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HOW JED MANOCHERIAN'S STEALTH CAMPAIGN FOR NIH WAS OUTED BY ITS OWN SUCCESS

By Matthew Bin Han Ong

Congress has been good to biomedical research over the past three years.

The NIH budget has gone up by 23 percent between 2016 and 2018, the 21st Century Cures Act has been passed, the Biden Moonshot continues into the Trump administration, and the FDA cancer center has been formed.

What changed? Why such success after a 13-year dry spell marked by flat budgets?

Washington insiders say at least some of the credit belongs to a philanthropist who had been determined to stay under the radar, and succeeded at doing so until legislative victories made his role hard to miss.

An argument can be made that Jed Manocherian, a real estate investor and developer, was ratted out by his success. Over the past four years, ACT for NIH, an organization Manocherian founded, has been channeling political clout to advance NIH.

In a conversation with The Cancer Letter, Manocherian said he became interested in securing funding for NIH when he joined the Board of Visitors at MD Anderson Cancer Center.

"Through this service, I learned about the enormous promise of biomedical science to ease human suffering," said Manocherian, whose company, Woodbranch Investments, holds property in New York and Texas. "I also learned about the alarming erosion of federal support for the National Institutes of Health, the most important biomedical research agency in the world."

The interview, a first for Manocherian in his role as an advocate, is posted on page 8.

"When I first met [Sen. Roy] Blunt (R-MO) in 2014, he envisioned a doubling of the NIH budget in the next 10 years, and he is not alone," Manocherian said to The Cancer Letter. "There is an ever-increasing number of NIH congressional champions who understand the tremendous promise of science to enhance the health and wealth of our nation. Our role is simply to support their vision."

When he founded ACT for NIH in 2014, Manocherian hired Patrick White,

then the associate director for legislative policy and analysis at NIH, to run the organization.

"Jed and Pat played key roles in helping me shape and pass the 21st Century Cures Act," said Rep. Diana DeGette (D-CO), who sponsored the measure with Rep. Fred Upton (R-MI) in 2014. "Their dedication to advancing and funding biomedical research through this legislation was truly inspirational.

"It was a bipartisan, bicameral effort requiring energy, creativity, passion and commitment," DeGette said to The Cancer Letter. "Thanks to Jed's vision and Pat's expert guidance, they made a real impact—we couldn't have done it without them."

Last month, congressional appropriators added $3 billion to NIH, the biggest increase in 15 years since the doubling effort led by John Porter, who was a key congressional appropriator and House representative from the 10th district in Illinois. Combined with the $2 billion increase in 2016 and another $2 billion in 2017, the textbook 25 percent inflationary loss to the NIH budget has been halved to 13 percent—from $8.6 billion to $4.8 billion.

It was, some say, a confluence of factors: pro-NIH congressional leaders, economic upturn, leeway in budget negotiations, and, as in the past, advocates eager to lobby. Even so, it was not pure luck that Manocherian's goal to obtain 10 percent annual increases for NIH had coincided with the $7 billion raise over three years, bringing the budget to $37.1 billion.

Manocherian has been compared to Mary Lasker, a philanthropist who was the leading campaigner for the National Cancer Act, and Michael Milken, a financier who used Hollywood glitz and public activism in an effort to build a grassroots constituency for cancer research.

Lasker was a high-profile socialite, famously a friend of Lady Bird Johnson during the Johnson presidency. Indeed, Lasker's advocacy led to the National Cancer Act of 1971, the fundamental document of the war on cancer. Milken's efforts culminated in the 1998 "march" on Washington, which some credit with the start of the doubling of the NIH budget.

> The key thing to understand about Jed Manocherian is that he does this for no other reason than he wants to help end human suffering. He is truly special—driven, generous in recognizing others, collaborative with other advocacy groups, respectful of others, and humble.
>
> *– Ronald DePinho*

And yet, Manocherian's efforts are different from Lasker's and Milken's. For starters, it's not publicly known whether anyone in his family has had cancer. By contrast, it's hard to miss the fact that Mary Lasker's husband, Albert, had died of colon cancer, and that Milken had prostate cancer. Milken is a member of the ACT for NIH advisory committee.

But more importantly, Manocherian clearly prefers to work behind the scenes.

Manocherian's family has been active in philanthropy and advocacy on societal issues, said Ronald DePinho, the Harry Graves Burkhart III Distinguished University Chair and professor in the Department of Cancer Biology at MD Anderson, and former president of the cancer center. Jed Manocherian's brother is involved in wildlife conservation, and their father founded the National Road Safety Foundation more than 50 years ago.

"ACT for NIH's success stems directly from the countless one-on-one meetings with members of Congress to educate them on why we must recommit our nation to a sizeable investment in research, discovery of treatments and cures to avert losing America's greatest scientific minds to other industry sectors or to other nations," DePinho said to The Cancer Letter.

In 2016, the Manocherian family poured close to $2 million into political contributions, placing them in the Top 20 Club of individual contributors, according to OpenSecrets.org. In the 2018 election cycle, Manocherian has thus far contributed $553,500 to candidate campaigns and political action committees (The Cancer Letter, March 30).

"The key thing to understand about Jed Manocherian is that he does this for no other reason than he wants to help end human suffering," DePinho said. "He is truly special—driven, generous in recognizing others, collaborative with other advocacy groups, respectful of others, and humble.

"Most importantly, congressional champions like Roy Blunt, Sen. Patty Murray (D-WA), Rep. Tom Cole (R-OK), and Rep. Rosa DeLauro (D-CT) were already focused on the dire need to restore NIH, and ACT for NIH helped build broad bipartisan support," DePinho said. "Without these visionary leaders, our new investments in our future would not have occurred.

"This is a great example of Congress working together for the people. We owe these congressional leaders, Jed Manocherian, Pat White, the ACT for NIH team and the community advocacy organizations an enormous debt of gratitude. Lives will be saved thanks to their devotion to others."

While DePinho's presidency at MD Anderson was marked by turbulence and controversy, his influence on the national level is emerging as game changing.

"When I first met Ron in New York, he was the incoming president of MD Anderson, and he outlined his bold vision for what became the cancer moonshots program," Manocherian said. "Some people thought it was too bold and ambitious, but I thought it was absolutely brilliant, and it is proving to be transformative. On many levels Ron is a true innovator and he will continue to have a major impact in 'making cancer history' both on a national and global level."

In addition to bringing Manocherian on the scene as an advocate for NIH and the 21st Century Cures Act, DePinho recommended his former colleague Norman "Ned" Sharpless for the NCI directorship (The Cancer Letter, Aug. 4, 2017).

Also, even as MD Anderson's Cancer Moon Shots took fire in Houston, former Vice President Joe Biden took inspiration from DePinho, and, in fact, the federal government licensed the trademark for the Beau Biden Cancer Moonshot.

Congress has authorized $1.8 billion over seven years for the national initiative, which was incorporated into the Cures Act at the end of the Obama administration (The Cancer Letter, Dec. 16, 2016). The FY18 omnibus allocates $496 million for the Cures Act, of which $300 million goes to the Moonshot, fully funding it for a second year (The Cancer Letter, March 23).

"There were so many champions in this process that deserve accolades including Ron, who played a significant role," said Ellen Sigal, founder and chair of Friends of Cancer Research. "He and Jed were relentless on a bipartisan, bicameral basis in dealing with the importance of funding NIH.

"Jed was instrumental in getting multiple stakeholders involved in the Cures Act from the grasstops and grassroots," Sigal said to The Cancer Letter. "Jed has a great understanding of what has to be done for NIH and he isn't disease-centric—which many of us can be—he has a big vision for research. He understood that all boats rise and fall on the importance of research and the investments in research.

"Jed is selfless. He's very quiet and very focused on the mission, the deliverables, and definitely does not like to call attention to himself and what he's done. He's highly modest."

Manocherian has the support of other members of MD Anderson's Board of Visitors, who also used their political connections and resources to advance his advocacy agenda, said Tom Johnson, a member of the board, and formerly the president of CNN, publisher of the Los Angeles Times, and executive vice-president of Texas Broadcasting Company.

"As I recall, Ron DePinho basically established with the board the history of what's happening with NIH funding, and the importance of NIH, not just to MD Anderson, but to all health-related issues," Johnson said to The Cancer Letter. "He introduced Jed to us. Most of us had not met Jed. I mean, we've read about him in some profiles on him, but the more I listened to Jed, to his commitment, to his willingness to take a leadership role, and to his passion for it, I think I just became one of many people around that table that said, 'Let's do what we can. This is one that can benefit all of us.'

"I went down a list of various people with whom I have longtime friendships. Even though I'm a Democrat, one of my close friendships over the years—going back to my time working in the Lyndon B. Johnson White House—was with Sen. Lamar Alexander (R-TN), and in fact, it led to Lamar coming and speaking to our board later.

"We went to work, and we first indicated to Jed that, 'Yes, we are enthusiastically behind you,' and second, we re-

> "The most significant role in all of this was led by Jed. There's no way to understate his role and I'm not somebody that overstates. I have no motive here but to be completely truthful with you."
>
> *– Tom Johnson*

alized that while this is not a campaign for MD Anderson alone, this is a campaign for all health care, we realized that we have a board made up of some of the finest—and I think some of the most bipartisan—people in the country. Let's do what we can. There's just a tremendous upside to supporting Jed and a tremendous downside if we let the funding continue to be cut.

"The most significant role in all of this was led by Jed. There's no way to understate his role and I'm not somebody that overstates. I have no motive here but to be completely truthful with you. Jed deserves a Presidential Medal of Freedom for what he's doing, and it will have implications for decades to come."

Manocherian's role as the "quiet storm" cannot be understated, said Margaret Anderson, former executive director of FasterCures.

"I certainly believe that luck plays a part in a lot of things in life," Anderson said to The Cancer Letter. "But luck plus preparation—I feel what Jed and Pat have brought to this issue is diligent preparation in terms of just educating, meeting, and being strategic about who needs to understand what the NIH does.

"With Jed, they've assembled this dream team of intelligence with the operational ability to navigate and get things done," said Anderson, who is now managing director of life science consulting at Deloitte. "In your article about Nancy Pelosi, even when she said that about the $3 billion, I'm not sure that everybody in the room was saying, 'Oh yeah, sure, that's going to happen.'

"Budgets change with circumstances, but Jed and Pat's ability to stay the course and continually push for increases with their kind of caliber of work—that's fairly extraordinary to me," said Anderson, who joined the ACT for NIH. board earlier this year. "I just want to punctuate that point about their deep humility and passion for this mission, and it's because they so believe in why they're doing it, in the cause."

In early conversations with Manocherian, DePinho said he discussed how a revolution in science would transform the prevention and treatment of cancer.

"He, like many others, was surprised to learn of our nation's steady decline in NIH funding at a time of great opportunity. He learned about the $5 billion NCI budget and very low grant success rates," DePinho said. "He remarked that it doesn't make sense that we spend $400 billion on a fighter jet program, and $5 billion on cancer, which kills 600,000 Americans every year. This fact, coupled with his desire to help others and his can-do nature, led to the founding of ACT for NIH.

"In fact Jed's initial idea was to double the NCI budget, but his engagement with these groups made him quickly realize that this needed to be done through NIH. He recruited Pat White, who has been brilliant in educating our legislators and their staff. As a vice chair of the BOD, I have been privileged to see first-hand how Jed and Pat worked across the aisle, sought support and guidance from members of the MD Anderson Board of Visitors, and engaged many other research advocacy groups, to get the job done."

As was the case with Mary Lasker, Manocherian has the interest and skills to work with a multifaceted community of advocates, said Mary Woolley, president and CEO of Research!America.

"It was immediately apparent to me when I met Jed that he is not about putting himself in the spotlight or being a celebrity of sorts, but rather about getting the job done and being persistent and determined in that way," Woolley said to The Cancer Letter. "Not just talking it but doing it. And that goes back to the willingness to spend his own time and money. And that matters. It really speaks volumes.

"Right from the start, people who knew Jed got in touch with me when they were hearing about some of his ambitions and passion for the cause for NIH. The analogy they drew is one that I have found holds up quite well, that is, he reminded them of a man named John Whitehead who came forward in the 90s to do something similar for NIH, and the predecessor before that is Mary Lasker, quite famously.

"They were people fortunate enough to have accumulated some wealth to put their own time and money into making NIH a priority for this nation. Similarly, all three of them kind of went from a particular, more focused interest, to a broader view of NIH, writ large, and carrying on their advocacy activities for the whole rather than, for example, cancer research only or basic research. They adopted this broader scope so that we don't get the advocacy community into a rob-Peter-to-pay-Paul kind of scenario, especially since all of us, and our families, are afflicted with more than one disease.

"When Jed came on board, he really put his shoulder to the wheel. And that was a good coincidence of timing because that was the point at which to key leaders in Congress stepped into their role as chairs of appropriations. It takes a village, but you know that leaders are hugely important. They're the kind of leaders—Tom Cole, Roy Blunt—whose names will be on a building at NIH one day.

"Then, somebody like Jed comes along and says, 'I'm going to make a difference here, try to set a high bar, assemble some smart people to work with me, make friends in the community, and get to work and not have it be all about me.'"

Q & A

Manocherian spoke with Matthew Ong, a reporter with The Cancer Letter.

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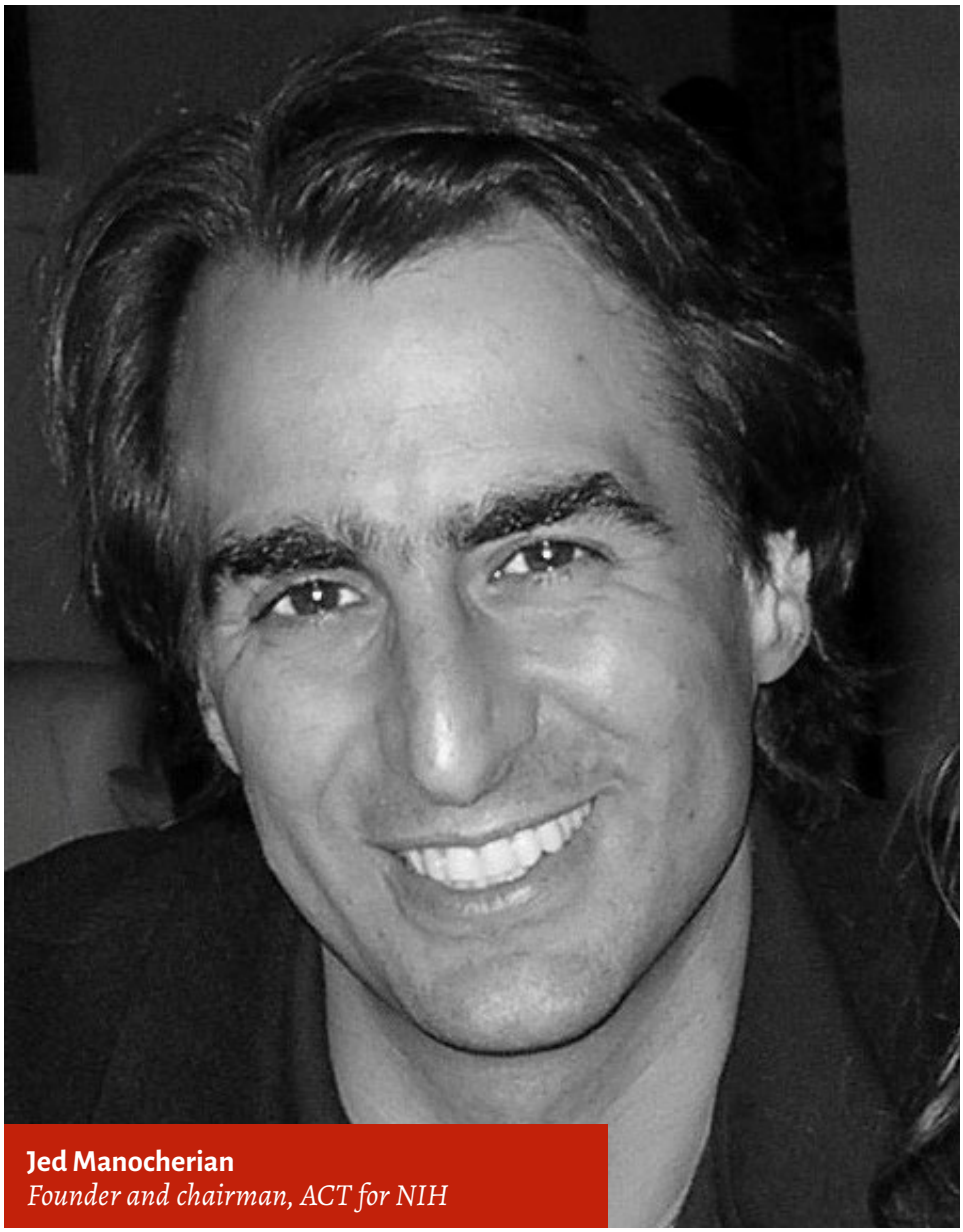
CONVERSATION WITH THE CANCER LETTER

Manocherian: We have been unapologetic in advocating for 10% annual increases to NIH

> NIH Restoration started in FY16, and could potentially also be completed in five years, by FY21. This would be one of the greatest legacies of any Congress in history, and in the history of scientific advancement. I cannot think of anything that could be more impactful to improve the human condition.



Jed Manocherian
Founder and chairman, ACT for NIH

Restoring the NIH budget is the singular mission of ACT for NIH, said Jed Manocherian, founder and chairman of the nonprofit advocacy organization.

"In the halls of Congress, and the science community, NIH Restoration is now defined as the inflationary loss to the NIH budget since 2003," said Manocherian, a real estate investor and developer whose company, Woodbranch Investments, holds property in New York and Texas. "Thankfully, over the last three years Congress has reduced the inflationary loss to 13 percent ($4.8 billion), and we hope Congress can race across the finish line in coming years, and complete restoration.

"Since we talk with almost everyone who determines annual NIH funding levels, we have a unique understanding of what is possible, and also the potential obstacles."

Manocherian spoke with Matthew Ong, a reporter with The Cancer Letter.

Matthew Ong: How did you get involved in medical research funding?

Jed Manocherian: I serve on the Board of Visitors for MD Anderson Cancer Center and our shared mission is "making cancer history." Through this service, I learned about the enormous promise of biomedical science to ease human suffering. I also learned about the alarming erosion of federal support for the National Institutes of Health, the most important biomedical research agency in the world.

Between 2003 and 2015, NIH lost nearly 25 percent of its purchasing power, severely impacting the search for treatments and cures. In the best of times, one-in-three NIH research proposals were funded. When we began our campaign that rate had fallen to one-in-six, its lowest level in history.

In 2014, I founded ACT for NIH: Advancing Cures Today, a nonprofit advocacy organization with the singular mission to restore federal funding for biomedical research.

In 2016, NIH received its first meaningful increase in 13 years, and now the largest in 15 years since the doubling. What role did ACT for NIH play in that conversation?

JM: Following 12 years of inflationary erosion, the downward spiral of NIH budgets has finally ended. The top Republicans and Democrats of the Labor, Health and Human Services Appropriations Subcommittees in the Senate and House have shown extraordinary commitment to NIH and have set a path to restoring the inflationary loss of the NIH budget.

In fact, when I first met Sen. [Roy] Blunt (R-MO) in 2014, he envisioned a doubling of the NIH budget in the next 10 years, and he is not alone. There is an ever increasing number of NIH congressional champions who understand the tremendous promise of science to enhance the health and wealth of our nation. Our role is simply to support their vision. We are part of a close community of advocacy groups and research institutions that have all contributed to the bipartisan groundswell of congressional support for NIH Restoration.

Of course, how difficult could it be to support [NIH Director] Dr. Francis Collins, who led the $3.8 billion NIH-funded Human Genome Project, which may be one of the most important scientific advancements in history, and has returned more than $1 trillion to our economy?

What was your role?

JM: When we have an opportunity to meet with NIH congressional champions and leadership, we discuss our high hopes for NIH funding levels, but mostly we seek their guidance. We also meet with representatives and senators that we hope will become NIH congressional champions. Since we talk with almost everyone who determines annual NIH funding levels, we have a unique understanding of what is possible, and also the potential obstacles.

We have met with numerous legislators since 2014, and the bipartisan support for NIH Restoration is overwhelming, in fact unanimous! What is also unanimous is that every single member we have met shares their personal story of how disease has touched their lives. Touched is too delicate a word for members that have lost parents, spouses, and children through the ravages of disease.

What are you doing that's different?

JM: Mary Lasker said it best, "if you think research is expensive, try disease." Disease is on an accelerating trajectory to bankrupt our economy. Alzheimer's care and treatment alone will cost the federal government trillions over the next 10 years. Our nation must also maintain its preeminence in science and technology that is fueling a life sciences revolution and will drive our economy in the years and decades ahead.

NIH-funded research is the lifeblood of multi-billion industries that create hundreds of thousands of jobs and it is of crit-

ical importance to our economy. Most importantly, it is priceless to the millions of patients anxiously awaiting cures.

Our singular mission is NIH Restoration. In the halls of Congress, and the science community, NIH Restoration is now defined as the inflationary loss to the NIH budget since 2003. The benefit is that there is a specific numerical target. It is a moving target because every year you need to factor the previous year's inflation. In 2015, the NIH budget had a nearly 25 percent, ($8.6 billion) inflationary loss.

Who did you hire? And who are some of the other players you work closely with?

JM: Former longtime appropriations committee staffer Mike Stephens was instrumental in launching our effort. Pat White, former associate director for legislative policy and analysis at NIH, is president and runs the operations, and our staff in D.C. is exceptional.

> When I first met Sen. [Roy] Blunt (R-MO) in 2014, he envisioned a doubling of the NIH budget in the next 10 years, and he is not alone. There is an ever increasing number of NIH congressional champions who understand the tremendous promise of science to enhance the health and wealth of our nation.

Thankfully, over the last three years Congress has reduced the inflationary loss to 13 percent ($4.8 billion), and we hope Congress can race across the finish line in coming years, and complete restoration.

We have been unapologetic in advocating for 10 percent annual increases to the NIH budget. We believe this is the appropriate level to restore NIH and also fund highly-merited research. Our sense is that Congress would like to embrace this level, but it is constrained by the necessity to work within its annual budget.

We enlisted FasterCures founder Michael Milken, Nobel Laureate Dr. David Baltimore, and Past President of MD Anderson, Dr. Ron DePinho as the first members of our Advisory Committee, which has grown to 13 members.

We also have alliances with countless advocacy organizations and research institutions such as FasterCures, Milken Institute, Friends of Cancer Research, the Parker Foundation, Ad Hoc Group, United for Medical Research, Lasker Foundation, Research!America, and the Alzheimer's Association.

With proposals for a 22 to 27 percent cut from the White House, and no more than $1.1 billion and $2 billion in the congressional appropriations bills, how did advocates for NIH secure $3 billion for fiscal year 2018—at very short notice?

JM: On March 16, 2017, the White House released the so-called "skinny budget," which called for across-the-board budget cuts to nearly all agencies. However, Congress controls the budget, and both parties are committed and working together to restore NIH.

In the president's inaugural address, he said he would like to "free the earth from the miseries of disease." The president's words inspired hope for patients and in the science community, and it would be wonderful if the president would join Congress in making this dream a reality.

The intention of both the House and Senate was to increase the NIH budget by $2 billion for FY18 if they could. Meaning, if there was a budget deal and not a yearlong continuing resolution, and they could agree on where to find the funds within the LHHS budget.

What most members also realized very early on is that there was a strong likelihood that we would increase the federal budget for both defense and non-defense, but it was unclear at what level. What we have been doing for almost a year is to advocate for an increase in excess of $2 billion, if the increase in the non-defense discretionary budget, and more specifically, the increase in the LHHS budget provided that opportunity.

When the final increase in non-discretionary spending and the budget allocation for LHHS were released, it was at a

higher level than most had anticipated, and we had high hopes that NIH would fare well. So did Chairman Tom Cole (R-OK) who said, "Let's just put it this way: I think the people in NIH are going to be very happy," he said, adding for emphasis: "I just said very happy, not just happy."

At the end of every year's budget negotiations there is a flurry of activity, and "horse trading" which takes place among a small contingent of House and Senate chairs, ranking members and leadership. Our role throughout the year is to make the case to everyone that determines NIH funding levels to prioritize NIH, especially during the final negotiations.

What worked right?

JM: The answer is simple, the incredibly compassionate and talented NIH congressional champions, including appropriators Sen. Roy Blunt (R-MO), Sen. Patty Murray (D-WA), Congressman Tom Cole, and Congresswoman Rosa DeLauro (D-CT), who have always understood and championed this cause, and continue to work together on a bipartisan basis for our nation and for all of humanity.

When we think about the most important people in history for the advancement of science and medical research, we think of Jonas Salk and Alexander Fleming, and we should also include living legends [NIAID Director] Tony Fauci and Francis Collins.

But let us not neglect to include the great political leaders that have unleashed thousands of brilliant young scientists to pursue their dreams of research that will lead to transformative treatments and cures for the most intractable diseases and conditions.

What's the outlook in Washington for NIH funding over the next few years?

JM: In one word, excellent!

Congress has elevated NIH Restoration as a bipartisan national priority, and seized this historic opportunity to reaffirm our nation's preeminence in science and technology. This renewed Congressional investment in NIH comes at a time when scientific and technological capabilities make this the greatest time in history to find remarkable scientific advances that aid understanding, treatment, prevention, and cures for thousands of diseases and conditions.

The overall budget level is set for FY19, and appropriators are already considering NIH levels for next year. Sens. Arlen Specter and Tom Harkin and Congressman John Porter led the doubling of the NIH budget over five years, 1999-2003. Then, 12 years of inflationary erosion caused the biomedical research crisis and historically low grant success rates.

NIH Restoration started in FY16, and could potentially also be completed in five years, by FY21. This would be one of the greatest legacies of any Congress in history, and in the history of scientific advancement.I cannot think of anything that could be more impactful to improve the human condition.

In the years ahead, there will be less misery and suffering, death and sorrow, for hundreds of millions across the globe ravaged by ALL the dreaded diseases.

ACT for NIH will continue our efforts working with the science community and with Congress on a shared mission to end pain and suffering through science. There are too many patients to be patient.

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AACR announces 2018 class of fellows of AACR Academy

The American Association for Cancer Research announced a class of fellows of the AACR Academy:

Alan Ashworth

President, UCSF Helen Diller Family Comprehensive Cancer Center; senior vice president for cancer services; professor of medicine, Division of Hematology/Oncology, Department of Medicine; E. Dixon Heise Distinguished Professor in Oncology, University of California, San Francisco

For characterizing the significance of cancer susceptibility genes, notably BRCA2, in the pathogenesis of cancer, and for his contributions to the establishment of PARP inhibitors as effective therapeutic options for the treatment of various cancers.

René Bernards

Professor, Molecular Carcinogenesis, Netherlands Cancer Institute, Amsterdam

For establishing innovative strategies to categorize biomarkers of treatment response and effective treatment combinations, and for pioneering the use of genetic screening tests to identify and stratify individuals at risk of developing breast cancer.

Bruce Beutler

Director, Center for the Genetics of Host Defense; Regental Professor; Raymond and Ellen Willie Distinguished Chair in Cancer Research, University of Texas Southwestern Medical Center, Dallas

For discovery of toll-like receptors and for deciphering the biological mechanisms and signaling events that govern tumor necrosis factor-mediated inflammation and innate immune system activation. For establishing innovative strategies to categorize biomarkers of treatment response and effective treatment combinations, and for pioneering the use of genetic screening tests to identify and stratify individuals at risk of developing breast cancer.

Michael Caligiuri

President and Physician-in-Chief, The City of Hope National Medical Center, Duarte, California

For elucidating the fundamental mechanisms of natural killer cell development and immune surveillance, and for his commitment to advancing cancer health disparities research and promoting the collection and use of clinical samples to guide screening, treatment, and surveillance protocols.

Chi Van Dang

Scientific sirector, Ludwig Institute for Cancer Research, New York; professor, the Wistar Institute, Philadelphia

For illuminating mechanistic links between the MYC oncogene and cellular metabolism, and for defining how tumor cell utilization of various energy sources contributes to cancer progression.

Gary Gilliland

President and director, Fred Hutchinson Cancer Research Center, Seattle

For identifying genetic drivers of various hematologic malignancies including leukemia, myelodysplastic syndrome, and myeloproliferative disease, and for his contributions to the development of monoclonal antibody-based immunotherapeutics.

Laurie Glimcher

President and CEO, Dana-Farber Cancer Institute; Richard and Susan Smith Professor of Medicine, Harvard Medical School; Director and Principal Investigator, Dana-Farber/Harvard Cancer Center

For her central discoveries in the fields of transcriptional regulation, lymphocyte differentiation, inflammation, and osteobiology, and for her trailblazing efforts to improve access to care, health policy, and medical education.

Elizabeth Jaffee

The Dana and Albert "Cubby" Broccoli Professor of Oncology; Deputy Director, Sidney Kimmel Comprehensive Cancer Center; Co-Director, Gastrointestinal Cancers Program, The Johns Hopkins University School of Medicine

For her groundbreaking efforts dedicated to the development of cancer vaccines and vaccine combinations that bypass tumor-associated immunotolerance, and for exploiting genomic and proteomic technologies to define biomarkers required for cancer onset, progression, and metastasis.

Richard Klausner

Founder and director, Juno Therapeutics; founder and director, GRAIL; executive chairman, Wisdo, a third-generation internet company; co-founder and executive chairman, Mindstrong, Los Altos Hills, California

For defining molecular mechanisms of intracellular trafficking, translation, and protein assembly, and for leading the creation of national and international programs to support the spectrum of cancer research, resulting in improved cancer diagnosis and treatment strategies.

Roger Kornberg

Winzer Professor in Medicine, Department of Structural Biology, Stanford University School of Medicine

For pioneering discovery of the structure and function of nucleosomes, and for revolutionizing the understanding of the molecular machinery and orchestrated mechanisms required for eukaryotic gene transcription.

Arthur Levinson

Founder and CEO, Calico Life Sciences LLC, South San Francisco

For visionary leadership and relentless commitment to the discovery and development of targeted therapeutics for the treatment of various malignancies, including HER2/neu monoclonal antibodies for the treatment of breast cancer.

Norman Sharpless

Director, NCI

For seminal contributions to stem cell biology and to demonstrating the relationship between tumor suppressor activation, cell cycle control, cellular senescence, and molecular aging in tumorigenesis.

Fellows of the AACR Academy are charged with:

- Identifying scientific priorities that will contribute to the AACR's programs and activities; influencing science and public policy and creating and/or signing letters addressed to members of the U.S. Congress and to the presidential administration regarding important scientific or policy issues as needed;
- Advocating for increased federal funding for cancer research and cancer-related sciences;
- Participating in special meetings to discuss how to accelerate advances in cancer research;
- Mentoring cancer researchers in training in all research settings;
- Assisting the AACR in educating the public about cancer, the importance of the AACR, and the value of cancer research to public health and the conquest of cancer.

Barker, Osborne, Sharp and Williams win AACR awards

The American Association for Cancer Research will present special recognition awards to four individuals whose work has made extraordinary contributions to the AACR's mission to accelerate the prevention and cure of all cancers through research, education, communication, and collaboration.

Anna Barker, C. Kent Osborne, Phillip Sharp, and James Williams will receive the awards at the AACR Annual Meeting 2018, April 14-18 at McCormick Place in Chicago.

These AACR Awards recognize groundbreaking, innovative work across the entire cancer community, and they reflect a wide range of contributions to cancer science and medicine. This year's award recipients represent meritorious work in research, patient care, policymaking, and advocacy.

This year's winners:

Anna Barker will receive the 2018 AACR Distinguished Award for Exceptional Leadership in Cancer Science Policy and Advocacy.

Barker is the director of the National Biomarker Development Alliance; the director of Transformative Healthcare Knowledge Networks; co-director, Complex Adaptive Systems; and a professor in the School of Life Sciences at Arizona State University.

Barker has been chairperson of the AACR Scientist↔Survivor Program since she conceptualized the program more than two decades ago. She also provided outstanding leadership in cancer science policy and advocacy for the AACR through her work as Chair of the AACR's Public Education Committee from 1993-2002.

She continues to serve on this committee, lending her expertise to its initiatives. In addition, she served on the AACR Board of Directors from 1995-1996 and 1998-2001. She was Deputy Director of the National Cancer Institute from 2002-2010.

C. Kent Osborne will receive the 2018 AACR Distinguished Award for Extraordinary Scientific Achievement and Leadership in Breast Cancer Research.

Osborne is the director of the Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine, where he is also a professor and the Dudley and Tina Sharp Chair for Cancer Research. Since 1992, he has been a codirector of the San Antonio Breast Cancer Symposium, the world's largest and most prestigious conference devoted to breast cancer.

Osborne's own research has focused on improving the effectiveness of endocrine and HER-2 targeted therapies in patients with breast cancer.

Phillip Sharp will receive the 2018 AACR Distinguished Award for Extraordinary Scientific Innovation and Exceptional Leadership in Cancer Research and Biomedical Science.

Sharp is an Institute professor and faculty member at Massachusetts Institute of Technology's David H. Koch Institute for Integrative Cancer Research. A world leader in molecular biology and biochemistry, he won the 1993 Nobel Prize in Physiology or Medicine for his co-discovery of RNA splicing. He was elected as an inaugural Fellow of the AACR Academy in 2013.

Sharp has been Chair of the Stand Up To Cancer Scientific Advisory Committee over the past decade, leading the selection of 23 "Dream Teams" of top researchers and other SU2C research groups.

He served as program chair of the AACR's Inaugural Special Conference in 1988. That conference, "Gene Regulation and Oncogenes," has been characterized as a watershed meeting in stimulating novel, transformative thinking about the molecular biology of cancer. In October 2018, he will lead the 30th Anniversary Special Conference on "Convergence: Artificial Intelligence, Big Data, and Prediction in Cancer."

Col. James E. Williams will receive the AACR 2018 Distinguished Public Service Award for Exceptional Leadership in Cancer Advocacy.

Williams, a retired Army colonel who served in the Vietnam War, was diagnosed with prostate cancer in 1991.

His advocacy efforts include serving as a member of the editorial advisory board of the AACR's Cancer Today magazine; serving as chairman of the board of the Intercultural Cancer Council; serving as chairman of the Pennsylvania Prostate Cancer Coalition; participating on the patient advocacy committee of the Alliance for Clinical Trials in Oncology; and serving as a board member of the Alliance for Prostate Cancer Prevention.

IN BRIEF

Primo Lara named director of UC Davis cancer center

Primo Nery Lara was named director of the UC Davis Comprehensive Cancer Center.

Lara replaces Ralph de Vere White, who retired in 2016. As director, Lara will hold the Codman-Radke Chair in Cancer Research and serve as executive associate dean for cancer programs. Lara has served as acting director since July 2016 and was selected for the permanent position after a national search.

He is the first Filipino-American to lead an NCI-designated cancer center, the cancer center said.

Known to most as "Lucky" Lara, the new director began his career at UC Davis as a hematology-oncology fellow specializing in cancers of the lung, prostate and bladder. He was invited to join the faculty in 1999.

Lara has served as the cancer center's associate director for translational research since 2008.

In March, Lara was named incoming deputy chair of SWOG, where he will also oversee the National Clinical Trials Network portfolio of treatment trials.

UC Davis is the only NCI-designated comprehensive cancer center that cares for patients throughout the Central Valley of California, a diverse region of more than five million people.

Lara serves as principal investigator of the NCI-funded K12 Paul Calabresi Clinical Oncology Training Grant, which trains junior faculty scholars to be independent, patient-oriented cancer researchers.

Lara's key priorities include building upon the multi-disciplinary programs and projects across UC Davis to develop novel approaches to diagnose, monitor and treat cancer:

- Comparative oncology, which teams medical, radiation, and surgical oncologists at the cancer center with veterinary oncologists to test novel therapies or biomarkers in canine cancer patients that can be more rapidly translated into human clinical trials. One study, for example, explores integrating immunotherapy with radiation therapy for dogs with cancer—which led to clinical research now underway at the cancer center in human patients.
- Biomedical engineering, to design and build tools to better diagnose, track and treat cancer. EXPLORER, for example, will be the world's first total-body PET scanner, capable of imaging the entire body with high resolution, while using less radiation and potentially transforming the way cancer treatments can be delivered and evaluated in the clinic.
- Nanotheranostics, a field of study that integrates imaging and therapy in a single platform, allowing scientists to develop drugs that specifically target cancer cells and monitor how drugs are released and distributed in the body. Nanotheranostics will allow providers to predict whether a drug reaches its tumor target and may be more effective than standard untargeted therapies.

Fitzpatrick steps down as CancerLinQ CEO; ASCO CMO Schilsky named interim CEO

Kevin Fitzpatrick will step down from his role as CEO of CancerLinQ LLC, a wholly owned non-profit subsidiarity of the American Society of Clinical Oncology, on April 13 to pursue a new opportunity outside of ASCO.

Richard Schilsky, ASCO chief medical officer, will serve as interim CEO. CancerLinQ LLC will initiate a global search for a permanent CEO to oversee the continued expansion and implementation of CancerLinQ.

"Under Kevin's leadership we've taken CancerLinQ from a bold and ambitious idea to a reality for physicians and researchers across the country who seek to learn from everyday patient care," Clifford Hudis, CEO of ASCO and chair of the CancerLinQ board of governors, said in a statement. "He played a crucial role in establishing CancerLinQ, overseeing its rollout to physician practices and securing novel strategic collaborations with government, for-profit and non-profit entities.

"We are fortunate to have Dr. Schilsky, with his extensive experience with CancerLinQ and oncology data, and his relationships throughout the oncology community, to step in to sustain our momentum through the transition," Hudis said.

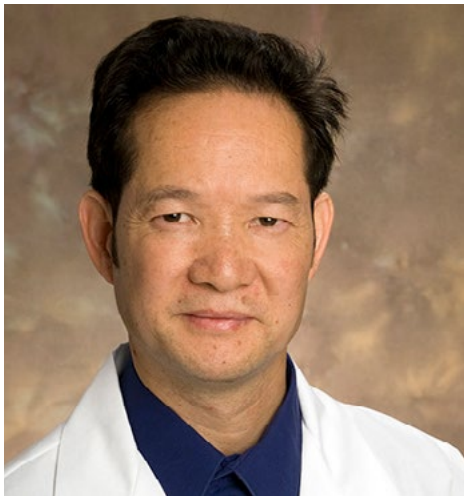
Schilsky is a past president of ASCO and has served as CMO since 2012. In addition to being closely involved with CancerLinQ since its inception. He leads ASCO's Center for Research & Analytics, which makes various cancer data sets—including CancerLinQ Discovery—available to the oncology community and provides consultation and support for research and analysis.

Last year, ASCO and two companies—Tempus and Precision Health AI—announced a deal to curate and license the data in CancerLinQ. The ten-year collaboration, announced Dec. 21, 1017, gives Tempus and PH.AI access to de-identified data from over a growing database of more than a million records contained in CancerLinQ (The Cancer Letter, Jan. 5)

Emory Winship awards three new endowed chairs

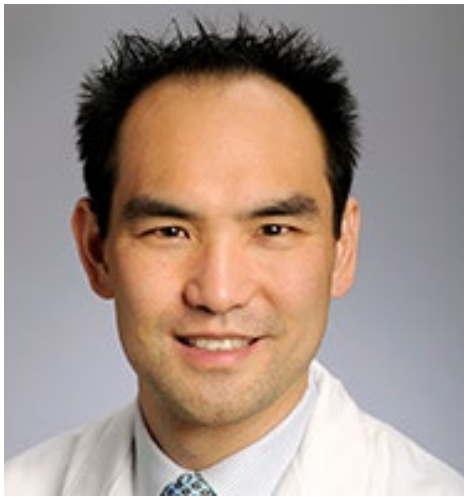
Three members of Winship Cancer Institute's Department of Radiation Oncology received endowed chair appointments:

- **Xingming Deng** is the inaugural holder of the Chair in Cancer Biology.
- **David Yu** is the inaugural holder of the Jerome Landry Chair of Cancer Research.
- **Hyunsuk Shim** is the inaugural holder of the Crocker Family Chair in Cancer Innovation.

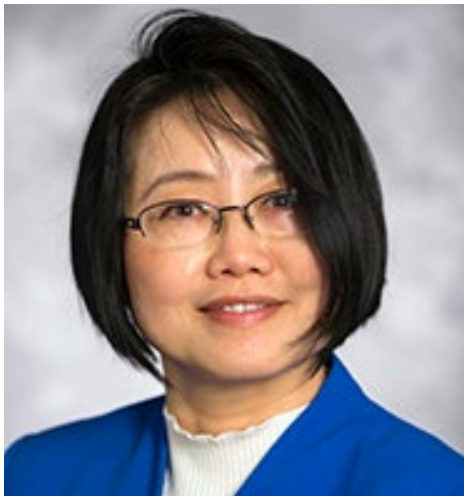


Deng, professor in the Department of Radiation Oncology and director of the discovery theme in Winship's Discovery and Development Therapeutics Research Program, joined Winship in 2009. He has unique experience in uncovering cell death and DNA repair mechanisms.

He has contributed the understanding of the Bcl-2 and Bax family of proteins and how their anti and pro-apoptotic functions influence the development of aerodigestive malignancies and their subsequent response to anticancer therapies. He has obtained four patents for new anticancer drug discovery.



Yu, associate professor and director of cancer biology in the Department of Radiation Oncology, began his faculty career at Winship in 2010. His research focuses on the role of acetylation in directing the replication stress response and whether it will translate to cancer therapeutics and diagnostics, especially for patients with pancreatic cancer. In 2014, Yu received the Michael Fry Research Award from the Radiation Research Society recognizing the most outstanding junior scientist in the field of radiation research.



Shim, professor and scientific director of medical physics in the Department of Radiation Oncology, is a molecular

oncologist with a specialty in diagnostic imaging and drug discovery. In her 16 years at Emory and Winship, she has contributed groundbreaking insights into the involvement of chemokine receptor modulation in cancer invasion and metastasis. She is known as a global expert in working with the alpha chemokine receptor CXCR4. Shim leads Emory's NCI Quantitative Imaging Network team on developing advanced 3D whole-brain spectroscopic MRI for the management of brain tumor patients.

Fisher named executive director, research, business administration at Siteman

Nick Fisher was named executive director of research and business administration at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine in St. Louis.

Fisher now leads the fiscal and managerial administration of research facilities, information systems, human resources and day-to-day operations of Siteman. He has 14 years of experience with academic clinical research and cancer center operations and was selected after a national search.

Fisher has worked in the School of Medicine's Division of Oncology and at Siteman Cancer Center since 2003. Since then, he has served in many positions, including director of operations, director of clinical research and manager of oncology clinical research.

Bill Louv named Project Data Sphere president

Bill Louv was named president of Project Data Sphere, LLC, an independent, not-for-profit initiative of the CEO Roundtable on Cancer, Inc.'s Life Sciences Consortium.

Louv is a former member of GlaxoSmithKline's corporate executive team.

A free digital library-data laboratory, the Project Data Sphere cancer research platform was launched in April 2014. The platform has grown to patient-level data representing more than 120,000 clinical trial cancer patients.

The registered user community has increased to more than 1,700 authorized users who have performed more than 8,800 downloads of data for research purposes for various cancer tumor types including bladder, breast, colorectal, gastric, kidney, lung, melanoma, pancreatic and prostate.

NCCN awards grants to five young investigators

The NCCN Foundation has announced five recipients for this year's Young Investigator Awards. The grantees come from National Comprehensive Cancer Network Member Institutions, and will each receive up to $150,000 in funding over a two-year period.

This marks the eighth year for the NCCN Foundation Young Investigator Awards supporting career development for innovative cancer researchers.

The 2018 awardees are:

Rebecca Arend, University of Alabama at Birmingham Comprehensive Cancer Center

The Role of TGF-β in Immune Suppression in Suboptimally Debulked Ovarian Cancer Patients

Yin Cao, Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

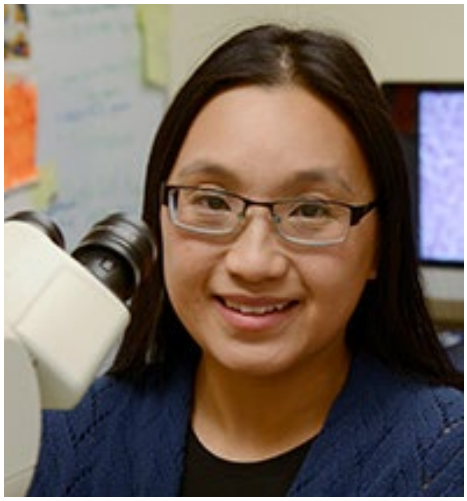
Disparities in Young-Onset Colorectal Cancer Survival According to Patient, Treatment, and Tumor Molecular Characteristics

Tim Luetkens, Huntsman Cancer Institute at the University of Utah

CD229 Chimeric Antigen Receptor T Cells for the Treatment of Multiple Myeloma

Edwin Manuel, City of Hope Comprehensive Cancer Center

Altering the Local Immune Landscape in Lung Cancer to Improve Anti-PD-1 Therapy

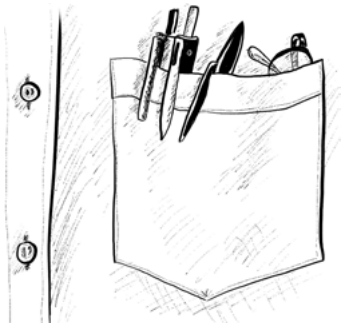


Cecilia Yeung, Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Optimization of a Rapid Point of Care Device for Acute Promyelocytic Leukemia Diagnosis and Therapy Guidance

These five awardees were selected out of a pool of 48 applicants nominated from across the 27 NCCN member institutions. The NCCN Oncology Research Program will manage and oversee the projects for the next two years. The awardees will then present the results from their research at the NCCN 25th Annual Conference in 2020.

THE CLINICAL CANCER LETTER



TRIALS & TRIBULATIONS

The importance of staging lung cancer consistently and correctly worldwide

By Fred R. Hirsch
CEO of the International Association for the Study of Lung Cancer

Despite much progress in lung cancer over the last decade, lung cancer is the most frequent cause of cancer death.

IASLC

Globally, 1.8 million patients are diagnosed with lung cancer, while in the U.S., more than 220,000 new cases are diagnosed per year. To ensure the best quality care for lung cancer worldwide, it's critical that patients are diagnosed and treated correctly. The IASLC, as the only global organization dedicated solely to the study of lung cancer and other thoracic malignancies, is in a unique position to facilitate the improvement of lung cancer care worldwide through education and research, and the development of standardized guidelines for detection, screening, and treatment.

The IASLC staging system is a well-validated and accurate system that has led to the development of several ac-

companying guidelines and educational materials. The IASLC Staging Manual in Thoracic Oncology is one such guideline and reports on the latest revisions of the tumor, node and metastasis (TNM) classifications of thoracic malignancies; namely, lung cancer, malignant pleural mesothelioma, carcinoma of the esophagus and of the esophago-gastric junction and thymic epithelial tumors.

Proper staging of lung cancer and other thoracic malignancies accurately is important for making treatment decisions and ensures the best standardized care for patients worldwide.

The history of the staging system

The IASLC established an international Staging Committee in 1997, now known as the Staging and Prognostic Factors Committee (SPFC). The IASLC SPFC collects and combines lung cancer data sets to inform changes to the lung cancer TNM staging system with worldwide representation including all treatment modalities.

The data sets include a large amount of data regarding the size of tumors, lymph node status, and metastasis. This data provided the basis for staging recommendations that were adopted by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). Before the IASLC Staging Project, data collected for staging of lung cancer came from a smaller group of patients, almost exclusively based in the U.S. and was based on about 6,000 patients.

The IASLC Staging and Prognostic Factors Committee (SPFC) proposed revisions to the lung cancer staging system for the 8th edition of the TNM Classification of Malignant Tumours. The Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) accepted these revisions, and the 8th edition of the TNM Classification was implemented in January 2017. In the United States and most of the world, implementation was delayed until January 2018; now, the new edition has been enacted worldwide.

Updating the staging system—impact on clinical practice

The new database, which informs the Eighth Edition of the TNM Classification of Lung Cancer (The IASLC added our data beginning with the Seventh Edition), consists of 94,708 eligible patients diagnosed around the world from 1999-2010. The objective was to further explore and analyze the impact on prognosis of tumor size and of the different T descriptors; the prognostic significance of tumor burden in hilar and mediastinal lymph nodes; and the confirmation of the revised M1 categories (M1a and M1b) of the seventh edition of the classification along with the prognostic impact of number and anatomic location of metastases.

Staging is a tumor classification system that, in principle, reflects the anatomical extent of the tumor based on the extent of the primary tumor (T), the nodal spread (N) and the distant metastases (M). Revisions from the 7th to 8th edition were made to achieve refined prognostic capabilities and to help clinicians stratify tumors/ patients based on expected prognosis. Treatment modalities are very much dependent on stages of the disease. Therefore, a uniform staging system is important for determining the best treatment modality for the individual patient. It is also important for comparisons of treatment results from clinical trials.

The second edition of the IASLC Staging Manual in Thoracic Oncology includes:

- Information on the four above-mentioned neoplasms, instead of the first edition's sole focus on lung cancer and mesothelioma.
- Besides the chapters describing the basic TNM classifications of the four thoracic malignancies, there are chapters on the history of the TNM classifications of the four tumors that give a lot of background information on the development of their staging systems.
- There are original chapters on the new recommendations proposed by the IASLC for classifying lung cancers presenting with multiple lesions, for measuring tumor size and for coding the newly described adenocarcinoma in situ and minimally invasive adenocarcinoma, as well as on prognostic factors.
- There are color atlases graphically describing the TNM classifications of the four thoracic malignancies.
- Additional chapters assist in the classification of tumors with characteristics that do not fit in the present official descriptors.

Differences in the TNM Classification of Lung Cancer

The main differences between 7th and 8th editions are the following:

T Descriptors

In the T component of lung cancer, the T1 category was divided into three subcategories (T1a-T1c) according to 1-cm cutoff points of the greatest dimension. The T2 category now includes tumors larger than 3 cm but no more than 5 cm and was divided into T2a and T2b according to 1-cm cutoff points. Tumors larger than 5 cm, but no more than 7 cm were classified as

T3, and tumors larger than 7 cm were classified as T4. Adenocarcinoma in situ (Tis(AIS)): tumors without a solid part on CT image or a pathologic invasive part) and minimally invasive adenocarcinoma (T1mi: tumors with a solid part of < 0.5cm on CT image or a pathologic invasive part of < 0.5 cm) were introduced. Sub-solid tumors 3 cm or less in the greatest dimension were recommended to be classified according to the size of the solid part on CT image or the pathologic invasive part. Involvement of main bronchus without carina was categorized as T2 regardless of distance to the carina. Total atelectasis or obstructive pneumonitis were downgraded from T3 to T2. Invasion of the diaphragm was upgraded from T3 to T4.

N Descriptors

The N component had no changes. However, analyses of the IASLC database revealed prognostic implications of the number of involved lymph nodes and of involved nodal stations. Exploratory analyses of survival showed that N1a (involvement of a single N1 nodal station) had better prognosis than N1b (involvement of multiple N1 nodal stations). N2a1 (involvement of a single N2 nodal station without N1 involvement) had a similar prognosis to N1b. N2a2 (involvement of a single N2 nodal station with N1 involvement) was correlated with a worse prognosis than N2a1 but a better prognosis than N2b (involvement of multiple N2 nodal stations).

M Descriptors

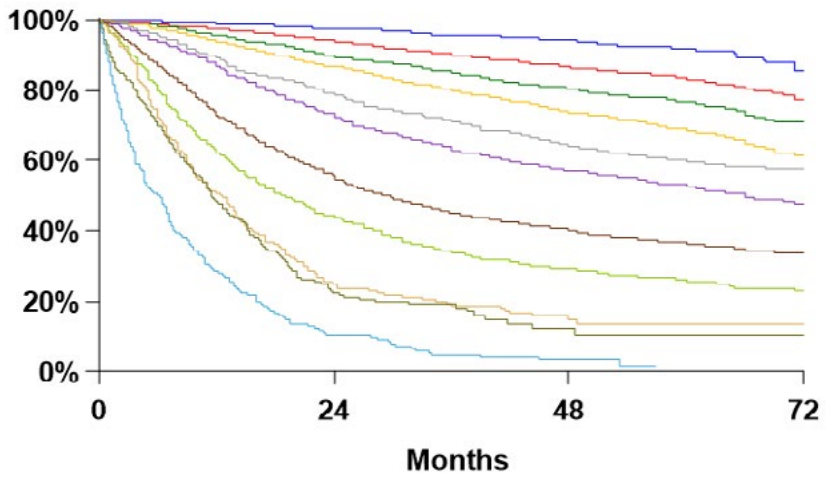
M1 categories were refined based on the number of the extrathoracic metastases. Single extrathoracic metastasis was categorized as M1b, and multiple extrathoracic metastases were categorized as M1c. M1a has not changed from the 7th edition, which included metastasis restricted to the thoracic cavity. Prognosis of M1a and M1b diseases were similar; however, due to the difference of anatomic extension of the tumor, M1a and M1b were categorized as different entities.

Tools and teaching aids to help clinicians worldwide

The IASLC offers a wealth of resources to help doctors and nurses worldwide stage lung cancer, including a *Staging Manual in Thoracic Oncology*, a *Staging Handbook in Thoracic Oncology*, a staging app, laminated staging cards and posters, a collection of peer-reviewed scientific articles, and a comprehensive website. These tools can assist with implementation of the protocol in routine daily care.

Finally, the IASLC Staging Articles contain the science behind the revisions introduced in the 8th edition of the TNM classification. These articles have to be read thoroughly because they provide all the necessary information on the database used for the revision, the methodology applied, the results of the numerous analyses and their interpretation. Any doubt that one may have reading the core information included in the laminates, posters and apps will be solved by reading the landmark paper (ref. Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Can-

OVERALL SURVIVAL BY CLINICAL STAGE



Proposed	Events / N	MST	24 Month	60 Month
IA1	68 / 781	NR	97%	92%
IA2	505 / 3105	NR	94%	83%
IA3	546 / 2417	NR	90%	77%
IB	560 / 1928	NR	87%	68%
IIA	215 / 585	NR	79%	60%
IIB	605 / 1453	66.0	72%	53%
IIIA	2052 / 3200	29.3	55%	36%
IIIB	1551 / 2140	19.0	44%	26%
IIIC	831 / 986	12.6	24%	13%
IVA	336 / 484	11.5	23%	10%
IVB	328 / 398	6.0	10%	0%

Source: Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2016;11:39-51.

cer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2016;11:39-51.)

While the 8th Edition of the international staging system was recently published, the IASLC is currently working on the 9th Edition, which will include molecular characteristics added to the TNM system. Given the rapid progress in the understanding of lung cancer, it's critical that our staging system keep up. Small changes in the precision of diagnosing and treating lung cancer can make large changes in a patient's outcome.

Future projects

The IASLC is a multidisciplinary organization that includes surgeons, medical oncologists, radiation oncologists, pulmonologists, radiologists, pathologists, epidemiologists, basic research scientists, nurses, allied health professionals, advocates, caregivers and patients involved in lung cancer prevention and management.

The organization has grown significantly from 3,000 (2013) to about 8,000 members in >100 countries. Data from survival curves clearly shows that the earlier lung cancer patients are diagnosed, the better their outcomes. Thus, lung cancer screening and prevention efforts have high priority in IASLC. The IASLC is working on a global database for screening lung cancer patients more effectively and efficiently, hopefully helping the field take another large step toward the goal of making lung cancer a curable disease.

The IASLC is, of course, also involved in developing other educational and research activities and recently published CAP/IASLC/AMP guidelines for molecular testing of patients with lung cancer (ref. Lindeman NI, Cagle PT, Aisner DL, et al. Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors: Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology. J Thorac Oncol. 2018;13(3):323-358.)

“Given the rapid progress in the understanding of lung cancer, it's critical that our staging system keep up. Small changes in the precision of diagnosing and treating lung cancer can make large changes in a patient's outcome.”

CLINICAL ROUNDUP

NIH completes in-depth genomic analysis of 33 cancer types

Researchers funded by the NIH have completed a genomic analysis, known as the PanCancer Atlas, on a data set of molecular and clinical information from over 10,000 tumors representing 33 types of cancer.

The PanCancer Atlas, published as a collection of 29 papers across a suite of Cell journals, sums up the work accomplished by the Cancer Genome Atlas, a collaboration initiated and supported by the NHGRI and NCI, both part of NIH. The program, with over $300 million in total funding, involved upwards of 150 researchers at more than two dozen institutions across North America.

The project focused on cancer genome sequencing, and different types of data analyses, such as investigating gene and protein expression profiles, and associating them with clinical and imaging data.

The PanCancer Atlas is divided into three main categories, each anchored by a summary paper that recaps the core findings for the topic. The main topics include: cell of origin, oncogenic processes, and oncogenic pathways. Multiple companion papers report in-depth explorations of individual topics within these categories.

In the first summary paper, the authors summarize the findings from a set of analyses that used a technique called molecular clustering, which groups tumors by parameters such as genes being expressed, abnormality of chromosome numbers in tumor cells, and DNA modifications. The paper's findings suggest that tumor types cluster by their possible cells of origin, a result that adds to our understanding of how tumor tissue of origin influences a cancer's features and could lead to more specific treatments for various cancer types.

The second summary paper presents a broad view of the TCGA findings on the processes that lead to cancer development and progression. Specifically, the authors noted that the findings identified three critical oncogenic processes: mutations, both germline and somatic; the influence of the tumor's underlying genome and epigenome on gene and protein expression; and the interplay of tumor and immune cells. These findings will help prioritize the development of new treatments and immunotherapies for a wide range of cancers.

The final summary paper details TCGA investigations on the genomic alterations in the signaling pathways that control cell cycle progression, cell death and cell growth, revealing the similarities and differences in these processes across a range of cancers.

Simultaneous chemo and immunotherapy may be better for some metastatic bladder cancers

Researchers from Mount Sinai and Sema4, a health information company and Mount Sinai venture, discovered that giving metastatic bladder cancer patients simultaneous chemotherapy and immunotherapy is safe and that patients whose tumors have certain genetic mutations may respond particularly well to this combination approach, according to the results of a clinical trial published in European Urology.

Though chemotherapy and immunotherapy have become standard options for the treatment of metastatic bladder cancer, it was previously unknown whether these therapies could be given together and whether chemotherapy's side effect of weakening the immune system would inhibit immunotherapy.

The phase II trial was conducted at six cancer centers, and patients in the trial did not show any additional or more severe side effects than patients given chemotherapy or immunotherapy alone, a finding that showed the combination therapy is a safe alternative.

Researchers also generated evidence showing that immunotherapy could boost immune cells in the blood of patients receiving concurrent chemotherapy, allaying previous concerns that chemotherapy might counteract the effects of immunotherapy.

One of the new trials, which Matthew Galsky, director of genitourinary medical oncology and professor of

urology, medicine, hematology and medical oncology at The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, and principal investigator of the study.

The study, headed by Galsky at Mount Sinai and other centers, gives chemotherapy and immunotherapy to a subset of patients with earlier-stage bladder cancer to determine if this combination can head off the need for surgery to remove the bladder, a standard treatment but one with quality-of-life-altering implications that include wearing a urostomy bag outside the body to collect urine. The other trial combines two different chemotherapy regimens with immunotherapy to determine the best types of chemotherapy drugs to combine with immunotherapy.

Galsky and Andrew Uzilov, director of cancer genomics for Sema4, and Huan Wang, Sema4 bioinformatics scientist, and other researchers hypothesized that patients with tumors with particular genetic mutations might respond best to the combination of chemotherapy and immunotherapy.

They found that certain types of mutations in DNA damage response genes were associated with better response to the combined chemotherapy and immunotherapy. If validated in subsequent studies, these findings could add a novel biomarker to the "precision oncology toolbox" and refine the selection of patients who might benefit from concurrent administration of chemotherapy and immunotherapy.

This study was supported by Bristol-Myers Squibb, Cancer Research Institute Clinical Strategy Team Grant, and National Cancer Institute grant P30 CA196521.

DRUGS & TARGETS

EC expands XGEVA indications for prevention of skeletal events in multiple myeloma

European Commission has approved an expanded indication for XGEVA (denosumab) for the prevention of skeletal-related events in adults with advanced malignancies involving bone.

The indication now covers patients with bone metastases from solid tumors and those with multiple myeloma. The approval is based on data from the phase III '482 study, the largest international trial ever conducted for the prevention of skeletal-related events in multiple myeloma patients.

XGEVA is sponsored by Amgen Inc.

In the '482 study, XGEVA met the primary endpoint, demonstrating non-inferiority to zoledronic acid in delaying the time to first on-study skeletal-related event in patients with multiple myeloma (HR=0.98, 95 percent CI: 0.85-1.14).

The median time to first on-study skeletal-related event was 22.8 months for XGEVA and 24.0 months for zoledronic acid. The safety profile was consistent with known adverse events of XGEVA.

XGEVA is the first fully human monoclonal antibody that binds to and neutralizes RANK ligand, a protein essential for the formation, function and survival of osteoclasts, thereby inhibiting osteoclast-mediated bone destruction.

On Jan. 5, FDA approved the supplemental Biologics License Application for XGEVA to expand the currently approved indication for the prevention of skeletal-related events in patients with bone metastases from solid tumors to include patients with multiple myeloma.

Additional regulatory applications for XGEVA for the prevention of skeletal-related events in patients with multiple myeloma are underway and have been submitted to health authorities worldwide.

The '482 study was an international, phase III, randomized, double-blind, multicenter trial of XGEVA compared with zoledronic acid in the prevention of skeletal-related events in adult patients with newly diagnosed multiple myeloma and bone disease.

In the study, a total of 1,718 patients (859 on each arm) were randomized to receive either subcutaneous XGEVA 120 mg and intravenous placebo every four weeks, or intravenous zoledronic acid 4 mg (adjusted for renal function at baseline) and subcutaneous placebo every four weeks, plus investigators' choice first-line antimyeloma therapy.

Skeletal surveys using conventional radiography were obtained every 12 to 24 weeks per protocol. The primary endpoint of the study was non-inferiority of XGEVA versus zoledronic acid with respect to time to first on-study skele-

tal-related event (pathologic fracture, radiation to bone, surgery to bone or spinal cord compression).

Secondary endpoints included superiority of XGEVA versus zoledronic acid with respect to time to first on-study skeletal-related event and first-and-subsequent on-study skeletal-related event and evaluation of overall survival.

Progression-free survival was a prespecified, exploratory endpoint and was not powered for statistical significance. The secondary endpoints, delaying time to first skeletal-related event and delaying time to first-and-subsequent skeletal-related events, did not demonstrate superiority.

Overall survival was comparable between XGEVA and zoledronic acid, with a hazard ratio of 0.90 (95 percent CI: 0.70, 1.16). Median progression-free survival was 46.1 months (95 percent CI: 34.3 months, not estimable, n=219) for XGEVA and 35.4 months (95 percent CI: 30.2 months, NE, n=260) for zoledronic acid.

The safety and tolerability of XGEVA were also compared with zoledronic acid. The safety profile was consistent with known adverse events of XGEVA. The most common adverse reactions (greater than or equal to 10 percent) were diarrhea, musculoskeletal pain, hypocalcaemia, and dyspnea.

NCI launches resource for specimens and data from clinical trials

NCI has launched a resource for cancer researchers interested in conducting studies using specimens and clinical data collected from cancer treatment trials in NCI's National Clinical Trials Network and former NCI Cooperative Group Program.

Known as NCTN Navigator, the resource includes information about specimens, such as tumor and blood samples, donated by patients in NCI-sponsored clinical trials. The clinical trials included in Navigator are published phase 3 studies that evaluated cancer treatments.

Investigators can use the NCTN Navigator website Exit Disclaimer to search the inventory for specimens with specific characteristics. Investigators who develop proposals and get approval can use the specimens, along with the trial participants' clinical information, in their research.

NCI has supported large cancer treatment trials for decades through what is now the NCTN. For many of the trials, donated specimens were collected and stored in NCI-funded specimen banks. The clinical data from the trials include detailed information about patient responses to treatments and their outcomes.

The NCTN Navigator inventory includes data from more than 80 trials, 50,000 patients, and 600,000 specimens.

Although the researchers who conducted these clinical trials have long been using the specimens and clinical data in studies, Navigator will now make the materials available to any investigators who submit research proposals that are approved by a scientific review board.

To ensure the optimal use of the resources in Navigator, the scientific review committee will consider the importance of a proposed project with the value of the specimens in mind.

In general, successful Navigator proposals will use the specimens and data to test a research question that builds on prior knowledge and has potential clinical implications, noted Mishkin. The specimens in Navigator will generally not be appropriate for studies that are more exploratory in nature, she added.

Before developing or submitting a research proposal to the Navigator program, investigators can perform searches on the program's website to ensure there are specimens and related data to meet their research needs.

If they would then like to move ahead, they can use the website to submit a proposal for how they would like to use the specimens.

There is no charge for the specimens or clinical data in Navigator, but investigators with approved proposals will be responsible for the costs associated with processing and delivering the specimens and clinical data.

Although Navigator currently includes only specimens and information from adults, specimens, and data from patients with pediatric cancers are expected to be added later this year.

Boehringer Ingelheim, OSE collaborate to develop checkpoint inhibitor

Boehringer Ingelheim and OSE Immunotherapeutics announced a worldwide collaboration and license agreement to jointly develop OSE-172, a SIRP-alpha antagonist targeting myeloid lineage cells.

SIRP-alpha is a receptor expressed by myeloid lineage cells such as dendritic cells, tumor-associated macrophages, and myeloid-derived suppressor cells. In targeting SIRP- alpha, OSE-172 prevents the ligand CD47 from binding to

and triggering the cellular inhibitory effects of SIRP-alpha.

OSE-172 has the potential to enhance anti-tumor immunity by improving T cell activity through enhancement of DC antigen presentation functionality, potentiating the phagocytic and inflammatory properties of macrophages in the tumor microenvironment and enabling differentiation of MDSCs to an effector state.

Boehringer Ingelheim has acquired the global rights to develop, register, and commercialize OSE-172, a monoclonal antibody targeting SIRP-alpha which is expressed in myeloid lineage cells, as part of their continued commitment to research and innovation in immuno-oncology.

Under the agreement, OSE Immunotherapeutics will receive a €15 million upfront payment from Boehringer Ingelheim, and potential additional short-term milestones of up to €15 million upon initiation of a phase 1 clinical study. OSE Immunotherapeutics stands to receive more than €1.1 billion upon reaching pre-specified development, commercialization and sales milestones, plus royalties on worldwide net sales.

Neoepitopes innovation (Tedopi) is in phase III in advanced lung cancers after checkpoint inhibitors failure (anti PD-1 and anti PD-L1). An option to license was exercised in July 2016 by Janssen Biotech to continue clinical development of FR104 (an anti CD28 mAb) in auto-immune diseases after positive phase I results.

A two-step license option was signed in 2017 with Servier Laboratories to develop OSE-127 (Effi-7) up to the completion of a phase 2 clinical trial planned in autoimmune bowel disease and Sjogren's syndrome.