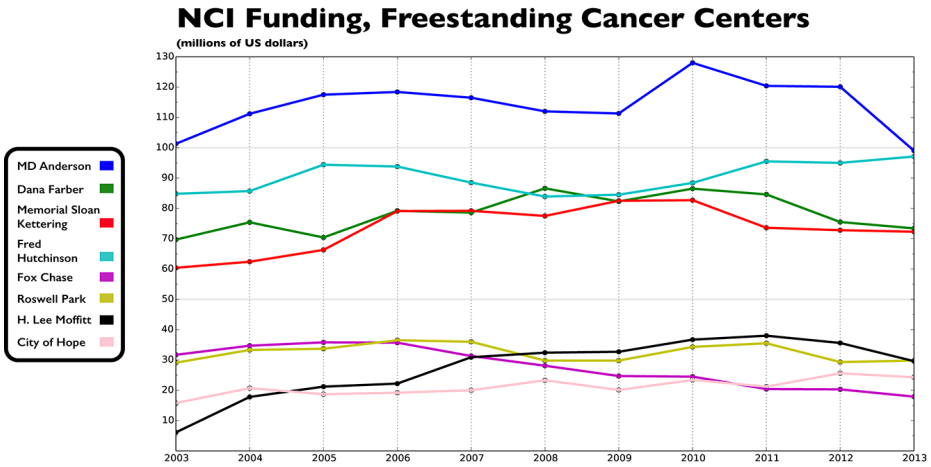
THE CANCER LETTER

Oct. 31, 2014 • www.cancerletter.com • Vol. 40 No. 41



How Elite Institutions were Affected By a Decade of Constricted Funding

By Will Craft and Matthew Ong

The ten-year period of erosion that followed the doubling of the NIH budget has hit some research institutions harder than others.

NIH appropriations figures provide a glimpse of the state of science funding in the U.S., but they don't shed light on how individual institutions and areas of research are affected.

To conduct an exploratory analysis of levels of funding at specific institutions, The Cancer Letter compiled NIH and NCI funding figures from 2003 to 2013 for eight freestanding cancer centers and nine other research institutions that include cancer centers. A focus on freestanding cancer centers provides a snapshot of funding at institutions engaged primarily in basic and clinical cancer research.

(Continued to page 2)

Guest Editorial

The Academic Difference: George Weiner On How America's Cancer Centers Are More Valuable Than Ever

By George J. Weiner

The nation's academic cancer centers are a national resource that will increase in value as remarkable changes continue in biomedical research, cancer care, and health policy.

(Continued to page 12)

In Brief

City of Hope Launches Blood Cancer Institute

CITY OF HOPE launched an institute focused on treating blood and bone marrow diseases: the **Hematologic Malignancies and Stem Cell Transplantation Institute**.

(Continued to page 16)

A Tough Decade: Tracing Funding at 17 Institutions

(Continued from page 1)

The other academic institutions that include cancer centers were chosen to illustrate NIH and NCI funding levels at institutions that focus on a broader range of research.

Relying on the NIH Research Portfolio Online Reporting Tools database, The Cancer Letter charted the impact of twin calamities that struck biomedical research: the end of the doubling of the NIH budget, which concluded in 2003, and the expiration of the American Recovery and Reinvestment Act in 2010.

A third misfortune—ongoing biomedical inflation, charted by the Biomedical Research and Development Price Index, or BRDPI—further reduced purchasing power by about 25 percent over a decade. These two graphs illustrate what NCI and NIH funding would be had their budgets kept pace with rising inflation.

The Cancer Letter looked at three data sets for each institution:

- NIH funding since 2003,
- NCI funding since 2003, and
- ARRA funding in 2009 and 2010.

The eight freestanding cancer centers are: MD Anderson Cancer Center, Dana Farber Cancer Institute, Memorial Sloan Kettering Cancer Center, Fred Hutchinson Cancer Center, Fox Chase Cancer Center, Roswell Park Cancer Center, H. Lee Moffitt Cancer Center, and City of Hope Cancer Center.

The Cancer Letter also focused on the following academic cancer centers that are components of larger institutions: Duke University, Stanford University, Johns Hopkins University, University of Pittsburgh, the Mayo Clinic, UT Southwestern, Ohio State University, the University of Southern California, and Baylor College of Medicine.

The data presented here are not adjusted for biomedical inflation.

Whether they are described as freestanding or as components of universities, many of these institutions are, in fact, consortia. Thus, "freestanding," a classification that has been around for decades, doesn't always constitute a meaningful category. Also, the manner in which data are submitted to the NIH Reporter may vary by institution and may not include other forms of funding, such as sub-contract arrangements.

With these caveats in mind, The Cancer Letter asked leaders of cancer centers, professional societies, and science advocacy organizations to comment on the data.

In this era of constricted funding, when the direct financial rewards of having an NCI designation have been declining, many institutions are nonetheless pursuing this mark of distinction, which gives them an advantage in fundraising, competition for healthcare dollars, and recruitment of researchers—particularly those who come with funded grants.

In an effort to distribute its funds more equitably, NCI has been redesigning the manner in which it sets the size of core grants, to eliminate the advantages of longevity in the centers program (The Cancer Letter, July 7, 2013; March 14, 2014; July 11, 2014).

The stakes are especially high because academic cancer centers are emerging as a conduit for adoption of precision medicine in oncology. A guest editorial on academic difference by George Weiner, director of the University of Iowa Holden Comprehensive Cancer Center and president of the Association of American Cancer Institutes, appears here.

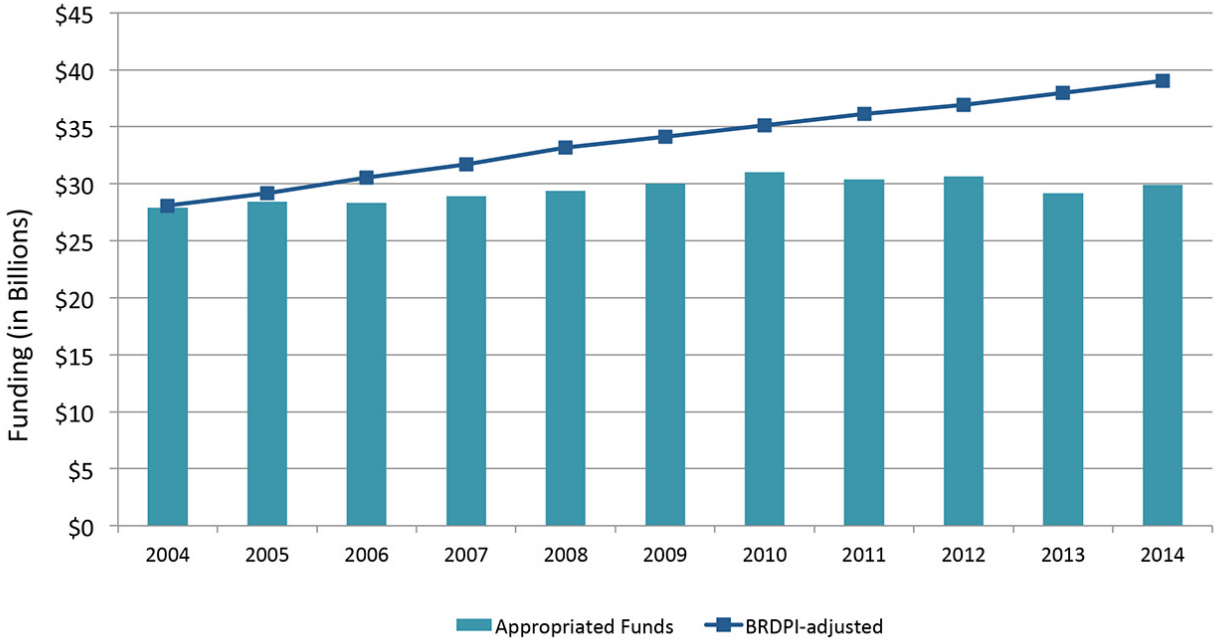
The graphs summarizing the state of NIH and NCI funding at selected institutions appear below. Corresponding tables can be found on The Cancer Letter website.

Editor & Publisher: Paul Goldberg
Associate Editor: Conor Hale
Reporter: Matthew Bin Han Ong

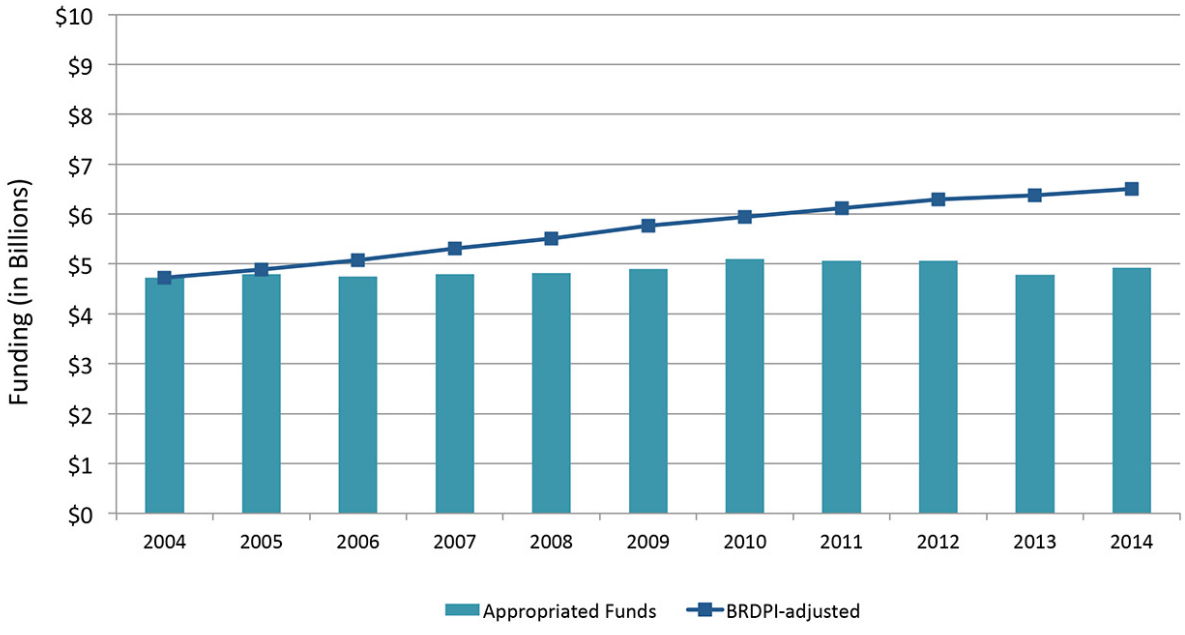
Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

The NIH Funding and Biomedical Inflation Discrepancy



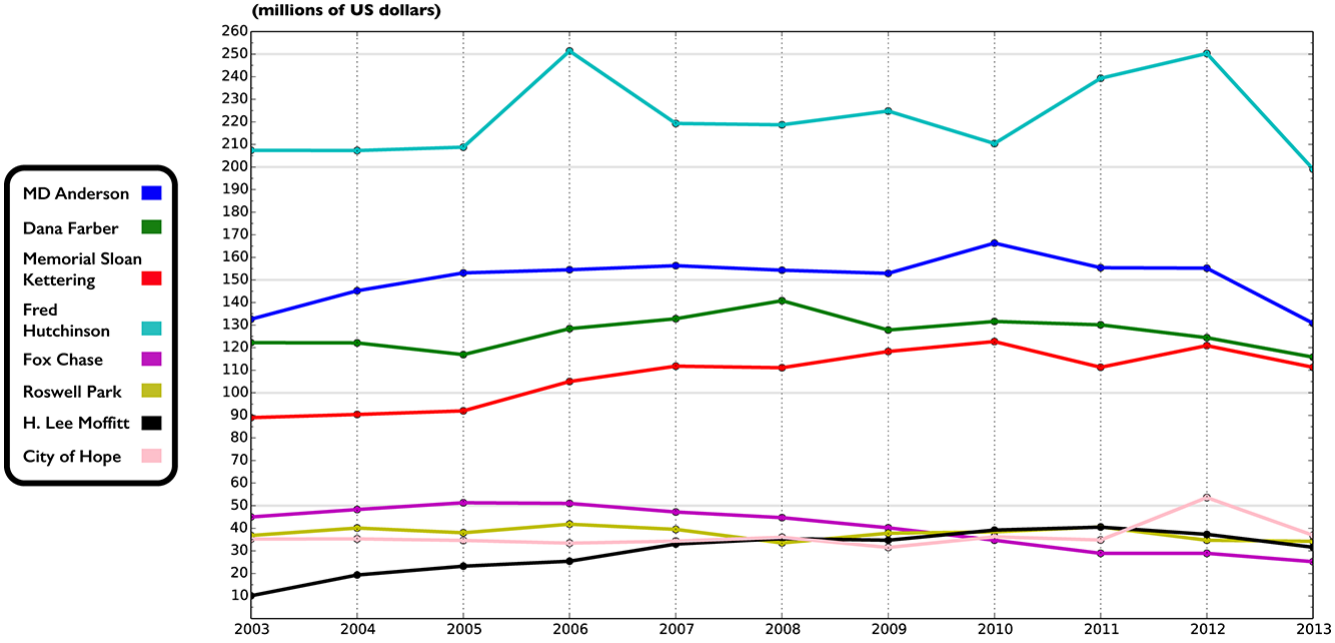
The NCI Funding and Biomedical Inflation Discrepancy



Source: AACR

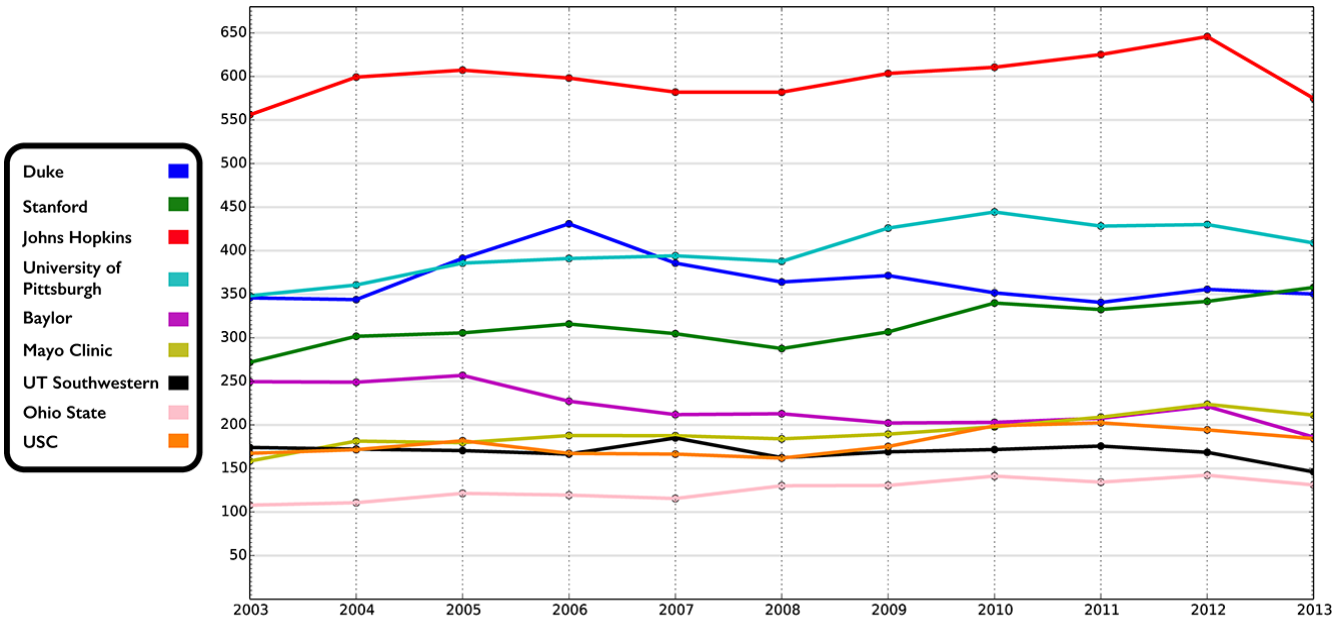
NIH Funding, Freestanding Cancer Centers

(millions of US dollars)

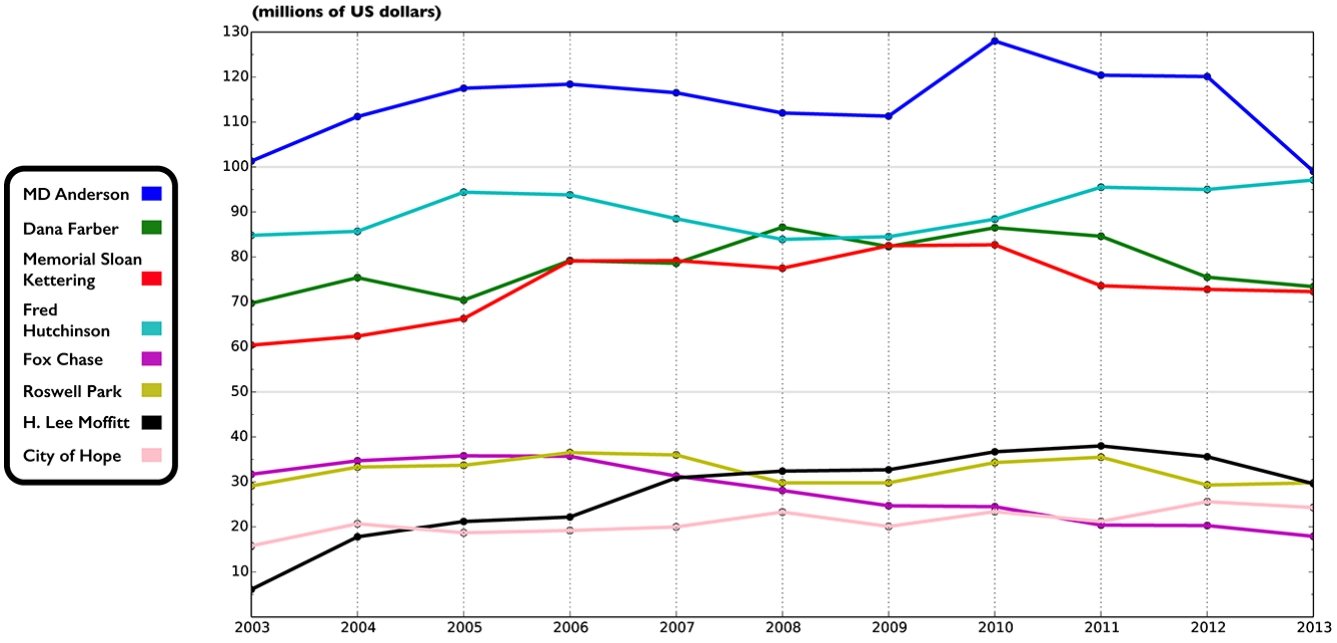


NIH Funding, Research Institutions with Cancer Centers

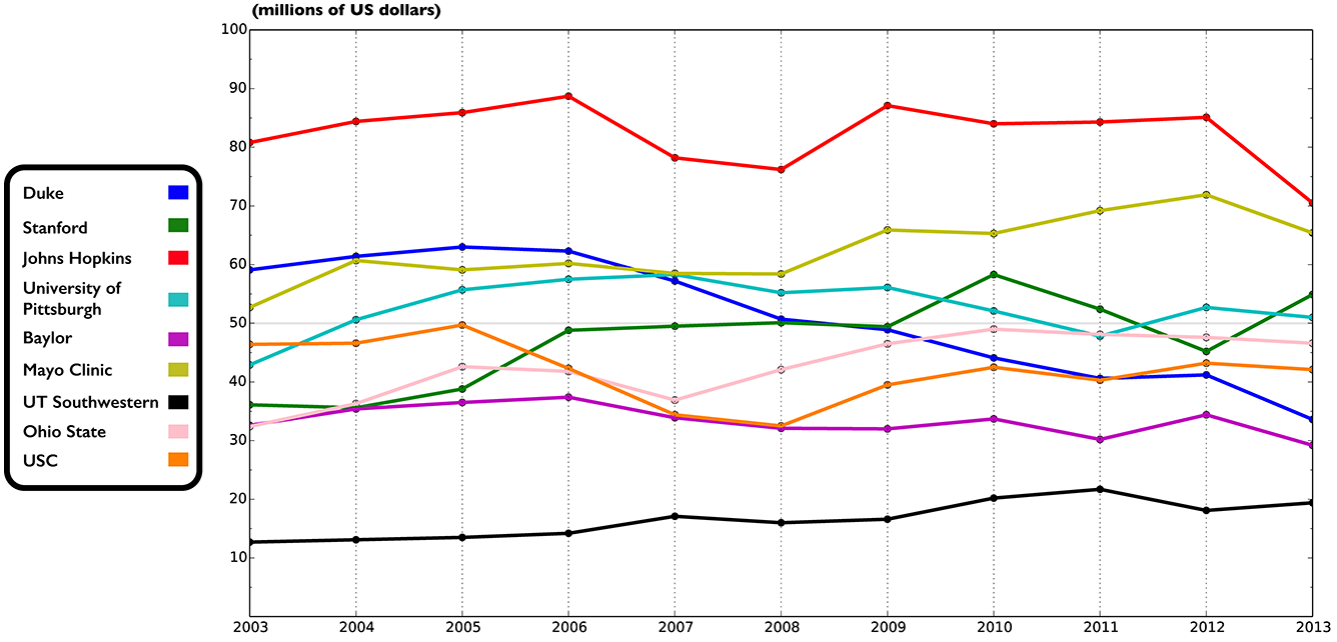
(millions of US dollars)



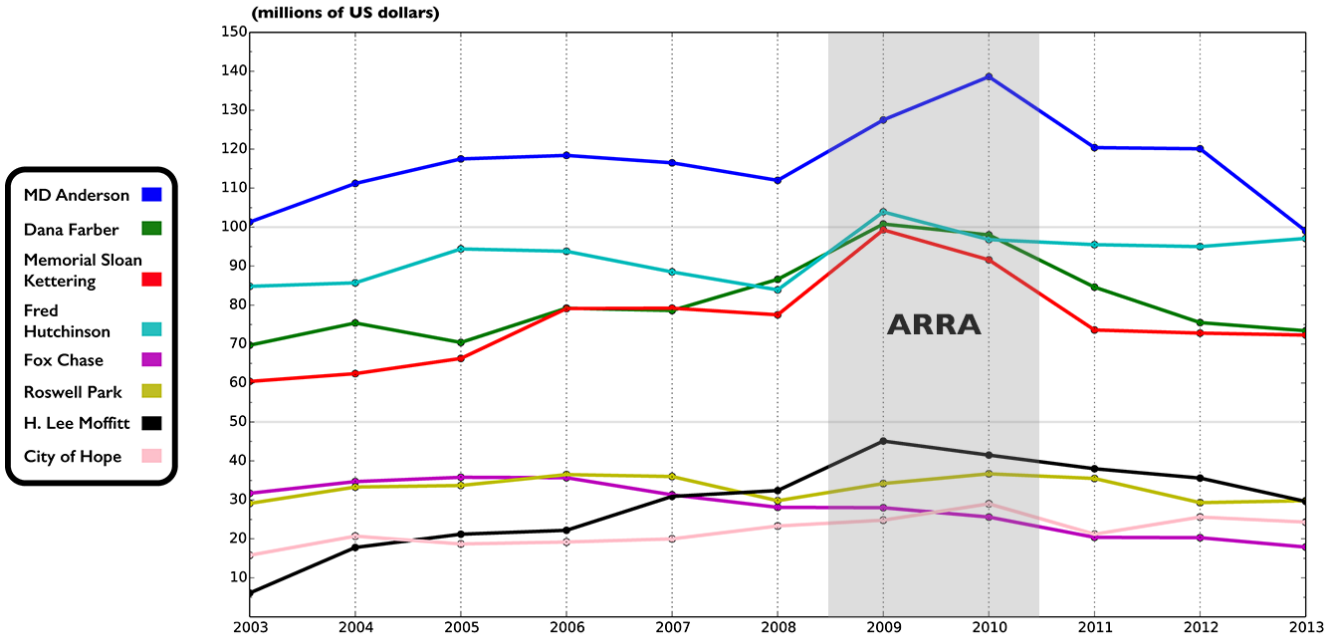
NCI Funding, Freestanding Cancer Centers



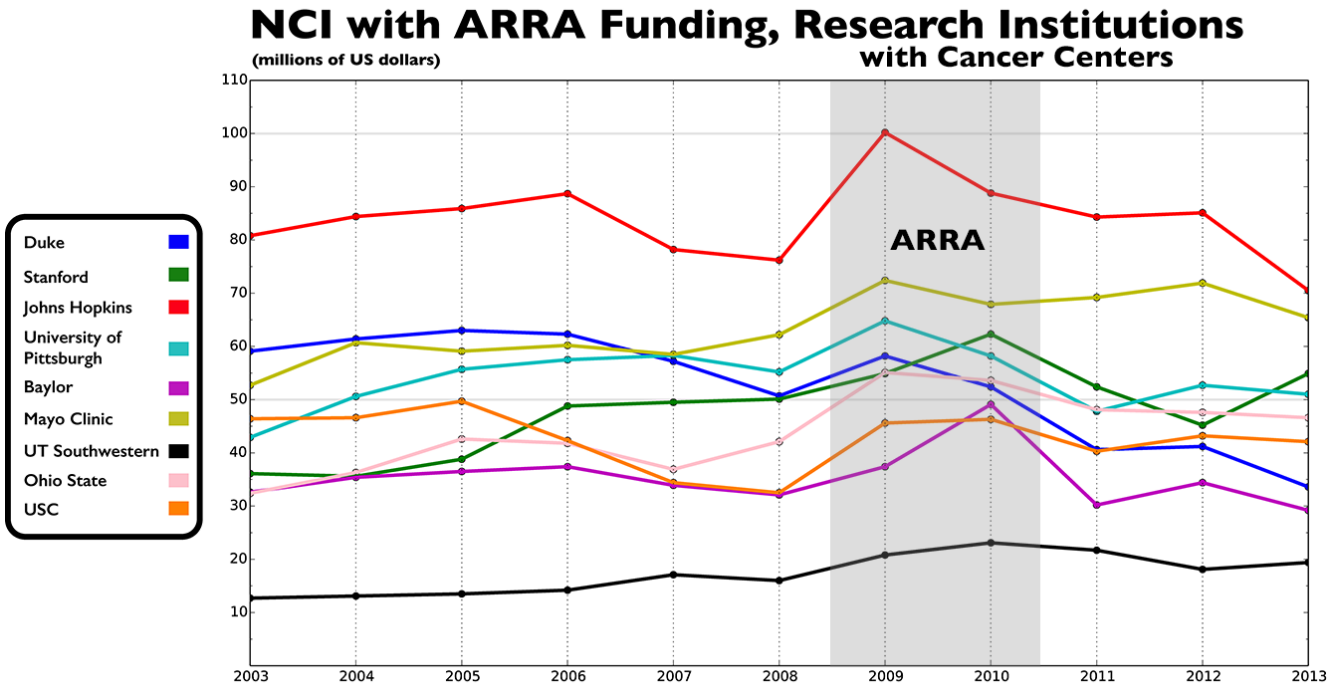
NCI Funding, Research Institutions with Cancer Centers



NCI Funding with ARRA, Freestanding Cancer Centers



NCI with ARRA Funding, Research Institutions with Cancer Centers



The Impact of Triple Calamities: Flat Funding, the End of ARRA, & a Loss of Purchasing Power

Reported by Matthew Bin Han Ong

The Cancer Letter asked leaders of cancer centers, professional societies, and science advocacy organizations to comment on declining levels of NIH and NCI funding at freestanding cancer centers and selected academic institutions that include cancer centers.

Their responses follow:

Kevin Cullen, director of the University of Maryland Marlene and Stewart Greenebaum Cancer Center

"I think the changes in funding you show here are very troubling and in some ways ominous. Many of the best cancer centers in the country have seen large decreases in their NIH and especially NCI funding in the last 5 years. Adjusted for inflation, the numbers are even worse.

"While the impact of these reductions at an individual center may be moderate or large, the impact across the totality of NCI designated cancer centers is huge.

"A tremendous and productive national cancer research infrastructure built up over the last 40 years is being eroded. Research that could contribute to new treatments and insights is lost. Clinical research and clinical trials are especially hard hit.

"Perhaps most worrisome of all, we are discouraging the next generation of investigators, especially physician scientists, from entering the field. I was one year out of training when I received my first major NCI grant. Now, we demand a junior faculty work until nearly the middle of his or her career before they can hope to get their first significant independent grant.

"The recent Ebola epidemic caught the international scientific community with its collective pants down because funding cuts, like you show here, prevented the work that would have averted the current crisis. These trends will mean the same for cancer."

Stephen Gruber, director of the USC Norris Comprehensive Cancer Center, professor of medicine at the Keck School of Medicine of the University of Southern California, and the H. Leslie Hoffman and Elaine S. Hoffman Chair in Cancer Research at Keck Medicine of USC

"These data tell an important story over the last decade, but what we are reading is actually a compilation of a lot of short stories. The most recent short story has a really bad ending.

"Our investigators are continually applying for grants, and we are fortunate that we have been able to sustain success despite decreased paylines and budgets.

"I remain very concerned about the downward trends that are particularly evident since sequestration."

Carlos Arteaga, president of the American Association for Cancer Research, professor of medicine and cancer biology, and associate director for clinical research at the Vanderbilt-Ingram Cancer Center of Vanderbilt University

"The charts that are included in this particular article are missing a key element, specifically that the budget numbers are not adjusted for inflation over the last ten years.

"By doing so, the charts would depict an even much more concerning and sobering picture because of the additional 22 percent decline in the budgets (when adjusting for inflation) that have occurred over the past decade for both NIH and NCI, as well as the institutions and cancer centers that are highlighted in the article.

"This important article underscores the importance of predictable and sustained budget increases for medical research, as this current long-term, significant reduction in funding for medical research is jeopardizing our ability to make critical advances against cancer and impeding long-term planning by the NCI and its parent agency, the NIH, as well as the scientists at the institutions and cancer centers that are supported by these two vital funding organizations."

"In fact, this is a time for our nation's policymakers to be prioritizing investments in medical research, as opposed to overseeing medical research budgets that are continually falling behind, which is resulting in missed scientific opportunities that ultimately may benefit patients.

"In light of this discouraging funding environment, it's also important to consider the fact that cancer is a growing health care challenge: 585,720 U.S. residents

are projected to die from some form of cancer in 2014, and this number is predicted to steadily increase in the coming decades without new preventive interventions and treatments."

"As the founding organizer for the past three Rally for Medical Research-related events, including the most recent Rally for Medical Research Hill Day on Sept. 18, the AACR is significantly focused on making a difference in the overall NIH and NCI funding situation.

"Therefore, we were just overjoyed with the enthusiastic response and participation from the 300 organizations that are joining together to call on our nation's policymakers to make funding for the NIH a national priority and raise awareness about the importance of continued investment in medical research."

Nancy Davidson, director of the University of Pittsburgh Cancer Institute and UPMC Cancer Center, associate vice chancellor for cancer research, Hillman Professor of Oncology, and Distinguished Professor of Medicine and Pharmacology and Chemical Biology at the University of Pittsburgh

"We think these statistics confirm the work that we've put in over the last several years to really grow our research at the university and also specifically at the cancer institute, and this reflects the amazing recruitment that we've done and the growth in our research, especially our clinical and translational research.

"A really important point is, we at the University of Pittsburgh are getting a bigger fraction of the pie, if you will—but there is a question that the pie is not big enough for anybody.

"The real cost of research has gone up considerably, and the fact that the NIH budget has definitely not kept up with it, and not only has it not kept up with it, but we have seen a substantial loss because of biomedical inflation. You know, we are 20 percent down from what we would be if we didn't have that inflation. I agree with you that there is a big mismatch between what we need, and where it can make a bigger difference in cancer, and what we are being provided. And that is true for our cancer institute, and every other cancer institute."

"For our cancer institute, we think that this data reflects what we have been trying to do, which has been to grow our cancer enterprise, to be more competitive, to do what we need to do to garner the resources to try to do the best possible research, and ultimately to try and provide the best possible cancer care. So, for use, this reflects our reality: we have been growing and building for the last ten years and our funding reflects that."

"So, good news from our perspective. We are a matrix cancer center and we're excited that our funding is going up because it reflects our hard work, and the excellence of our faculty."

William Nelson, director of the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

"Overall cancer death rates throughout the nation are trending downward thanks in large part to state and federal programs aimed at research, screening and treatment.

"Cancer medicine is transforming from a model of treating disease only when patients experience multiple symptoms and often have widespread disease to one that detects, manages, and many times eradicates cancers well before their deadly stage.

"This change is being driven by pioneering discoveries in cancer genetics and epigenetics, funded largely by federal sources. We have the opportunity to build on our scientific successes and improve the way we preserve health by preventing cancers, very accurately predicting who will get them, and personalizing treatments to each individual patient, making sure he or she gets the treatments that will work against the unique cellular characteristics of the cancer.

"Our ability to continue these successful trends is tied directly to philanthropic, industry and federal funding of cancer research.

"From FY07 to FY13, our cancer center's government funding decreased 17.6 percent while industry funding increased 142.4 percent and foundation/other funding is up 82.6 percent. Our overall funding is up 15.3 percent over that period, but down 4.6 percent from our peak in FY10.

"Many cancer centers' funding has been reduced or flattened to levels not seen in more than a decade, due in part to an absolute 5 percent cut in funding to the NIH because of sequestration. Many research institutions experienced sequestration-related cuts double that amount.

"Cancer research funding is limited and very competitive. The federal commitment to cancer research is not adequate enough to keep up with scientific opportunity. We are fortunate at the Johns Hopkins Kimmel Cancer Center to have talented faculty who compete well among federal research grants. However,

limited funding that is affected by economic and governmental changes discourages investigators from pursuing novel and challenging ideas.

"Funding cancer and other types of biomedical research goes far beyond our potential to eradicate disease. Many of our cancer centers and research institutions are leading employers in our states. We help young scientists establish careers and compete for larger, national grants.

"These funded investigators hire technicians, administrative and clerical staff. They purchase equipment and service from local and national businesses, invent new products, and start new companies. Moreover, the jobs created are ones that spark opportunity, are secure, and provide health insurance, education, and retirement benefits.

"The return on investment, in the form of salaries from job creation and tax revenue, far exceeds the nation's original investment.

"We hope the current trends in federal funding of cancer research are reversed. Congress should complete the FY2015 appropriations bills and, at a minimum, restore funds lost to sequestration. We have millions of cancer patients and survivors depending on it."

Steven Patierno, deputy director of the Duke Cancer Institute and professor of medicine, pharmacology and cancer biology at Duke University School of Medicine

"On the surface, these data suggest that most large, research-intensive cancer centers, whether freestanding or matrix centers, have either lost some fraction of their NCI funding, or remained relatively stable since 2003.

"The most disturbing trend evident from these data is the consistent decrease in NCI funding since 2011 at nearly all cancer centers.

"What is not evident from these data is the dramatic loss in purchasing power of each awarded research grant since 2003, which compromises scientific productivity of each grant period.

"The marked increased difficulty in obtaining individual investigator grants is resulting in increased attrition of experienced investigators, fewer first-time investigators, and potential loss of the next generation of cancer researchers.

Follow us on Twitter: @TheCancerLetter

Thomas Sellers, director of the H. Lee Moffitt Cancer Center, and Brian Springer, vice president of research administration

"These data underscore the reality that cancer funding, adjusted for inflation, is the same today as it was a decade ago. We are losing ground at a time when the opportunities for progress are greater than ever, and this weakens our ability to bring scientific findings to patient care.

"We must increasingly utilize other non-traditional sources of funding to make up for this, which can further complicate our research and require more sophisticated models for intellectual property and conflict-of-interest.

"Free-standing cancer centers can be more susceptible than matrix centers to funding swings, because of a (usually) more limited number of faculty, and less opportunity to spread revenues and indirect costs across a smaller, focused line of business. The end of ARRA funding affected all cancer centers.

"Since the support from the government doesn't seem to be changing soon, all of us are being forced to explore alternative sources of revenue to secure the funds that are critical to the prevention and cure of cancer, requiring more sophisticated models for intellectual property and conflict-of-interest."

Steven Rosen, provost and chief scientific officer of City of Hope

"The key ingredient and the reason that City of Hope has been successful—and we anticipate will be more successful going forward—is because it's mission driven, which is obviously very important.

"It is a modest institution in comparison to some larger medical centers: we have about 100 laboratory-based scientists. In general, they are very productive and a significant majority of them are cancer-focused.

"At the present time, we are blessed with significant revenues from philanthropy and royalties that are allowing us to expand the research base that we'll have on campus, and recruit additional investigators. And so I think we have a very bright future ahead of us.

"Most of our research is NCI-directed. The state of our funding is positive, considering the environment, and it's allowed us to maintain incredible stability.

"The philanthropy and royalties has created a sound foundation and we'll be able to expand the

number of investigators being recruited and attract top talent. I'm anticipating that the next decade will actually be even more productive.

"We're one of few places that have the resources to expand dramatically."

Kent Osborne, director of the Dan L. Duncan Center at Baylor College of Medicine

"NIH funding for cancer research has gone down significantly over the past decade, and this is certainly affecting our ability to advance some of the most exciting discoveries to improve outcome of patients as quickly as possible."

Aman Buzdar, vice president of clinical research at the University of Texas MD Anderson Cancer Center

"The flat NCI budget is not very conducive for researchers to carry out innovative research—it is causing challenges for investigators trying to discover potential treatments that could be tested subsequently.

"I think resources have been constrained for the past few years. It is kind of disheartening for investigators everywhere, including institutions like MD Anderson.

"It affects all of us the same way. MD Anderson doesn't have any special privileges—we are measured against the same yardstick like everyone else. All the investigators do.

"NCI funding has also not increased because of inflation. If you look at it realistically, even at the lowest inflation rates, it is just staying flat. You are losing 1 or 2 or 3 percent, depending on how much the inflation is each year. Essentially, if you look at it realistically, we are losing the resources that are available to the institutions and investigators each year by the increasing degree of inflation.

"If the NCI budget continues to remain flat, it means we are losing ground."

Richard Schilsky, chief medical officer of the American Society for Clinical Oncology

"Federal funding for cancer research has steadily eroded over the past decade and threatens to stall the major progress that has been achieved in recent years.

"NCI plays a vital role in all federally funded cancer research and supports research projects conducted by universities and cancer centers across the United States and in other countries.

"These institutions provide the intellectual core of our nation's research efforts to better understand cancer and to transform that understanding into better treatments for people with cancer.

"To ensure these institutions have the means to support high-quality cancer research projects requires that the federal government take bold action to improve funding for the core infrastructure and innovative research conducted at our nation's cancer centers and universities.

"ASCO will continue to call on Congress to provide a sustained investment in federal research and ensure our current pace of progress continues to accelerate."

Howard Garrison, deputy executive director for policy and director of public affairs at the Federation of American Societies for Experimental Biology

"While there are some annual fluctuations, particularly at the smaller institutions, the most striking pattern is the overall lack of growth. When these budgets are adjusted for rising costs, they reflect a cut nearly 25 percent. This is part of an unprecedented reduction in research capacity that will haunt us for years."

Mary Woolley, president and CEO of Research!America

"While research has helped reduce new cancer cases and annual cancer deaths over the last decade, more than 1.6 million Americans are newly diagnosed and we lose nearly 600,000 Americans to cancer each year.

"Those numbers alone call for a greater commitment to research, but here are more: The most recent estimates by the National Cancer Institute place the annual cost of cancer at $216.6 billion. Annual funding for the National Cancer Institute has hovered at about $4.9 billion over the last several years.

"So we're spending hundreds of billions on care and productivity losses each year, and a few billion a year to wrestle those costs down. That disconnect is emblematic of the broader issue: the power of research to save lives and tax dollars justifies far higher levels of investment than our nation is making.

"It's a strategic error, and now is the time to correct it. The downward trajectory of research funding is a sad state of affairs particularly for patients struggling to beat the odds and improve their quality of life."

Carrie Wolinetz, president of United for Medical Research and deputy vice president for federal relations at the Association of American Universities

"Generally speaking, I see a fair amount of steady support over time. Obviously, if you adjust for biomedical inflation, that steady support ends up being a downturn. But the steady state indicates a couple of things:

"One, continued interest in solving the incredibly complex problem that is cancer and its many different diseases. Given that the data starts at the tail end of the doubling of the NIH budget, the fact that interest hasn't declined since the doubling is good news.

"Two, the support also probably speaks very well to the exciting state of science. In the last decade, competition has gotten so fierce in the research community in general. The fact that we're seeing steady, and in some institutions, an uptick, really speaks to where we are in science.

"If you're looking at the steady state of funding, it doesn't seem to be—I hate to say falling off in popularity—a reduced portion of the NIH portfolio, for sure.

"As I keep factoring in inflation, the figures are showing a lack of growth—somewhat reflective of the overall lack of agency growth, but also not a sharp decline either."

Guest Editorial

George Weiner on Cancer Centers And "The Academic Difference"

(Continued from page 1)

Research advances stemming from academic cancer centers have had an immense impact on the care of patients with cancer. Breakthroughs including development of signal transduction inhibitors such as imatinib, monoclonal antibodies such as rituximab, stem cell transplantation and newer advances such as checkpoint blockade and chimeric antigen receptor T cells, would never have happened without research conducted at academic cancer centers. The same is true for advances in cancer prevention and early detection. Untold numbers of individuals in the U.S. and beyond have benefited from these advances.

Research conducted at academic centers has been at the center of the realization that cancer is much more complex at the molecular level than previously imagined. Cancers that we previously considered "common" can now be classified based on their molecular makeup, and increasingly are viewed and treated as distinct entities.

Thus, essentially all cancers are proving to be rare cancers. This complexity is already resulting in new treatment paradigms for a variety of cancers even though we are just at the dawn of this revolution, all made possible in large part by our academic cancer centers. Our ability to probe, understand and leverage this complexity to help individual cancer patients is progressing at an unprecedented rate, in large part because of the ability of

academic cancer centers to integrate their major missions of research, clinical care and education.

With this rapid evolution and ever-increasing enhanced understanding of the complexity of the many diseases known as cancer, it is difficult for even the most outstanding general oncologist to keep up. Academic cancer centers are well positioned to collaborate with general oncologists to minimize the gap between state-of-the-art therapy based on this new knowledge, and the actual care provided to patients. Academic cancer centers are home to multidisciplinary teams of clinicians and investigators with expertise in specific cancer types.

These teams are often involved in generating the scientific and clinical advances. They are able to keep up with rapidly changing and complex factors, including molecular analysis, that increasingly affect the provision of optimal patient care. Providing the highest quality, affordable cancer care based on state-of-the-art science will require close collaboration between academic, multidisciplinary teams of experts and community oncologists. Only through such collaborations can we assure the most effective treatments are selected and provided to patients as efficiently and conveniently as possible.

While some patients will require specialized care that can only be delivered in the academic setting, many others will be able to receive their care closer to home. In the area of research, the pharmaceutical industry is increasingly relying on discoveries made in academia. The highly collaborative and interdisciplinary nature of academic cancer centers, as well as the access they afford to patient samples and patient data, serves as an incubator for ideas that provide great value to the pharmaceutical and biotech industries. These commercial entities are also dependent on academic cancer centers to train laboratory and clinical investigators who chose industry as a career path. The cancer centers provide a skilled pool of clinicians who are in short supply across the country, at a time when cancer is becoming more common in our aging population.

Academic cancer centers have an outsized positive economic impact on both their local communities and the nation. Each research laboratory is the equivalent of a small business providing jobs for highly skilled employees. The ideas and discoveries generated by academic cancer centers have played a central role in the development of the biotech industry, which in turn has been a leading economic engine for the U.S. and a key to country's competitive edge internationally.

The current inflationary rate of health care expenditures cannot be sustained. Cancer care is responsible for a significant fraction of this inflation. Academic cancer centers are vital if we are to respond effectively to this challenge as well. They conduct health services research and are central to development and implementation of guidelines and pathways that will be increasingly important as both academic and community oncologists seek to provide evidence-based, optimal patient care while not bankrupting the nation.

Those of us who work in academic cancer centers and have the privilege of participating in this incredible era of advancement know that the statements made above concerning the role of academic cancer centers are true. However, as believers in data-driven decision-making, we know that simply making that statement is not enough. We need to back it up with evidence.

With this in mind, the Association of American Cancer Institutes (AACI) has begun an initiative to gather information on the value of academic cancer centers with respect to clinical care, research, education and economic impact. We will use various platforms to share this information with various audiences including the general public, leadership at academic institutions, payers, corporations, chambers of commerce and government officials at the federal, state, and local levels. The goal of the initiative is to gather and distribute data that highlights the unique and indispensable role played by academic cancer centers and why these efforts should be supported.

Academic cancer centers are an incredible success story. They leverage their three mutually supportive missions of research, clinical care and education to create knowledge, provide complex cancer care, serve as a resource for community oncologists and educate the next generation of investigators and clinicians all while having a positive effect on the economy. They must continue to be supported based on their unique ability to play a leading role in leveraging the remarkable scientific opportunity before us to reduce the pain and suffering caused by cancer. The AACI "Academic Difference" initiative is designed to help us do a better job of explaining why.

The author is director of the University of Iowa Holden Comprehensive Cancer Center.

He became president of the Association of American Cancer Institutes Oct. 26, during the association's annual meeting in Chicago, where he delivered a talk about his presidential initiative, "The Academic Difference."

Bennett, Federal Prosecutors Reach $475,000 Settlement

By Paul Goldberg

Charles Bennett, an oncologist and cancer researcher whose work focuses on adverse events caused by pharmaceutical products, settled a federal complaint brought by a whistleblower alleging irregularities in the management of R01 research grants administered by Northwestern University.

Northwestern paid $2.93 million in 2013 to settle allegations of mismanaging five of Bennett's R01 grants.

In an agreement made public Oct. 30, the government said it would dismiss its suit, filed under the False Claims Act, in exchange for a payment of $475,000 by Bennett. The deal, which was based on analysis of Bennett's finances, allowed the parties to "avoid the delay, uncertainty, inconvenience, and expense of protracted litigation," court documents state.

However, the announcement also included some parting shots: "Dr. Bennett expressly denies the allegations of the United States."

Countering, the government "contends that it has certain civil claims against Dr. Bennett arising out of his improper submission of claims to Northwestern University for grant expenditures for: professional and consulting services, airfare and other transportation, conference registration fees, food, hotel, travel, meals, and other expenditures for items that were for the personal benefit of Dr. Bennett, his friends, and his family that were incurred in connection with certain grants as to which Dr. Bennett was a PI."

The settlement agreement and the complaint are available on The Cancer Letter website.

Bennett made important contributions to describing adverse events associated with erythropoiesis-stimulating agents (The Cancer Letter, June 1, 2007; June 8, 2007; Feb. 29, 2008; March 21, 2008; Aug. 8, 2008; Oct. 3, 2008).

Bennett's R01-funded research has resulted in multiple "Black Box" warnings from FDA. His supporters say his research has saved billions of dollars in expenditures by government agencies and private health insurers as well as thousands of lives, while making powerful enemies in the pharmaceutical industry. He continues to be supported with funding from NIH and has authored over 350 publications, many in top-tier medical journals.

Through much of his career, Bennett was on the faculty of Northwestern University's Robert H. Lurie Comprehensive Center for Cancer.

A temporary employee hired by the Northwestern University Faculty Foundation in 2008 filed a whistleblower lawsuit claiming that he had improperly submitted reimbursement requests to Northwestern University for activities related to his NIH and NCI grants. In 2010, Bennett accepted an offer to be one of 47 SmartState endowed professors in South Carolina. He leads the only state-funded pharmaceutical safety program in the nation.

The Two Settlements

The government's suit against Northwestern was unsealed last year, in conjunction with the university's agreement to refund money to the federal government (The Cancer Letter, Aug. 9, 2013).

Northwestern's settlement, which similarly didn't acknowledge wrongdoing, left Bennett open to civil actions by the U.S. Department of Justice. Now, these actions have concluded, but Bennett may still be open to administrative sanctions.

"The settlement with the government is similar to the settlement agreement of Northwestern submitted on July 30, 2013, i.e. it contains an explicit denial by Dr. Bennett of the government's allegations," Bennett's attorney James McGurk said to The Cancer Letter.

"The settlement was entered into by Dr. Bennett to avoid the expense and the drain of a trial," McGurk said. "The grants which are the subject of the government's complaint are, in some cases, 11 years old.

"Dr. Bennett has continued his work including recent significant publications in the New England Journal of Medicine on May 22 and a publication last week in the Journal of Clinical Oncology on Oct. 20.

"Dr. Bennett continues his work at the University of South Carolina," McGurk said. "There has never been any suggestion that Dr. Bennett's very significant scientific work was flawed or unsound in any way."

Bennett's supporters say that his work is first-rate.

"Charlie was a pioneer in tracing adverse drug reactions," said Steven Rosen, former director of Northwestern's cancer center who is now the provost, chief scientific officer and director of the cancer center at City of Hope. "His work had a profound effect on American medicine and lives were saved."

At Northwestern, Bennett founded the Research on Adverse Drug Events and Reports (RADAR) project and, subsequently, at the University of South Carolina, he founded the Southern Network on Adverse Reactions (SONAR).

The two programs review physician queries,

published and unpublished clinical trials, case reports, FDA databases and manufacturer sales figures to identify serious adverse drug and device reactions. According to a recent paper these programs have reported 50 serious ADRs. Data sources include case reports, registries, referral centers, and patients. SONAR, which is funded by NCI, has identified 20 ADRs.

The two programs flagged ticlopidine- and clopidogrel-associated thrombotic thrombocytopenic purpura, rituximab- and brentuximab vedotin-associated progressive multifocal leucoencephalopathy, erythropoietin- and darbepoetin-associated venous thromboembolism and mortality, erythropoietin-associated pure red cell aplasia, and thalidomide- and lenalidomide-associated venous thromboembolism.

Bennett was the first academic to jointly file a petition to the FDA with a state attorney general—Richard Blumenthal, who was then attorney general of Connecticut—requesting that a Black Box warning be added to the package label of a drug. This petition was granted in 2006.

The allegations against Bennett were made in a civil lawsuit filed under seal in 2009 by Melissa Theis, who came to Northwestern in 2007 and later became a purchasing coordinator for the Division of Hematology and Oncology at Northwestern's Feinberg School of Medicine. She left the university in 2008.

The division, which is separate from the cancer center, administered all but one of the grants in question, the NIH database shows.

In actions of this sort, the individual plaintiff, called "relator," is usually an insider who has worked for several years at a company and brings forward information the government couldn't otherwise obtain. The relator is rewarded with a portion of recovered funds. Theis collected $498,100 from Northwestern's settlement with the government and will collect $80,750 from Bennett's.

The suit remained under seal until July 30, 2013, when it was released in conjunction with the memorandum of settlement between the prosecutors and Northwestern.

When the action and the settlement deal in the case against Northwestern were unsealed, documents showed that the relator also made allegations against then-center director Rosen. However, the final settlement document contains no allegations against Rosen.

Sources close to Rosen said that until the settlement he was unaware of having been a defendant in the sealed federal lawsuit.

Days before the settlement with Northwestern was announced, a former research administrator at the Division of Hematology and Oncology at the university's medical school pled guilty to felony charges stemming from administration of Bennett's NCI grants.

According to documents filed in the U.S. District Court for the Northern District of Illinois, Feyifunmi Sangoleye, the administrator for Bennett's grants, set up an elaborate scheme to divert $86,000 to her personal accounts. The proceeds financed a wedding and a honeymoon in Europe, court documents say.

Legal experts said to The Cancer Letter that the final plea agreement between Sangoleye and the government would have weakened Northwestern's position in negotiating the settlement. The final version of the plea agreement with Sangoleye was filed on July 25, 2013, five days prior to the announcement of the government's settlement with Northwestern.

In 2005, Northwestern paid $5.75 million to settle similar allegations of grant mismanagement of NIH-funded projects, including one grant supporting the Pediatric Oncology Group.

Drugs and Targets

Lymphoseek Label Expanded To Include Mapping Solid Tumors

FDA approved the expanded use of Lymphoseek (technetium Tc 99m tilmanocept) injection for lymphatic mapping in solid tumors, and adding sentinel lymph node detection for breast cancer and melanoma to the approved indications.

The FDA also allowed expanded utilization of Lymphoseek with or without scintigraphic imaging, known as lymphoscintigraphy, to enable pre-operative imaging and mapping of lymph nodes to facilitate node localization during surgical procedures. Lymphoseek is developed by Navidea Biopharmaceuticals Inc.

Lymphoseek is the first and only FDA-approved radiopharmaceutical agent for sentinel lymph node detection, is the only FDA-approved agent for lymphatic mapping of solid tumors, and will be immediately available using existing reimbursement codes for this expanded population of cancer patients.

The expanded approval is supported by data from Navidea's combined analysis of Lymphoseek's prospective phase III data in melanoma, breast cancer, and certain head and neck cancers from more than 500 subjects. Findings indicated that Lymphoseek accurately identified lymph nodes for assessment in the trial subjects, and is likely to be predictive of overall node pathology status.

THE CENTERS FOR MEDICARE AND MEDICAID SERVICES published a draft local coverage determination for the **Decipher Prostate Cancer Classifier** developed by GenomeDx Biosciences. The determination describes coverage and payment policy for use of the Decipher test in men who have undergone radical prostatectomy.

Under Medicare policies, a 45-day comment period will commence on Nov. 10. After comments are received and revisions, if any, are made to the draft LCD, the final LCD will be posted within 45 calendar days.

Palmetto GBA, a national contractor that administers Medicare benefits, has issued the draft LCD through the MolDX Program for Decipher. MolDX, developed in 2011, facilitates the clinical review, coverage and payment policies for molecular diagnostic tests. The MolDX Program is a contractor to Noridian, a national contractor that administers Medicare benefits for Jurisdiction E, where GenomeDx is located.

Decipher is a unique genomic test intended for men who have had prostate surgery and are considered by guidelines to be at high-risk for their cancer returning. These are men who have specific risk factors for cancer recurrence, including positive surgical margins, stage T3 disease (seminal vesicle invasion, extraprostatic extension, bladder neck invasion) or rising PSA after initial PSA nadir.

THE NATIONAL COMPREHENSIVE CANCER NETWORK approved the **VeriStrat predictive proteomics test** for inclusion in its Clinical Practice Guidelines in Oncology for Non-Small Cell Lung Cancer. The test is developed by Biodesix Inc.

The updated guidelines recommend clinicians' use of VeriStrat, a blood-based protein profiling test, to help determine whether patients entering the second line of treatment for NSCLC should be considered as candidates to receive the targeted drug erlotinib (Tarceva).

The guidelines state: "Recommended proteomic testing for patients with NSCLC and wild-type EGFR or with unknown EGFR status. A patient with a 'poor' classification should not be offered erlotinib in the second-line setting." Erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor therapy, is commonly used in NSCLC patients who harbor an activating EGFR mutation.

An independent phase III clinical trial (PROSE) for VeriStrat confirmed the test's results are prognostic and specifically predictive of differential overall survival benefit for erlotinib versus chemotherapy in the second-line setting. Successful trial results were recently published in The Lancet Oncology.

MYRIAD GENETICS INC. established a **Tumor BRACAnalysis CDx** laboratory in Munich.

The test is a companion diagnostic used to identify patients with BRAC mutations who may benefit from treatment with PARP inhibitors, such as olaparib, a novel PARP inhibitor being developed by AstraZeneca.

The European Medicines Agency's Committee for Medicinal Products for Human Use recently recommended marketing authorization for olaparib as monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

UNIVERSITY HOSPITALS Case Medical Center and **UH Seidman Cancer Center** selected GO Clinical Workbench developed by **GenomOncology** for workflow management of next generation sequencing data.

The platform allows molecular pathology laboratories to produce an actionable clinical report using the molecular profile of an individual patient's tumor.

QIAGEN N.V. and **Astellas Pharma Inc**. will collaborate to develop and commercialize companion diagnostics paired with Astellas drugs for use in cancer and other diseases.

Two initial projects in the collaboration focus on oncology and aim to pair Qiagen diagnostics with Astellas compounds in early-stage clinical trials: ASP5878, a fibroblast growth factor receptor inhibitor, and ASP8273, an EGFR inhibitor. Financial terms were not disclosed.

The scope of the agreement is not restricted to certain sample types, platforms, indications or biomarkers, giving Astellas access to Qiagen's assays based on PCR, next generation sequencing and multi-modal testing technologies using liquid and tissue biopsies.

In Brief

City of Hope Launches Blood Research Institute

(Continued from page 1)

The institute will be composed of six centers, individually focused on research in lymphoma, myeloma, leukemia, T cell immunotherapy, stem cell transplantation, and gene therapy. These include the Toni Stephenson Lymphoma Center and the Gehr Family Center for Leukemia Research.

The institute has recruited several prominent researchers, including **Larry Kwak**, chairman of the Department of Lymphoma/Myeloma at MD Anderson Cancer Center and associate director of its Center for Cancer Immunology Research; **Jasmine Zain**, associate director for the Bone Marrow Transplantation Program at the College of Physicians and Surgeons at the New York Presbyterian Hospital and Herbert Irving Comprehensive Cancer Center at Columbia University; **John Chan**, co-director of the Center for Leukemia and Lymphoma Research and co-leader of the Lymphoma Research Program at the University of Nebraska; **Guido Marcucci**, professor of internal medicine and molecular virology, immunology and medical genetics, and pharmaceutics in the Division of Hematology at Ohio State University Comprehensive Cancer Center; and **Christiane Querfeld**, dermatopathologist and lymphoma specialist at Memorial Sloan-Kettering Cancer Center.

The institute is currently launching several T cell immunotherapy clinical trials for treatment of leukemia and lymphoma, with others being developed for myeloma and transplantation.

LISA RICHARDSON was named director of the **CDC Division of Cancer Prevention and Control**.

Richardson served for over a decade in medical and scientific leadership roles in the division and will rejoin the center Nov. 16.

She first joined CDC in 1997 as medical officer in DCPC's National Breast and Cervical Cancer Early Detection Program and was then selected as medical officer of the Hematologic Diseases Branch in the National Center for Infectious Diseases.

She left CDC in late 2000 to practice clinical care and serve as assistant professor at the University of Florida's School of Medicine. Richardson then returned to CDC in 2004 as medical officer and served as lead of the Scientific Support and Clinical Translation Team in the Comprehensive Cancer Control Branch and as the division's associate director for science. She then left DCPC in April 2013 to direct the Division of Blood Disorders in the National Center for Birth Defects and Developmental Disabilities.

Pamela Protzel Berman, who served as acting director of DCPC, will return to her full-time duties as DCPC's deputy director.

MILAN MRKSICH was appointed associate director for research technology and infrastructure at the **Robert H. Lurie Comprehensive Cancer Center** of Northwestern University.

Mrksich is the Henry Wade Rogers Professor of Biomedical Engineering, Chemistry and Cell and Molecular Biology, with appointments in the McCormick School of Engineering and Applied Science, Weinberg College of Arts and Sciences, and Feinberg School of Medicine.

He will be responsible for oversight of the Lurie Cancer Center's research shared resource facilities. Currently, 15 shared resource facilities are supported by the Lurie Cancer Center, including the Center for Advanced Microscopy, Medicinal & Synthetic Chemistry Core, Targeted Transgenic & Mutagenesis Laboratory, and the High Throughput Analysis Laboratory.

Mrksich's research combines synthetic chemistry with materials science to study important problems in cell biology. He is a co-founder of Arsenal Medical Inc., a medical devices company that has a stent product in clinical trials, and recently co-founded SAMDI Tech, an early-stage technology company based on his new platform for analyzing biochemical reactions.

RONAN SWORDS received the Pap Corps Endowed Professorship in Leukemia at the **University of Miami Sylvester Comprehensive Cancer Center**. Swords is assistant professor of medicine and director of the Leukemia Program at Sylvester.

The endowment comes from The Pap Corps: Champions for Cancer Research, a volunteer organization that raises money solely for cancer research at Sylvester. The organization has donated more than $51 million to the center, including this year's $4.5 million as part of an overall pledge of $25 million to University of Miami's Momentum2 campaign.

Swords is a fellow of the Royal College of Physicians in Ireland and the Royal College of Pathologists in London. He came to the U.S. in 2009 for an advanced fellowship in drug development at the University of Texas Health Science Center. Swords joined Sylvester in 2012.

LAURA BROD was named CEO of **GeneSegues Therapeutics**. Brod is an at-large member of the University of Minnesota Board of Regents and is chair of the university's Audit Committee. She was a member of the Minnesota House of Representatives from 2002 to 2010, during which time she served as assistant majority leader.

GeneSegues is based in Minneapolis and develops DNA and RNAi cancer therapeutics using sub-50 nanometer nanocapsule technology, including GS-10, for the treatment of a range of solid tumor cancers including head and neck, prostate and breast, as well as their related metastases.

MERCK SERONO awarded its first Grant for Oncology Innovation, who will receive grants totaling EUR 1 million. The grant supports researchers focused on personalized treatment of solid tumors.

The 2014 winners were formally announced at the annual meeting of the European Society for Medical Oncology in Madrid. They are:

• **Clara Montagut**, of Hospital del Mar, in Barcelona, Spain; for proposed research on ultra-selection and molecular monitoring of CRC patients treated with anti-EGFR therapy using NGS platforms and serial liquid biopsies.

• **Stefan Sleijfer**, of the Erasmus MC Cancer Institute, in Rotterdam, Netherlands; for proposed research on non-invasive monitoring of breast cancer therapy using cell-free tumor DNA in blood.

• **Ulrich Güller**, of Cantonal Hospital, in St. Gallen, Switzerland; for a prospective, double-blinded, placebo-controlled, phase III randomized trial of adjuvant aspirin treatment in PIK3CA mutated colon cancer patients.

MARTINE EXTERMANN received the **2014 Paul Calabresi Award** from the International Society of Geriatric Oncology. Extermann is the senior member of the Senior Adult Oncology and Health Outcomes & Behavior Programs at Moffitt Cancer Center.

Named after the first president of the society, the award recognizes individuals who have significantly contributed to the advancement of geriatric oncology. It is the highest award granted by the society.

Extermann received the award during the society's annual meeting in Lisbon, Portugal. She gave a lecture on translational and clinical opportunities in geriatric oncology, focused on Moffitt's Total Cancer Care Protocol and how it can be utilized for older cancer patients. The protocol provides a standard system for tracking patient molecular, clinical and epidemiological data and follows the patient throughout his or her lifetime.

APTOSE BIOSCIENCES Inc. joined the **Beat AML** collaboration, developed by **The Leukemia & Lymphoma Society** and the **Knight Cancer Institute** at Oregon Health & Science University.

Aptose's lead investigational anticancer therapeutic APTO-253 will be profiled extensively against primary cells from hundreds of AML patient samples collected by Beat AML contributors.

Under the agreement, Aptose and the Knight Cancer Institute will collaborate on research related to APTO-253, which is designed to provide further insights into the optimal genetic profile of patients likely to benefit from APTO-253 therapy.

APTO-253 is a small molecule that acts through induction of the innate tumor suppressor gene Krüppel-like factor 4 and expression of the downstream cell cycle regulator p21.

THE CLEVELAND CLINIC will use **IBM Watson** technology to accelerate the use of genomic-based medicine.

The Lerner Research Institute's Genomic Medicine Institute at Cleveland Clinic plans to evaluate Watson's ability to help oncologists develop more personalized care to patients for a variety of cancers. The goal is to use Watson to correlate data from genome sequencing to medical journals, studies and clinical records, identifying patterns in genome sequencing and medical data.

The pilot initiative is an extension of Cleveland Clinic programs focused on big data in healthcare. Given the depth and speed of Watson's ability to review massive databases, the objective of the collaboration is to increase the number of patients who have access to care options tailored to their disease's DNA.

MD ANDERSON CANCER CENTER and **Summit Medical Group** signed a letter of intent to develop a joint, outpatient cancer center, as an extension of MD Anderson's partnership with Cooper University Health Care, that will provide an integrated, multidisciplinary approach to oncology care in northern New Jersey.

Summit Medical Group will become a member of MD Anderson Cancer Network. The agreement is the first of its kind between MD Anderson and a physician-owned and governed multispecialty group.

MD Anderson will provide clinical oversight and management for the program, which will include radiation oncology, medical oncology, infusion and diagnostic imaging.

MERIDIAN HEALTH and **Hackensack University Health Network** agreed to enter into discussions to merge the health systems that will result in one, integrated health care delivery system.

The signing of the memorandum of understanding will now enter a period of due diligence which could take up to four months prior to the signing of a definitive agreement.

"Our combined organization would serve a much broader geography, expanding access to services and developing a vast array of new non-hospital services," said Robert Garrett, president and CEO of Hackensack University Health Network.

The new organization, which would be known as Hackensack Meridian Health, would have a corporate board comprised of an equal number of trustees from each system. Garrett will serve as co-president and CEO of the new organization with John Lloyd, president and CEO of Meridian, for a period of two-and-a-half years, after which Garrett would become president and CEO.

THE KNIGHT CANCER INSTITUTE at Oregon Health & Science University launched a program to aid communities statewide in addressing cancer-related needs.

The institute made a decade-long commitment to invest $1 million annually through this program to assist groups that want to reduce the cancer burden in their communities.

Three tiers of grants are available to support a wide variety of projects: early stage grants provide up to $10,000, developmental grants offer up to $25,000 and program advancement grants supply up to $50,000. These grants will fund community-identified projects anywhere along the cancer continuum from prevention to early detection and treatment through survivorship.

Projects will be paired with an academic collaborator who will share best-practices, support program development and aid in evaluation measures. The information will be shared between organizations, academic collaborators, and the OHSU Knight Cancer Institute.

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY endorsed a guideline published by the **American Urological Association** and the **American Society for Radiation Oncology** on the use of adjuvant and salvage radiotherapy after prostatectomy. The endorsement was published in the Journal of Clinical Oncology.

The AUA/ASTRO guideline recommends that physicians discuss adjuvant radiotherapy with patients who have adverse pathologic findings at prostatectomy (i.e., seminal vesicle invasion, extensive positive surgical margins) and salvage radiotherapy with patients with detectable postoperative prostate-specific antigen or local recurrence after prostatectomy.

Patients should be informed that, while adjuvant radiotherapy reduces the risk of recurrence and disease progression, its impact on preventing metastases and extending survival is less clear, the guideline states. The recommendations were published August 2013 in the Journal of Urology.

The society added one qualifying statement that not all men who are candidates for adjuvant or salvage radiotherapy have the same risk of recurrence or disease progression, and thus, not all men will derive the same benefit from adjuvant radiotherapy. Those at the highest risk for recurrence after radical prostatectomy (including men with seminal vesicle invasion, Gleason score 8 to 10, extensive positive margins, and detectable postoperative PSA) are likely to derive the greatest benefit.

Funding Opportunity

Leukemia & Lymphoma Society Launches Myeloid Program

THE LEUKEMIA & LYMPHOMA SOCIETY launched a program to fund research projects focused on myeloid diseases, such as myelodysplastic syndromes and myeloproliferative neoplasms, both of which can progress to acute myeloid leukemia.

Janssen Research & Development is co-sponsoring the program, and together the organizations have committed to providing a combined $1.7 million for the initiative.

LLS is issuing a request for proposals with the intent of funding research projects at $400,000 each for a period of three years. The grants will be administered as part of LLS's new "Transforming Cures Initiative—Intercepting Progression to Advanced Myeloid Blood Cancers."

Researchers who apply for these grants will focus on identifying the molecular drivers that cause progression to leukemia and/or working toward development of treatment strategies for early interception of the disease. More information is available at www.lls.org/tci.