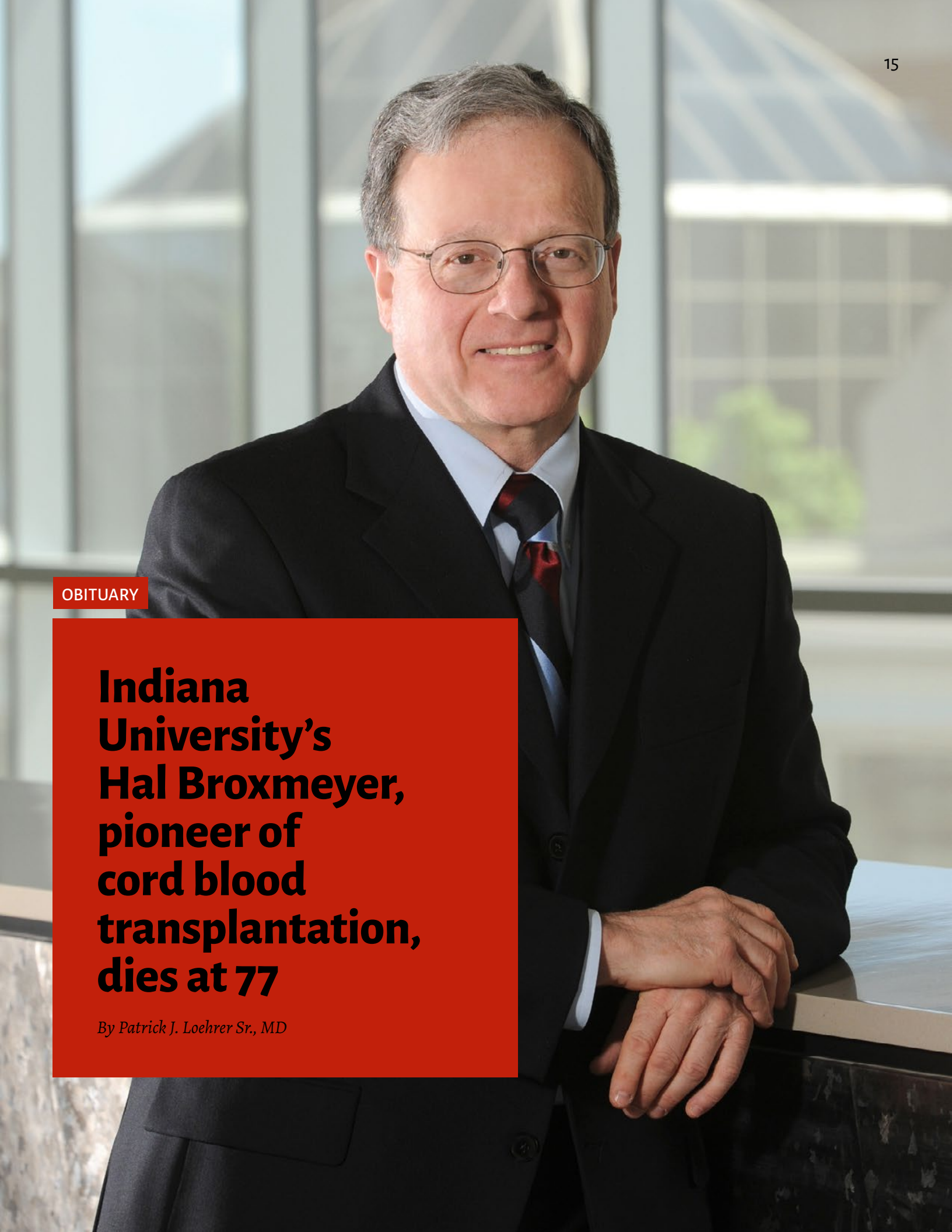
Benno, you get the "Richard". Dr. Letton, if you will step forward. The President of the American Cancer Society. You get the last name.

DR. LETTON: Thank you, Mr. President.

We would like to think that this is a wonderful Christmas present in the signing of this bill today for the 52 million people in our country who will develop cancer who are now living.

This bill, we feel, is a real great opportunity for America, probably the greatest thing that has ever been done by the United States. To you, sir, who asked for this to be a national priority and to our friends in the Congress who gave us this bill, two and a half, two and a quarter million of the volunteers of the American Cancer Society asked that I express their appreciation. We are truly grateful, sir.

THE PRESIDENT: Thank you, Doctor.



OBITUARY

Indiana University's Hal Broxmeyer, pioneer of cord blood transplantation, dies at 77

By Patrick J. Loehrer Sr., MD

Hal E. Broxmeyer, PhD, lost the final round of his battle with thyroid cancer on Dec. 8. Hal was our father, he was our brother, he was our mentor, and he was our friend. His was a life of impact.

On any given day or evening, you could drop by Hal's office and find him next to a stack of Petri dishes, peering into his microscope counting cells. Well after automated cell counters were invented, Hal, whose research was instrumental in pioneering the field of cord blood transplantation, seemed most at peace when counting cells, notably stem cells.

If there was another place that Hal found joy, it was when he was lifting weights. It was his nerdy appearance with his thick glasses that disguised his chiseled frame. Over a half century ago, this led his future wife to nickname him "Clark Kent."

At his core, Hal never did things halfway—he was passionate, relentless, and most of all, Hal Broxmeyer was competitive. Weightlifting was not a casual hobby but a vocation that led him to multiple national titles well into his 50s.

Hal won the Master's Weightlifting National Championship in 1990 and 1994 in his age and weight division. He also competed in the Master's World Championship in 1993.

Hal was born on Nov. 27, 1944, in Brooklyn, NY. Ron Hoffman, the second chief of Hematology-Oncology at Indiana University, recruited the Brooklyn native from Memorial Sloan Kettering to join our faculty in 1983. This was the same year that George Sledge, Asok Antony, Scott Boswell, and I also joined the faculty.

It was clear from the beginning that Hal was a cut above all of us. Years later, my self-esteem was assuaged as I realized that he was a cut above everyone.

It was his work that made possible the first umbilical cord stem cell transplantation, which took place in Paris on Oct. 6, 1988.

He had the cryopreserved cord blood flown to Paris for the transplantation, buying a separate seat on the Pan Am flight for the "Big Boy" dry shipper cryopreservation tank that contained the cord blood. The foundational publication on the viability of cord blood transplantation followed in 1989. He also started the first cord blood bank at Indiana University.

Since then, an estimated 40,000 cord blood transplantations have been performed worldwide.

This work would lead Hal to receive numerous national and international awards.

He was a recipient of the Karl Landsteiner Award of the American Society of Blood Banks (2002), the E. Donnall Thomas Prize of the American Society of Hematology (2007), the Donald Metcalf Award of the International Society of Hematology and Stem Cell Research (2011), the President's Medal of Honor from Indiana University (2019), the Lifetime Achievement Award from the Cord Blood Association (2019), and the Gold Medal of the City of Paris (1993).

Hal would become the first PhD to be elected president of the American Society of Hematology (2010). He was also president of the International Society for Experimental Hematology and Stem Cell Research (1991). His research achievements are reflected by his record of more than 838 peer-reviewed published scientific papers, which have been cited more than 72,552 times.

Hal was the first director of the Walther Oncology Center and chair of Microbiology and Immunology. At the time of his death, he was an IU Distinguished Professor, Mary Margaret Walther Professor Emeritus and professor of microbiology and immunology at IU School of Medicine, and senior advisor to the director of the Indiana University Melvin and Bren Simon Comprehensive Cancer Center.

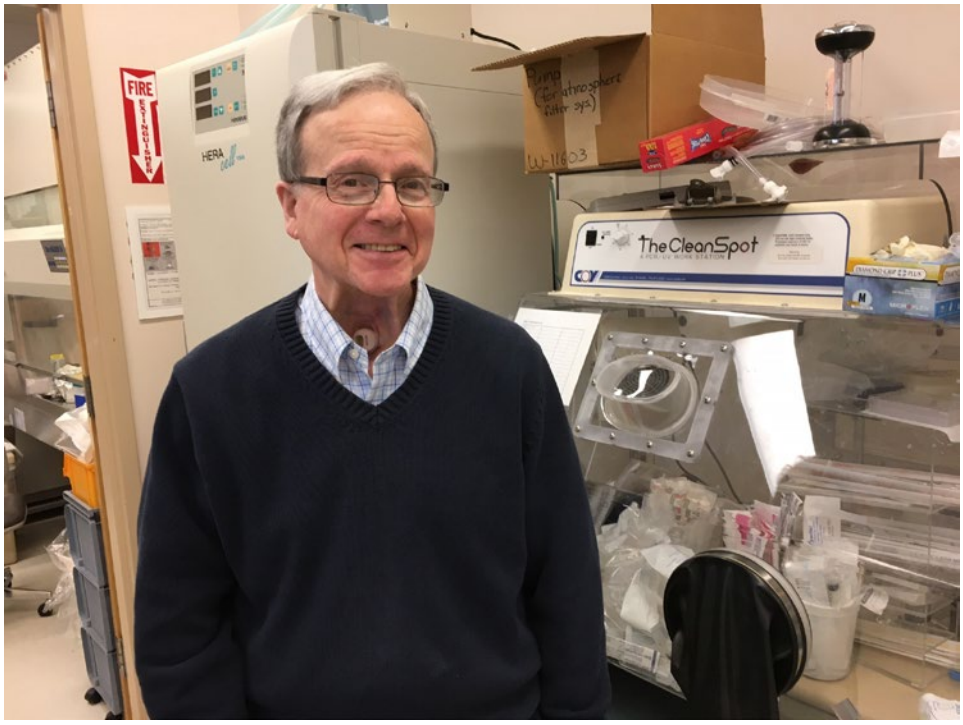
He mentored scores of pre-doctoral and post-doctoral students, of which many went on to highly productive academic careers.

Hal was a pillar for the IU Simon Comprehensive Cancer Center. Well before we were initially awarded NCI-designated Cancer Center status, then-Director Steve Williams appointed him to lead the Hematopoiesis, Malignant Hematology and Immunology research program (now HHM). Under his direction, this program was consistently designated as "outstanding," setting the bar for the other programs.

When Dr. Williams succumbed to melanoma, I became the acting director.

During the first external advisory board meeting under my leadership, our performance was mediocre at best. Despite putting on a strong face, I was disappointed, and Hal saw that in my face. He pulled me aside and gave me pointed and strong words of encouragement that a coach would give to a freshman quarterback thrown into a varsity game. From that day on, I was ready to play.

Cancer is rough, and some kinds of cancers are really rough.



> Well after automated cell counters were invented, Hal, whose research was instrumental in pioneering the field of cord blood transplantation, seemed most at peace when counting cells.

Hal's was one of those cancers. He gracefully went through surgery, subsequently had a recurrence that required a tracheostomy, radiation therapy, and more systemic therapies. He privately kept this years-long battle to his family and a select few.

Though he obviously couldn't hide his tracheostomy, he still managed to give talks with effort and self-deprecation.

One such talk was on behalf of the HHM program at our center's competing renewal. His presentation was a tour de force and helped lead us to achieve comprehensive status from the NCI.

To say that Hal was hard working and dedicated would be an understatement. From time to time during the pandemic, we would text each other. When I inquired as to how he was doing, he would deflect the obvious intention of my question and give me a detailed report on his research.

A few weeks ago, Hal sent me his final text, which is abbreviated here:

> Good to hear from you. I had a number of very rough days but was able to keep working. Reviewed journal papers and have been working on our own papers. Two submitted last week (to Haematologica and JBC) … I should be able to submit a paper of mine next week and will begin on working on a paper that I started a long time ago with Charles Abrams from U. Penn as soon as we get the last bit of data …Today I feel better than I have for weeks. Hope it lasts, but I am thankful for each good day I have. … What about you? What is new? Best, Hal.

Hal is survived by his wife of 52 years, Beth Broxmeyer (formerly Biller); sons, Eric Jay Broxmeyer (and his wife, Annie Owens) and Jeff Daniel Broxmeyer (and wife, Shira Roza); sister, Claire Goldstein and family; grandchildren, Naomi Francis Roza-Broxmeyer and Issac Louis Roza-Broxmeyer.

Donations can be made in his honor to the Leukemia & Lymphoma Society of America, the American Society for Hematology, the IU Simon Comprehensive Cancer Center, or the Indianapolis Hebrew Congregation.

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NCI BSA approves 11 new and reissued concepts

By Alice Tracey

The NCI Board of Scientific Advisors approved 11 new and reissued concepts at a joint meeting of the BSA and the National Cancer Advisory Board Dec. 7-9.

Also at the meeting, NCI Director Ned Sharpless welcomed 14 new BSA members and seven new NCAB members, while recognizing the NCAB members retiring this year—Peter C. Adamson, Deborah Watkins Bruner, Timothy J. Ley, Max S. Wicha, and Yuan Chang.

The following concepts were presented and approved. Presentation slides are available here.

Global Implementation Science for Equitable Cancer Control (New RFA)

The goal of this RFA is to bridge gaps in the implementation of cancer interventions in low- and middle-income countries. The project aims to build LMIC-based implementation science hubs that can:

- Address implementation gaps in cancer control in LMICs
- Build research capacity for cancer control implementation science in LMICs
- Foster stakeholder engagement between LMIC researchers and practitioners
- Enhance the ability of LMIC institutions to serve as regional experts in implementation science

The project, submitted by the Office of the Director, will receive funding through the U54 grant.

The RFA anticipates supporting four research projects lasting five years. $4 million is slated to be set aside for the first year of each project, with a total budget of $20 million for the whole project period.

Each award will include two investigator-initiated research projects and two core projects. The award date is summer 2023.

These research projects may focus on, for example, understanding modifiable barriers and facilitators to implementation, evaluating implementation processes and better integrating cancer control services, or testing the cost-effectiveness and impact of strategies to deliver cancer control interventions.

Priority research questions include:

- How do we adapt cancer control interventions to LMIC settings?
- How do we efficiently bundle cancer control services?
- How do we integrate cancer control into primary care and other care settings?
- What are the best ways to decentralize cancer control services to community settings?
- How do we enhance retention across the continuum of cancer care in typically fragmented systems?

Eligibility criteria for institutions include:

- PI or MPI must be from an LMIC-based institution
- Applicants from US-based institutions must have LMIC-based MPI
- Applicants must propose two implementation research projects and two cores (i.e., administrative and research capacity-building)

Additional review criteria include:

- Demonstrate strong partnerships and history of collaboration
- Demonstrate implementation science expertise
- Address high priority cancer control implementation gaps in LMIC
- Use appropriate implementation science approaches
- Demonstrate LMIC institutional support for implementation science

There are several metrics that may indicate the success of this RFA, such as: the number of new LMIC-based investigators trained in implementation science and applying for implementation science grants; the number of new collaborations across LMIC-based institutions; peer-reviewed publications demonstrating the use of implementation science approaches in LMIC-based studies; and the generation of evidence that informs national and international policies and practice in LMICs.

PREVENT Cancer Preclinical Drug Development Program (Reissue RFP)

This reissued RFP aims to develop innovative agents and biomarkers for cancer prevention toward clinical translation, with a focus on molecularly targeted or immuno-preventive agents and response-predictive biomarkers.

The RFP was submitted by the Division of Cancer Prevention. PREVENT is not a grant program.

PREVENT was established 10 years ago. Over this time, the focus of the project has shifted from organ-site centric preventative agents to precision prevention. Since 2011, PREVENT has expanded its portfolio of molecular agents, developed higher-tech research capabilities, and improved oversight of its projects. PREVENT has advanced seven agents to clinical development, six of these since 2017.

Key research questions, based on lessons from terminated projects, include:

- Are preclinical models based not only on organ-site specific pathology, but the involvement of oncogene(s) of interest?
- Are molecular or antigenic targets expressed in the target tissue?
- Are the phenotypic outcomes of new animal models reproducible?
- Have PK/PD studies been incorporated to ensure test agents reached the target tissue?

- Is immunogenicity linked to antitumor activity?
- Have specific target cohort(s) been envisioned at the outset? Have clinical trial teams been consulted for input?

Applications for PREVENT projects are peer-reviewed, ranked by an external review panel, and then selected by a management committee. PREVENT projects are contract-based.

The already approved FY22 budget for PREVENT totals $11 million, with $3.6 million dedicated to efficacy, $3.7 million to toxicology and pharmacology, and $3.7 million to Current Good Manufacturing Practice adherence. With the expectation that PREVENT will expand over the next five years, the projected budget increases annually to a total of $17 million in 2027.

Cancer Epidemiology Cohorts: Research Opportunities in Established Studies (PAR)

This program announcement with review (PAR) aims to provide continued support for established cohort studies that address novel research questions across the cancer control continuum. It replaces the expiring PAR 20-294 (Cohort Infrastructure for Cancer Epidemiology Cohorts), such that projects funded by PAR 20-294 must see through the expiration of their current grants before applying for more funding.

Proposed by the Division of Cancer Control and Population Sciences, the PAR will receive funding through the U01 grant.

There is no specific budget cap for projects under this PAR; projects will receive funding twice per year for three years, and applicants should propose up to five years of funding. There must be an Awaiting Receipt of Application for above $500,000 in direct costs per year and pre-submission meetings are required for budgets above $700,000 per year.

A program announcement with review by a special emphasis panel is requested.

There are currently 31 cancer epidemiology cohorts in the DCCPS portfolio, with the following characteristics:

- 1.1 million participants
- More women (76%) than men
- Racial/ethnic distribution: 66% white, 17% Black, 7% Asian, and 6% Hispanic
- Many of the longstanding cohorts have older populations (>65 years old)
- Distribution roughly reflects the proportion of white, Black, and Asian Americans, but the number of Hispanics included in these cohorts is considerably less than current U.S. population (18% in the 2020 Census)

Guidelines for applicants include:

- Must address key scientific gaps
- Aims must include hypothesis-based research questions
- Core infrastructure support is expected
- Must justify study methods (e.g., data collection, proposed assays) based on the research in aims
- Priority given to novel research that includes understudied populations or directly informs future interventions, guidelines, and/or clinical management strategies

Projects that do the following will not be reviewed:

- Initiate new cohorts
- Do not include hypothesis-based research based on data from an established longitudinal cohort study in the specific aims
- Have data and/or resource sharing plans that do not comply with NIH policy and follow the FAIR (Findability, Accessibility, Interoperability, Reusability) principles.

The NCAB Working Group on Population Science made several recommendations related to this PAR, advising that: NCI should continue providing sufficient infrastructure support for cohorts to conduct or facilitate research that addresses critical scientific gaps; peer-review processes should include review of justification for continued follow-up of the cohort, including scientific yield; cohorts should consider current and emerging gaps in research and comprise appropriate populations; and survivor cohorts should address current and emerging research gaps by cancer type and/or treatment.

Cancer Epidemiology Cohorts: Building the Next Generation of Research Cohorts (Clinical trials not allowed) (PAR)

The goals of this proposed concept are to support the next generation of population-based cancer epidemiology cohorts that address critical scientific and resource gaps, such as emerging and unique exposures in relation to cancer

risk and outcomes and understudied populations.

The PAR was submitted by the Epidemiology and Genomics Research Program/ Division of Cancer Control and Population Sciences.

The concept will receive funding through the U01 grant.

No budget cap for projects under the PAR is specified. Projects will receive funding twice a year for three years; applicants can propose up to five years of funding. There will be a review process to assess the scope and appropriateness of budgets. There must be an Awaiting Receipt of Application for above $500,000 in direct costs per year and pre-submission meetings are required for budgets above $700,000 per year.

According to the presentation of this PAR, new cohorts are needed for a number of reasons:

- Changing demographic and environmental landscape
  - Evolving cancer-related burden with implications on cancer control and prevention
- Next generation cancer epidemiology cohorts
  - Meet critically needed resource gaps
  - Enable investigations of new scientific questions
  - Foster scientific innovation and adaptation of new technologies

Criteria for applicants include:

- Must address key scientific and resource gaps
  - Review existing cohorts
  - Justify sample size, study population, and data collection
- Key features: Methodological work and community engagement
- Applicants responsive may include, though not limited to:
  - Testing of recruitment and retention strategies, relevant for hard-to-reach populations
  - Testing novel methods/ approaches for data collection and/or assessment
  - Assessing intermediate markers of carcinogenesis, behavioral outcomes, or healthcare utilization
- Established cohorts are not appropriate for this funding opportunity announcement

The PAR prioritizes methodological work to assess the achievement of identified scientific and resource gaps. This permits investigators to focus on:

- Approaches to engage, recruit, and retain
- Optimal and novel methods for data collection and assessment
  - Diverse exposures and biospecimens
  - Linkage to existing databases to obtain other information/data (SES-factors, neighborhood factors, geographic/environmental, healthcare delivery)
- Short-term research questions

Cancer Control Research in Persistent Poverty Areas (RFA/Coop. Agr.)

This RFA/Coop. Agr. aims to conduct cancer control and prevention research in partnership with communities and clinics in persistent poverty areas. Its goals include:

- Developing data integration and sharing processes, leveraging existing data resources, and/ or conducting preliminary data collection to improve understanding of the cancer burden
- Conducting multilevel/multifactorial interventions developed with communities and clinics located in or serving persistent poverty areas
- Developing and implementing training of transdisciplinary teams of junior researchers to conduct research in underserved communities for cancer prevention and control

Submitted by the Division of Cancer Control and Population Sciences, the RFA/Coop. Agr. will receive funding through the U54 grant.

The RFA/Coop. Agr. is requesting $10 million per year to support four U54 centers, for a total cost of up to $50 million over five years (with funding beginning FY2023). There is an anticipated direct cost of $1.5 million per center per year.

Persistent poverty areas are defined as having poverty rates of 20% or more in U.S. Census data from the 1980, 1990, and 2000 decennial censuses and the 2007-11 American Community Survey 5-year estimates. There are 353 counties across 30 states matching this definition; 85.3% of the counties are nonmetro and nearly 84% are located in the South.

Identifying persistent poverty using the county level definition is limited because it excludes smaller areas of extreme poverty. The NCI has worked with USDA to extend the definition to the census tract level for this funding announcement, to achieve broader representation.

Targeting persistent poverty areas for cancer prevention control is important because an NCI study found that people who live in persistent poverty counties are more likely to die from cancer than people in other counties. This risk was greater than the heightened risk seen in areas experiencing current—but not persistent—poverty.

Each research center can be managed by multiple PIs, and may include multiple institutions, health systems, and community partners—therefore, the estimated ceiling per research center is based on the structure of each grant and the need to include both full research and pilot studies.

The grant supports two pilot projects, for which applicants are asked to set aside 1.5% of the direct costs per year for the entire funding period. One pilot project will be an intervention study. The RFA/Coop. Agr. also encourages a cross-center (multisite) pilot. Pilot projects will be decided by the steering committee.

Study criteria include:

- Studies should be proposed from the provided list of census tracts
- To address issues related to persistent poverty, studies are to focus on community, institutional, and structural levels
- Studies should be multilevel and multifactorial
- Studies should include measures of the social context and needs of the population(s)
- Intervention studies can adopt quasi-experimental designs (RCT is preferred but not required)
- No drug or clinical trial recruitment studies are allowed
- Studies should address issues of sustainability of the program and training

Proposed centers must include the following required components:

- Administrative core
- Research/data infrastructure core
- Research projects (minimum two, with one intervention project)
- Pilot research projects (minimum two, with one intervention project)
- Investigator development core

Projects should focus on investigating the effects of poverty and its associated factors at the structural and institutional levels. This may involve studying interrelated factors inherent to the economy—like employment, income, and education.

Targeted outcome examples include:

- Increase cancer screening (mammography, colonoscopy, low-dose CT, Pap test)
- Increase cancer control prevention strategies (physical activity, nutrition, smoking)
- Improve care coordination
- Increase HPV vaccination rates
- Improve survivorship care

Evaluation methods include:

- Formation of a steering committee comprised of NCI staff, project PIs, and collaborators will meet monthly to assess both short- and long-term accomplishments that determine whether the major scientific aims are being met among the various project components
- Formation of working groups (and ad hoc groups) in accordance with the needs of the centers, such as junior investigators, methodology, etc., will assist in providing feedback to the steering committee.
- Annual meetings and monthly calls will allow for progress on projects to be assessed periodically

Pediatric Immunotherapy Network (RFA/Coop. Agr.)

The Pediatric Immunotherapy Network aims to develop translatable novel immunotherapy approaches for children and adolescents with solid tumors, including brain tumors, toward eventual clinical applications, with clinical trials optional.

The project has identified several gaps and opportunities in the treatment of pediatric solid and brain tumors, including:

- Targetable antigenic epitopes, binders, and immunotherapy agents
- Elucidation of immune evasion mechanisms
- Pediatric preclinical models especially for brain tumors

- Resources for developing protein therapeutics, IND-enabling studies, and cGMP manufacturing
- Predictive biomarkers, analytical technologies for immune monitoring and opportunities for reverse translation

This RFA will receive funding through the U01 grant. PIN was submitted by the Division of Cancer Treatment and Diagnosis/Division of Cancer Biology.

PIN anticipates six to eight awards between 2023-2027, each with a yearly total cost of $450,000. Collaborative administrative supplement awards (given between years 2-4) and network support funds are anticipated to cost $0.5-1 million in total cost per year, depending on the number of awards given.

Thus, the total cost per year of PIN is anticipated to be $6 million and the total network cost over five years is $30 million.

PIN will include a steering committee, consisting of the U01 project investigators and NCI staff. Patient advocates and additional NIH-funded pediatric immunotherapy researchers will be added as associate members. Administrative coordination for PIN will be provided by one of the U01 sites in partnership with NCI staff.

Example implementation plans include:

- Discover novel pediatric tumor-associated antigens
- Analyze pediatric-specific immune responses associated with response or resistance
- Molecular and immune profiling of pediatric solid tumors
- Modulate the pediatric tumor microenvironment to make immunotherapy agents (e.g., CAR T cells) more effective
- Develop, test, and optimize preclinical agents for cold pediatric tumors
- Reverse translation studies using clinical specimens to interrogate mechanisms of action or resistance to immunotherapy

Successes of PIN at the end of a five-year cooperative agreement term may include:

- Discovery, development, and validation of novel immuno-oncology targets
- Pre-clinical testing and development of single or combination of immunotherapy agents
- Novel mechanistic insights into the tumor microenvironment, response or resistance to immunotherapies
- Conduct of IND-enabling studies
- Promotion of novel immunotherapy agent(s) into a pilot clinical trial

Integrating Health Disparities into Immuno-Oncology Research (RFA)

This RFA aims to integrate health disparities into immuno-oncology research. The end goal is to build a cohort of immuno-oncology P01s, or other multidisciplinary research projects, with integrated health disparities research.

There are currently research gaps in health disparities in immuno-oncology, such as:

- Understanding inflammatory, metabolic, and immune profiles of immunotherapy treatment response across under-represented populations
- Investigating genetic, immune signatures, immune infiltrates, and/or distinct tumor immune microenvironments that may underlie the cancer health disparities

An analysis found that between FY2017-21, 333 investigator-initiated P01 applications were submitted to NCI. Out of these applications, 18% (n=59) had to do with immunotherapy—12 were awarded, none addressing health disparities. Just 1.5% of the applications submitted (n=5) addressed health disparities—one was awarded, but it wasn't related to immunology.

Example research projects integrating health disparities include:

- Characterizing unique gene expression and immune infiltration profiles in breast cancer subtypes across African American and Caucasian patients
- Understanding how distinct genetic and immune signatures in the tumor microenvironment are associated with colon cancer disparities
- Developing animal models that recapitulate the breadth of immune responses across underrepresented populations
- Characterizing disparities in immunotherapy response, resistance, and immune-related adverse events

This RFA was submitted by the Division of Cancer Biology/Office of the Director. It will be funded through the P20 grant.

The budget accounts for two to three awards, each lasting two years, capped at $250,000 in direct costs per year. The total budget allotted for the first year is $1 million.

Multidisciplinary research projects funded through this initiative will support ongoing NCI programs through NOSIs (Notice of Special Interest) and will use P20s (exploratory grants) to launch feasibility and planning studies to build collaborations, compile appropriate sample sets, and generate preliminary data for subsequent application submissions.

These P20 grants will generate:

- Initial studies to establish sufficiently powered and/or well-curated specimens from groups under-represented in clinical trials
- Feasibility/pilot studies to test exploratory or novel hypotheses on immune mechanisms, immune response, and/or treatment response/resistance underlying cancer health disparities
- Planning studies to build collaborations/teams, generate resources (e.g., tools, reagents), or other collaborative research infrastructure

Requirements for funding include:

- Integration of underserved populations
- Multidisciplinary teams with complementary expertise in both cancer health disparities and immuno-oncology research

Evaluation criteria and metrics of success include:

- Establishment of complementary, multidisciplinary research teams with strengths in both cancer health disparities and immuno-oncology research
- Pre-application or submission of well-integrated multidisciplinary research projects (e.g., P01s or R01s)
- If the P20 team is developing an investigator-initiated program project (P01), has the P20 team formed an advisory board to review an initial P01 application submission plan?
- Publications and metrics of collaboration

A Data Resource for Analyzing and Supporting Blood and Marrow Transplants and Cellular Immunotherapy Research (Reissue RFA/Coop. Agr./Limited Comp.)

This reissued limited competition RFA/Coop. Agr. aims to renew the Center for International Blood and Marrow Transplant Research Registry.

The RFA was submitted by the Division of Cancer Treatment and Diagnosis. It will receive funding through the U24 grant.

Funded by NCI for 30-plus years with support by NHLBI and NIAID, the CIBMTR is:

- The only publicly available, comprehensive U.S. Data Resource for hematopoietic stem cell transplant (HCT) and adoptive cell therapy (ACT) research
- A resource for researchers, clinicians, HHS policymakers, and pharmaceutical companies
- Supporting FDA CAR T-cell product safety and efficacy data and CMS coverage with evidence development trials

CIBMTR accomplishments between 2018-2020 included:

- Enrolled ~72,000 new cell therapy patients
- Enrolled 5,000 recipients receiving ACT for transplants or as a primary therapy
- Adapted forms to collect COVID-19 data, producing five scientific papers
- Created new forms to capture data on solid tumors
- Published 267 data analysis and research manuscripts
- Distributed 13,000 samples for secondary research
- Enhanced data quality by training 85 data managers
- Piloted technology platforms to automate data acquisition and reduce the burden of data entry
- Engaged in five Medicare Coverage with Evidence Development Trials

CIBMTR facilitates CAR T-cell data collection via public and private partnerships. With its industry partners, CIBMTR has launched five long-term follow-up studies for FDA required Post-Market Safety Reporting since 2018. The organization also works with NCI-funded collaborators, such as the AIDS Malignancy Consortium, Blood and Marrow Clinical Trials Network, and National Clinical Trials Network.

Plans for the RFA reissuance include:

- Expand HCT and ACT data collection used to treat malignant and non-malignant blood disorders
- Focus on special initiatives including HHS evidence gathering programs:
  - FDA-required long-term follow-up studies with industry—expected to be over 9000 ACT annually in next few years
  - CMS Medicare Coverage with Evidence Development Trials
- Adapt the database for the collection of ACT for solid tumors as well as new ACT products (as appropriate)
- Support trial designs and data analyses for observational and interventional studies

Patient Derived Xenograft Development and Trial Centers Network & PDX Data Commons and Coordinating Center for PDXNet (Reissue RFA)

The original goals of the Patient Derived Xenograft Development and Trial Centers Network (PDXNet) in 2017 were to:

- Develop PDX trials that test original therapeutic strategies in large scale PDX collections, that could then provide preclinical in vivo evidence to support novel early phase clinical trials
- Address critical scientific issues related to the use of PDXs as predictive models for clinical benefit through the collaborative network structure of PDXNet
- Contribute new PDX models to NCI's Patient Derived Models Repository (PDMR) for distribution to the wider research community

For this reissued RFA, the following goals were added:

- Increase diverse representation and study of racial/ethnic minority populations in PDXNet and in the PDMR
- Advance cancer health disparity research

The reissue RFA was submitted by the Division of Cancer Treatment and Diagnosis (DCTD)/Office of the Director. The reissue for the PDXNet: Patient Derived Xenograft (PDX) Development & Trial Centers (PDTCs) uses the U54 grant and the PDX Data Commons and Coordinating Center (PDCCC) for PDXNet uses the U24 grant.

The current annual total cost for PDXNet is $10.5 million. The estimated total cost for the full project period (FY23-27) is $40 million.

Currently, the four Division of Cancer Treatment and Diagnosis U54 PDTCs cost $1.25 million each. The two Center to Reduce Cancer Health Disparities (CRCHD) U54 PDTCs cost $1.25 million each. The one PDXNet U24 PDCCC costs $1.5 million total per year. The supplement program costs $1.5 million total per year.

The proposed annual total cost for the second grant cycle is $8 million per year. The breakdown of this proposed budget follows:

- A decrease from six U54 PDTCs to five U54 PDTCs (three or four from DCTD and one or two from CRCHD based on priority score), costing $6.25 million per year (a decrease of $1.25 million)
- PDXNet U24 PDCCC will cost $1 million per year (a decrease of $0.5 million)
- The supplement program will cost $0.8 million per year (a decrease of $0.7 million)

In its first four-year grant cycle, the collaborative PDXNet achieved the following steps:

- Established collaboration with CRCHD to bring in two PDTCs focused on disparity research
  - Developed a culture of collaboration among all grantees with multiple collaborative research projects
  - Demonstration of multicenter experimental reproducibility of drug response studies using PD models published in *Cancer Research*
  - Demonstration of CNV fidelity in successive PDX passages published in Nature Genetics
  - Demonstration of therapeutic target pathway identification in PDXNet PDX collections published in *Nature Communications*
  - Ongoing cross-network collaborative study of drug efficacy evaluation methods in PDX models, manuscript in preparation
  - 10 other active intra-network collaborations coordinated by PDCCC
- 690 unique PDX models donated to the NCI PDMR
  - Most in the process of expansion and characterization prior to public distribution

- Preclinical evidence developed for 10 CTEP LOIs
- Website established for internal network collaboration and public access
  - Development of the PDXNet portal as a platform for data sharing, described in a paper submitted for publication and posted online
- Collaborative projects necessitated development of workflows to facilitate collaboration; 15 validated workflows publicly shared via PDXNet portal
- 88 publications from original research projects

Deliverables in the second grant cycle will include:

- Develop and apply drug response evaluation standards across PDXNet; advocate for these to be adopted across the wider research community
- Provide robust preclinical in vivo data of targeted agent combinations to prioritize at least 20 clinical trials in NCI clinical trials networks (double from first cycle)
- Establish more strategic donations of models to PDMR—identify significant gaps in the NCI PDMR PDX repository collection, and orchestrate targeted contributions to fill those gaps
  - Ex. racial/ethnic underserved and clinical relapsed/resistant models
- Create methods and workflows to integrate complex omic and imaging data from multiple sites into a searchable PDX database for model selection; make these tools available
- Create productive collaborations between PDXNet scientists and early phase clinical trialists

The U54 grants and U24 grants support different research projects with different requirements.

PDX Development and Trial Centers (PDTCs) (U54) comprise:

- Research projects (at least two) in mechanism-based drug combinations in genetically or histologically defined tumor subgroups that explore the relation of the tumor characteristics to tumor drug response
  - Primary goal is preclinical evidence generation to support early phase studies of NCI-IND agents in NCI-funded clinical trial networks
  - Focus on new NCI-IND agents coming into portfolio to accelerate trials
  - CRCHD track: Focus on models relevant to cancer health disparities
- Four required cores
  - Administrative core
  - Bioinformatics core—to facilitate data sharing and to interact with PDCCC data commons
  - PDX core—including PDX maintenance and animal facilities
  - Pilot projects core—for PDXNet intra-network collaboration and to interact with investigators chosen through administrative supplement program

The PDXNet Data Commons and Coordinating Center (PDCCC) (U24) will comprise:

- Bioinformatics Core
  - Lead development and implementation of data collection standards, workflows, and SOPs for harmonization and data integration across different PDTCs
  - Centralized center for analysis of PDX response to agents across PDTCs
  - Maintain the PDXNet website and database
  - Share PDXNet data with NCI GDC and the larger research community
- Administrative Core
  - Grant administration of the PDTC and PDCCC
  - Scientifically-informed project management of PDXNet collaborative projects
  - Logistical and administrative assistance in arranging network-wide meetings, workshops and PDXNet Executive Committee

Non-U54 investigators may apply for PDXNet collaboration through an administrative supplemental award application process. In the current RFA, laboratory scientists apply to collaborate with PDXNet scientists. In the proposed RFA, to boost productivity, clinician scientists can apply to collaborate with PDXNet scientists.

Systematic Testing of Radionuclides in Preclinical Experiments (PAR)

Systematic Testing of Radionuclides in Preclinical Experiments (STRIPE) is requesting a PAR to solicit proposals that address knowledge gaps in how radiopharmaceutical therapy (RPT) agents affect the biology of cancer cells, normal cells, and the microenvironment.

The project seeks to support interdisciplinary collaborations across the fields of RPT and pre-clinical cancer biology, strengthening the pre-clinical foundation of the RPT field and promoting advances in biology-based targeting strategies.

This PAR was submitted by the Division of Cancer Treatment and Diagnosis/Office of the Director. The PAR will solicit R01 and R21 applications, with funding from a research project grants source—there is currently no funding set aside for the project. STRIPE anticipates 7-10 applications per round for three years.

STRIPE seeks to address the following gaps:

- Unmet needs in foundational pre-clinical RPT research
  - Limited knowledge on radionuclide radiation biology effects in tumor and normal tissues (e.g., guide particle choice, low dose-rate exposure, optimizing combinations (RPT + chemo, timing), late effects)
  - Inadequate level of pre-clinical research to catalyze targeting strategy development
  - Integration of RPT with –omic, molecular characterization, and enabling technologies
- Threshold for wider adoption of RPT into cancer research
  - Radioactivity license (open-source lab) can be an impediment for non-RPT researchers
  - Isolating effect on RPT field in leveraging full range of cancer modeling for discovery, optimization, and validation

With these unmet needs in mind, the goal of STRIPE is to form interdisciplinary projects that will launch pre-clinical experiments to understand RPT effects on the biology of cancer cells, normal cells, and the microenvironment toward the development of targeted interventions.

This research will help identify new targeting strategies for RPT and test/optimize novel RPT-molecular targeted therapy combinations.

Informatics Technology for Cancer Research (Reissue RFA/Coop. Agr.)

The Informatics Technology for Cancer Research (ITCR) at NCI promotes the integration of IT development with cancer research, supports different stages of the IT development lifecycle, enables technology dissemination and software reuse, and fosters communication among development teams.

The program has granted 130 awards to date. Some example areas of research include:

- Data management, storage, organization, and data sharing resources
- Data mining, visualization, and analytics tools and platforms
- Data annotation tools, including common data elements and ontologies
- Statistical methods and machine learning methods
- Natural language processing and text mining approaches
- Clinical decision support and treatment planning tools
- Technology to support next generation clinical trials and clinical trial matching

The ITCR toolkit can be found here.

Submitted by the Office of the Director, this ITCR renewal proposal includes the goals of balancing early and late stage development funding through program team prioritization, engaging SBIR for collaboration with industrial partners and focused contract topics, and discontinuing Competitive Revisions due to a low response rate.

There are a number of new awards included in the ITCR renewal.

The proposed budget accounts for: five R21 awards per year, each costing $275,000 over two years; five U01 awards per year, each costing $300,000 annually for three years; four U24 Advanced Development awards per year, each costing $600,000 annually for up to five years; and one U24 Sustainment award per year with no funding cap, lasting up to five years. Out of these award amounts, 10% will be set aside annually for collaborations.

The total requested budget for the renewal is $8 million.

IN THE ARCHIVES

CANCER HISTORY PROJECT

A 50 year war: The cancer community commemorates a milestone—and plans the road ahead

Cancer reflects on progress

On Dec. 9, 1971, Benno C. Schmidt delivered a speech that sets the stage for the new era slated to begin exactly two weeks later, on Dec. 23, with the signing of the National Cancer Act by President Nixon:

> It is now time to put aside any differences which have existed—and, happily, that should be relatively easy because many of the alleged differences never really existed—and work together to produce the best cancer program of which American science and American medicine is capable. Without arousing false hopes or false expectations, without minimizing in any way the complexities or difficulties of this implacable foe, let us all join together to give the American people what they want: the best cancer effort that lies within our capacity.

Schmidt, an attorney and industrialist credited with coining the term "venture capital," delivered these remarks at the Conference on Planning Cancer Centers, which was sponsored by the American Cancer Society. He had just spent a year as chairman of the National Panel of Consultants on the Conquest of Cancer, a group that advised the U.S. Senate on launching a government-wide effort aimed at the eradication of cancer, and he would soon be appointed the first and arguably most effective chairman of the President's Cancer Panel.

Schmidt's speech was published in the American Cancer Society's journal *Cancer* in April 1972 and republished in the Dec. 15, 2021, issue of the journal, to mark the 50th anniversary of the National Cancer Act.

Fadlo Khuri, president of American University of Beirut and former editor of the journal, writes in the introduction to the Schmidt paper:

> The speech is adroit, eloquent without being wordy, and forward-looking without the slightest hint of jingoism. It, like the National Cancer Act, has worn remarkably well. Schmidt was an attorney, entrepreneur, and industrialist, and he worked well with others of diverse backgrounds, including scientists, philanthropists, and political leaders. He shepherded the efforts of 5 of the original standalone US academic cancer centers, the American Cancer Society, and the National Institutes of Health through a process that set the stage for much of the progress that we have seen over the last 5 decades in the war against cancer.

The Schmidt paper is published as part of *Cancer*'s special issue dedicated to the 50th anniversary of the National Cancer Act.

The issue also includes an editorial by Suresh Ramalingam, editor or *Cancer* and director of Emory University Winship Cancer Institute, and Khuri. The editorial concludes:

> The 50th anniversary of the National Cancer Act provides an opportunity to reflect on our progress, review our challenges, and plan the future of cancer care and research… As we turn the page to a new chapter, it is clear that much work remains to be done. This is perhaps the end of the beginning and a prelude to new possibilities with another historic opportunity to rededicate ourselves to the next frontier in the fight against cancer, just as the visionaries of the National Cancer Act did in 1971.

The package of papers also includes a commentary by Otis W. Brawley, of Johns Hopkins University, and Paul Goldberg, of *The Cancer Letter*, assessing and quantifying the impact of the National Cancer Act.

Some highlights:

- The National Cancer Act increased support (politically and monetarily) for investigator-initiated research. This change—getting the government to pay for basic science—was still a relatively new concept early in the National Cancer Act, and it immediately won over the same medical school deans who were once opposed to the law.

- Consider the SARS-CoV-2 pandemic. When the pandemic struck, technologies that had been developed for cancer enabled rapid sequencing of the virus. The Chinese health authorities and the World Health

Organization announced on Jan. 9, 2020, that a novel coronavirus was confirmed as the pathogen responsible for the pneumonia cases in Wuhan province. Then, over the weekend—Jan. 11 to 12—Chinese scientists shared the full sequence of the coronavirus genome as detected in samples from the first patients. Next, using messenger RNA technology, which was also developed for cancer research, scientists constructed a vaccine. This latter task took 12 weeks of engineering, but the technologies used were based in part on 50 years of cancer research. Similarly, monoclonal antibodies, a modality that has been used in the treatment of COVID-19, were developed for the treatment of cancer and are used for multiple cancer indications.

- An unfortunate but important finding from outcomes research is that a substantial number of Americans do not enjoy the fruits of research. Approximately 600,000 Americans die of cancer annually. It is estimated that if all Americans had the advantages of college-educated Americans, including access to prevention, appropriate screening, diagnostics, and therapy, 132,000 would not die. They are the unnecessary casualties. Perhaps the most pressing question not adequately addressed by the National Cancer Act is the following: "How can we get more Americans necessary optimal care?"

Brawley and Goldberg are co-editors of the Cancer History Project.

Quote of the week

"Ending cancer as we know it means increasing access to screening to traditionally underserved communities. It means taking clinical care to people instead of having them come to us. It means having a two-way conversation about prevention, early detection, treatment and survivorship. It means connecting with those around us to enhance and save lives."

– Robert A. Winn

NCI on "ending cancer as we know it"

Ending cancer as we know it.

NCI has created a Twitter Moment highlighting the steps it is taking to "end cancer as we know it," an initiative by President Joe Biden.

"We want to use many approaches, including better screening and prevention and early diagnosis and treatment. All of these different approaches to end that tragedy of cancer," NCI Director Ned Sharpless said in a video. "I believe by using these combined modalities we can and we will beat the president's goal of ending cancer as we know it."

The field of oncology responded with their own videos on what "ending cancer as we know it" means to them:

"Ending cancer as we know it means increasing access to screening to traditionally underserved communities. It means taking clinical care to people instead of having them come to us. It means having a two-way conversation about prevention, early detection, treatment, and survivorship. It means connecting with those around us to enhance and save lives. Nothing will stop us from fighting cancer," said Robert A. Winn, director and Lipman Chair in Oncology at VCU Massey Cancer Center, and senior associate dean for cancer innovation and professor of pulmonary disease and critical care medicine at VCU School of Medicine.

"My vision of ending cancer as we know it is through engaging patients, survi-

vors, post-survivors, those at high risk, helping them use their voice to make research patient-centered, and impacting the cancers across our catchment area," said Hope Krebill, executive director of Masonic Cancer Alliance.

"Ending cancer as we know it means that when an oncologist meets a new patient, they will say 'you have cancer. And these are the multiple ways we're going to help you get better,'" said David A. Tuveson, president of the American Association for Cancer Research, Roy J. Zuckerberg Professor of Cancer Research, and cancer center director of Cold Spring Harbor Laboratory.

"Ending cancer as we know it means addressing the disproportionate cancer burden in underrepresented groups and making meaningful interventions to not only stop cancer in its tracks, but prevent it from happening in the first place," said Anil K. Rustgi, director of the Herbert Irving Comprehensive Cancer Center at NewYork-Presbyterian/Columbia University Irving Medical Center.

"Ending cancer as we know it ensures that every cancer patient becomes a long term survivor. Cancer needs to be addressed with the same urgency that we're seeing in response to the COVID-19 pandemic. That means funding and acceleration of research across the cancer continuum," said Sung Poblete, chief executive officer of Stand Up to Cancer.

"To me, ending cancer as we know it means reducing or eliminating the burdens of that disease for our patients," said Steven K. Libutti, director of Rutgers Cancer Institute of New Jersey, vice chancellor for Cancer Programs, Rutgers biomedical and health sciences senior vice president, Oncology Services, RWJBarnabas Health professor of surgery, and Rutgers Robert Wood Johnson Medical School Affiliated Distinguished Professor in Genetics in the Rutgers School of Arts and Sciences Department of Genetics. "If we could convert the disease, through early detection and development of new therapeutics, into a disease we could manage, akin to diabetes or hypertension, I think that would be a worthy goal to achieve."

"Ending cancer as we know it means that we've effectively integrated our efforts in research, cancer prevention, and early detection and treatment, so that millions of people worldwide have benefitted," said Brenda Marion Nevidjon, chief executive officer of the Oncology Nursing Society.

Watch the Nixon National Conference

- Nixon National Cancer Conference - Panelists and Keynote by Dr. Ned Sharpless
  By Richard Nixon Foundation | Dec. 15, 2021

Leaders in oncology gathered to commemorate the 1971 signing of the National Cancer Act at the Nixon National Conference Dec. 2.

A full recording of the conference appears here.

The conference began with a panel including James P. Allison, David Baltimore, Phillip Sharp, and Andrew von Eschenbach, titled "The National Cancer Act – Discovering Cancer's Secrets." Later in the day, Stephan A. Grupp, Lori J. Pierce, Peter Pisters, and Steven T. Rosen spoke during the panel "The National Cancer Act - Saving Lives, From Hopelessness to Hope."

The third panel, "The National Cancer Act - Changing the Future of Cancer," included William W. Li, Stephen Hahn, Mauro Ferrari, Larry Norton, and Anna Barker.

NCI Director Ned Sharpless, the event's keynote speaker, focused on the National Cancer Act's role in modernizing NCI.

Recent contributions

- The National Cancer Act at 50: A Memorial Sloan Kettering Timeline
  By Memorial Sloan Kettering Cancer Center | Dec. 15, 2021
- I Live to Conquer Cancer: Dr. Raymond U. Osarogiagbon
  By ASCO | Dec. 14, 2021
- What's on the Horizon for Cancer Drugs? Dr. Charles Sawyers on MSK Podcast
  By Memorial Sloan Kettering Cancer Center | Dec. 13, 2021
- Quality Care in Oncology Shifts to Implementing Change: A Look at Quality Research in Lung Cancer
  By ASCO | Dec. 13, 2021

This column features the latest posts to the Cancer History Project by our growing list of contributors.

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.

Access to the Cancer History Project is open to the public at CancerHistoryProject.com. You can also follow us on Twitter at @CancerHistProj.

Is your institution a contributor to the Cancer History Project? Eligible institutions include cancer centers, advocacy groups, professional societies, pharmaceutical companies, and key organizations in oncology.

To apply to become a contributor, please contact admin@cancerhistoryproject.com.

IN BRIEF

WHO and St. Jude form $200M collaboration to increase global access to childhood cancer medicines

The World Health Organization and St. Jude Children's Research Hospital Dec. 13 announced plans to establish the Global Platform for Access to Childhood Cancer Medicines to provide an uninterrupted supply of quality-assured childhood cancer medicines to low- and middle-income countries.

St. Jude is making a six-year, $200 million investment to launch the platform, which will provide medicines at no cost to countries participating in the pilot phase. This is the largest financial commitment for a global effort in childhood cancer medicines to date, cancer center officials said.

"Close to nine in 10 children with cancer live in low- and middle-income countries," Tedros Adhanom Ghebreyesus, WHO director-general, said in a statement. "Survival in these countries is less than 30%, compared with 80% in high-income countries. This new platform, which builds on the success of the Global Initiative for Childhood Cancer launched with St. Jude in 2018, will help redress this unacceptable imbalance and give hope to many thousands of parents faced with the devastating reality of a child with cancer."

The platform aims to provide safe and effective cancer medicines to approximately 120,000 children between 2022 and 2027, with the expectation to scale up in future years. The platform will provide end-to-end support—consolidating global demand to shape the market; assisting countries with the selection of medicines; developing treatment standards; and building information systems to track the provision of effective care and drive innovation.

"As I reflect back on the journey, this will be one of the most important things St. Jude Children's Research Hospital ever does," St. Jude President and CEO James Downing said in a statement. "This is a program that will provide a cornerstone of quality care to children everywhere

in the world. And so, moving forward, I see this as essential for us to do this collaboratively with all the participants across the globe focused on childhood cancer. We will change the outlook for children everywhere."

Medicine availability in low- and middle-income countries is often complicated by higher prices, interruptions in supply, and out-of-pocket expenditures that result in financial hardship.

According to a WHO Noncommunicable Disease Country Capacity survey published in 2020, only 29% of low-income countries report that cancer medicines are generally available to their populations, compared with 96% of high-income countries.

By consolidating the needs of children with cancer globally, the new platform will curtail the purchasing of substandard and falsified medicines that results from unauthorized purchases and the limited capacity of national regulatory authorities.

"For many years, we've struggled with getting essential medicines to children," WHO Cancer Control Officer André Ilbawi said in a statement. "And it's because of a variety of factors—whether it's a lack of money, a lack of infrastructure, or lack of the treatment guidelines that are needed to give the best possible care. But by consolidating this request, by bringing governments and partners to the table, we will change this and in the near future."

During an initial two-year pilot phase, medicines will be purchased and distributed to 12 countries through a process involving governments, cancer centers, and nongovernmental organizations already active in providing cancer care. Discussions are already ongoing to determine the countries that will participate in this pilot phase. By the end of 2027, it is expected that 50 countries will receive childhood cancer medicines through the platform.

"This is, I think, for the pediatric oncology community, the next frontier," St. Jude Global Director Carlos Rodriguez-Galindo said in a statement. "We cannot stop now."

The World Health Organization and St. Jude Children's Research Hospital first collaborated in 2018, when St. Jude became the first WHO Collaborating Centre for Childhood Cancer and committed $15 million for the creation of the Global Initiative for Childhood Cancer (*The Cancer Letter*, Oct. 12, 2018; May 14, 2021).

The Global Platform for Access to Childhood Cancer Medicines synergizes with the Global Initiative, which supports more than 50 governments in building and sustaining local cancer programs and aims to increase survival to 60% by 2030.

Jonathan W. Riess named medical director of UC Davis Thoracic Oncology Program

Jonathan Wesley Riess was named medical director of UC Davis Comprehensive

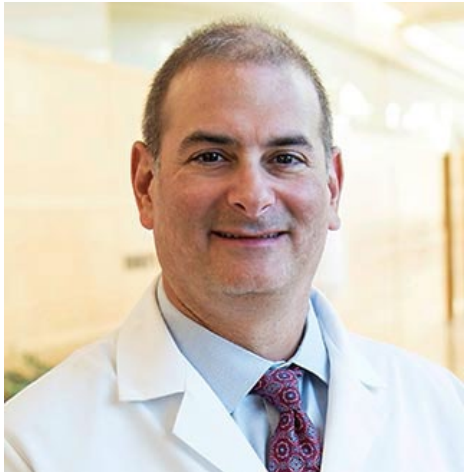
Cancer Center's Thoracic Oncology Program, replacing David R. Gandara, who will soon be co-directing a new center in experimental cancer therapeutics. Riess' appointment is effective immediately.

Riess' clinical interests include lung cancer and other thoracic cancers (mesothelioma and thymoma). He currently serves on the Non-Small Cell Lung Cancer/Malignant Pleural Mesothelioma/Thymomas and Thymic Carcinomas Panel for the National Comprehensive Cancer Network.

Riess' research interests encompass novel diagnostics, targeted therapies, and immunotherapy in lung cancer and other thoracic malignancies.

Riess is the past recipient of the NCI Cancer Clinical Investigator Team Leadership Award. He is also the past recipient of the Addario Lung Cancer Foundation and Van Auken Foundation Young Innovators Team Award and is a former Paul Calabresi K12 Scholar. Riess was recently awarded an NCI R01 grant for an NCI-sponsored clinical trial.

Eric Horwitz named chair of Fox Chase's Department of Radiation Oncology, integrated into Temple



Eric M. Horwitz was appointed chair of the Department of Radiation Oncology at Temple University's Lewis Katz School of Medicine, following an announcement that Fox Chase Cancer Center's Department of Radiation Oncology has been integrated within Temple University Health System.

These changes are part of the Temple University Health System's plan to integrate its Cancer Service Line.

Horwitz joined Fox Chase in 1997 and has led a clinical and research program that has grown exponentially in size and patient volumes. He will continue that leadership across TUHS in his new role, health system officials said.

Curtis Miyamoto, former chair of radiation oncology, was appointed to the new role of chair of the system integration committee of the TUHS Oncology Service Line. Fox Chase Chief Operating Officer Joel Helmke will co-chair the committee, which will launch in the spring and include constituents from all campuses and mission areas in oncology.

Miyamoto's guidance will coordinate Temple's efforts to integrate its clinical cancer programs, expand research activities and clinical trial participation, and develop unified cancer data systems across its campuses.

United for Medical Research publishes tribute to Francis Collins

United for Medical Research released a video tribute honoring NIH Director Francis Collins, who plans to step down this year.

Collins will continue his research at the National Human Genome Research Institute after this transition. Lawrence Tabak will serve as NIH interim director.

Members of the biomedical research community described Collins as a "trusted voice" who has been able to "make NIH a bipartisan priority" with "great charm and elegance," UMR officials said.

Collins, a physician-geneticist, is the longest-serving presidentially appointed NIH director, having served three U.S. presidents over more than 12 years. Under his leadership, the NIH has undertaken health issues including Alzheimer's disease, cancer, opioid use disorder, rare diseases, and the COVID-19 pandemic—and the NIH budget has grown from $30 billion in 2009 to $41.3 billion in 2021.

Collins is known for his commitment to developing and retaining young researchers and working to make biomedical research more accessible and equitable, recently encouraging an end to "manels"—all-male speaking panels.

Leaders from the following organizations participated in the video: Alzheimer's Association, American Association for the Advancement of Science, Association of American Universities, Association of Public and Land-grant Universities, Corning Life Sciences, Harvard University, Johns Hopkins University, Northwestern University, Stanford University, Thermo Fisher Scientific, Vanderbilt University, Vanderbilt University Medical Center, and Washington University in St. Louis.

A transcript of their full statements is available here.

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THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Tiragolumab plus immunotherapy improves PFS in PD-L1-positive metastatic NSCLC

A phase II trial investigating the anti-TIGIT cancer immunotherapy tiragolumab plus Tecentriq (atezolizumab) compared with Tecentriq alone as a first-line treatment for people with PD-L1-positive metastatic non-small cell lung cancer showed that the combination improved progression-free survival.

The full results from the CITYSCAPE trial, sponsored by Genentech, were featured as an oral presentation at the European Society for Medical Oncology Immuno-Oncology Congress 2021.

After 2.5 years median follow-up, tiragolumab plus Tecentriq continued to show an improvement in the intention-to-treat population (n=67), driven by the PD-L1-high population (TPS ≥ 50%) (n=29). In the ITT population, the combination improved PFS by 38% (median PFS=5.6 vs. 3.9 months; HR=0.62, 95% CI: 0.42-0.91) and improved overall response rates (38.8% vs. 20.6%) compared with Tecentriq alone.

A predefined exploratory analysis in the PD-L1-high population showed a 71% reduction in the risk of disease worsening or death (median PFS=16.6 vs. 4.1 months; HR=0.29, 95% CI: 0.15-0.53) and a clinically meaningful improvement in ORR (69% vs. 24.1%) with the combination compared with Tecentriq alone.

The analysis also showed that tiragolumab plus Tecentriq improved overall survival, a secondary endpoint of the study, in the ITT population, which was driven by the PD-L1-high population.

After 2.5 years median follow-up, median OS was 23.2 vs. 14.5 months (HR=0.69, 95% CI: 0.44-1.07) in the ITT population. The exploratory data in the PD-L1-high population showed a clinically meaningful OS improvement. The median was not reached for the tiragolumab regimen and is projected to be greater than 30.3 months based on the lower confidence interval (NE [30.3-NE] vs. 12.8 months [4.7-24.2]; HR=0.23, 95% CI: 0.10-0.53).

Data suggest that the combination was generally well-tolerated, showing similar rates of Grade 3-4 treatment-related adverse events when adding tiragolumab to Tecentriq, compared with Tecentriq alone (22.4% vs. 25%).

The phase III SKYSCRAPER-01 trial is currently ongoing to confirm these results in the PD-L1-high population, with the goal of bringing the treatment option to patients. Earlier this year, tiragolumab was granted Breakthrough Therapy Designation by FDA.

Since 2020, Genentech has initiated five phase III trials evaluating tiragolumab plus Tecentriq in early and metastatic disease in lung (SKYSCRAPER-01, SKYSCRAPER-02, SKYSCRAPER-03) and esophageal cancers (SKYSCRAPER-07, SKYSCRAPER-08). Tiragolumab is also being evaluated in other solid tumors as well as in hematological cancers.

Study raises concerns about clinical trial bias from undisclosed censoring

A University of Toronto-led study found that only 59% of oncology clinical trials studied provided adequately-defined rules for censoring.

The study, "Quantifying Withdrawal of Consent, Loss to Follow-Up, Early Drug Discontinuation, and Censoring in Oncology Trials," was published in the *Journal of the National Comprehensive Cancer Network*.

The researchers examined published randomized control trials supporting FDA approval for treatments for solid tumors from Jan. 2015 through Dec. 2019—and found that for 33 out of 81 studies, it was not clear in the publication why or how patients were being censored.

Censoring is defined in this context as the practice of removing patients from follow-up before experiencing the out-

come of interest; for instance, if the main outcome of a cancer treatment trial is survival and the patient experiences a heart attack and withdraws from the trial, they may no longer be followed up on.

If the proportion of patients who are censored is not evenly balanced between comparison groups, this can introduce bias and makes it difficult to interpret the results of trials.

"We hope that our findings will prompt investigators and journals to report early drug discontinuation, withdrawal of consent, loss to follow-up, and censoring more transparently in trial publications," lead researcher Brooke E. Wilson of the University of Toronto said in a statement. "This would allow patients and clinicians to make more informed decisions regarding the potential benefits of a treatment."

The authors compiled a list of goals and recommendations to improve transparency and reporting in clinical trials, including:

- Minimize the chance of post-randomization bias
- Improve transparency regarding censoring methods in oncology trials
- Explore the impact of censoring on trial results
- Improve the handling of transparency of missing outcome data in trial results
- Acknowledge the potential impact of censoring on the interpretation of results
- Provide transparent information regarding early drug discontinuation and withdrawal of consent or loss to follow-up

DRUGS & TARGETS

FDA approves Orencia for prevention of acute graft vs. host disease following unrelated donor HSCT

FDA approved Orencia (abatacept) for the prophylaxis of acute graft vs. host disease (aGVHD), in combination with a calcineurin inhibitor (CNI) and methotrexate (MTX), in adults and pediatric patients two years of age and older undergoing hematopoietic stem cell transplantation from a matched or one allele-mismatched unrelated donor.

Orencia is sponsored by Bristol-Myers Squibb. This is the first drug approved to prevent aGVHD.

The application included use of real world data in the determination of clinical effectiveness. Efficacy was evaluated in two studies in patients six years and older undergoing HSCT from a matched or one allele-mismatched unrelated donor.

GVHD-1 (NCT 01743131) was a randomized (1:1), double-blind, placebo-controlled clinical trial of patients who underwent an 8 of 8 Human Leukocyte Antigen-matched HSCT and received Orencia or placebo in combination with a CNI and MTX.

While severe (grade III-IV) aGVHD-free-survival assessed at day 180 after transplantation was not significantly improved in patients who received Orencia compared to patients who received a placebo (HR 0.55; 95% CI:0.26-1.18), the OS rate at day 180 after HSCT was 97% (95% CI: 89-99%) for patients who received Orencia compared to 84% (95% CI: 73-91%) for patients who received a placebo (HR 0.33; 95% CI: 0.12-0.93).

The moderate-severe (grade II-IV) aGVHD-free survival rate at day 180 after HSCT was 50% (95% CI: 38-61%) for patients who received Orencia compared to 32% (95% CI: 21-43%) for patients who received a placebo (HR 0.54; 95% CI: 0.35-0.83).

Additional evidence of effectiveness was provided by GVHD-2, a clinical study using data from the Center for International Blood and Marrow Transplant Research in patients who underwent a 7 of 8 HLA-matched HSCT between 2011 and 2018.

This registry-based study analyzed outcomes of 54 patients treated with Orencia for the prophylaxis of aGVHD, in combination with a CNI and MTX, versus 162 patients randomly selected from the CIBMTR registry treated with a CNI and MTX alone.

The OS rate at day 180 after HSCT was 98% (95% CI: 78-100%) for patients who received Orencia in combination with CNI and MTX compared to 75% (95% CI: 67-82%) for patients who received CNI and MTX alone.

Full prescribing information for Orencia can be found here.

EU CHMP adopts positive opinion for Keytruda as adjuvant therapy in RCC following surgery

The Committee for Medicinal Products for Human Use of the European Medicines Agency has adopted a positive opinion recommending approval of Keytruda (pembrolizumab), an anti-PD-1 therapy, as monotherapy for the adjuvant treatment of adults with renal cell carcinoma at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Keytruda is sponsored by Merck.

The positive opinion is based on results from the pivotal phase III KEYNOTE-564 trial, in which Keytruda demonstrated a statistically significant improvement in disease-free survival, reducing the risk of disease recurrence or death by 32% (HR=0.68 [95% CI: 0.53-0.87]; p=0.0010) compared to placebo, in patients at increased risk of recurrence (defined in the clinical trial protocol as intermediate-high or high-risk following nephrectomy and those with resected advanced disease).

The CHMP's recommendation will now be reviewed by the European Commission for marketing authorization in the European Union, and a final decision is expected in the first quarter of 2022.

Inceptor Bio in-licenses CAR-M Technology from UCSB

Inceptor Bio executed an in-licensing agreement with the University of California, Santa Barbara for an investigational chimeric antigen receptor macrophage (CAR-M) therapy targeting difficult-to-treat tumors.

Macrophage cells naturally engulf viruses and bacteria through phagocytosis; when combined with a CAR construct to form a CAR-M, they can selectively target and engulf cancer cells and generate an immune response via modulation of the tumor microenvironment. Inceptor's CAR-M technology plans to optimize the effectiveness of this therapeutic approach.

The technology was licensed from Denise Montell's research lab at UCSB.