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MD ANDERSON RESEARCHERS OUSTED AS NIH AND FBI TARGET DIVERSION OF INTELLECTUAL PROPERTY

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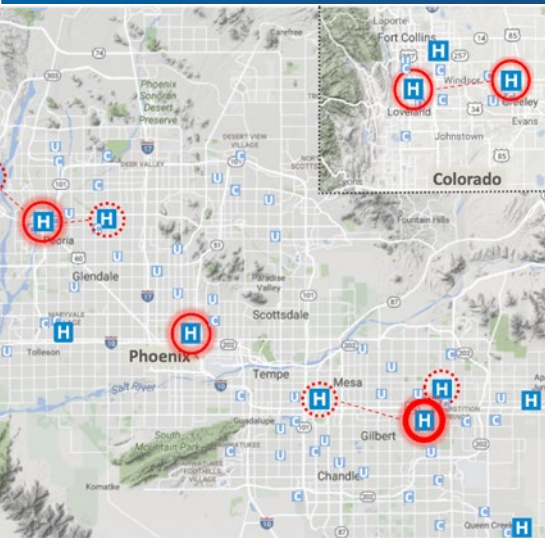
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Director

Banner MD Anderson Cancer Center Phoenix, Arizona



Banner MD Anderson Cancer Center (BMDACC), formed in 2011, has already become Arizona's largest cancer center with over 150,000 annual patient visits, 7000 new patients annually and over employed 150 providers. The Center did 75 stem-cell transplants and performed the first adult Car-T procedure in Arizona.

BMDACC employs approximately 100 physicians representing over 20 specialties, and nearly 60 advanced practice providers. The Center has a robust and growing research program, with more than 80 active clinical trials, over 400 patients accrued and over 40 research staff. In a recent survey, BMDACC was ranked as the number one choice for cancer care in the region.

The Center is increasingly recognized in the Southwest for its multidisciplinary disease-site teams and expertise, exceptional patient experience, and the extent of its treatment, diagnostic and support services. Today the program provides services at eight Banner Hospital campuses in Arizona and Colorado. A major expansion at the Banner University Medical Center in downtown Phoenix is underway, as is expansion at other hospital campuses in Arizona and Colorado. The goal is to have a fully functional, integrated service line across all Banner Health locations.

The Director will provide vision, direction, and leadership for all clinical and research programs across BMDACC system-wide in both Arizona and Colorado. S/he will provide financial, strategic and operational leadership working with executive business partners. This position reports to Banner Health's Chief Clinical Officer and works closely with a dyad business executive partner.

We are seeking a leader with the skill and vision to direct an integrated, high-performing, and interdisciplinary cancer center operating in multiple sites across multiple states. The ideal candidate will be an inspiring leader who possesses a relentless focus on clinical quality, outcomes and ease of use for customers; the ability to execute strategically and tactically across a large, complex system; and clarity and vision about the rapid evolution of cancer care.

Candidates must possess 10 years experience post-fellowship (surgical, radiation, or hematology/oncology) including leadership experience in a high-quality academic cancer environment. S/he will have demonstrated success in recruitment, mentorship, and fostering research; in clinical operations and administrative leadership; and in the development and execution of strategic plans. Candidates must be board-certified, fellowship trained, and eligible for unrestricted medical licensure in Arizona.

Banner Health is one of the leading non-profit integrated health systems in the country. Headquartered in Phoenix, Arizona, Banner Health operates 28 hospitals, including three academic medical centers, two large multi-specialty medical groups, one large physician network and other related health entities, services and insurance products.

Banner Health is one of the leading providers of healthcare services in Arizona and Northern Colorado and has revenues of \$8bn and nearly 50,000 FTEs. Banner Health is a leader in population health management with over 400,000 members in value-based commercial, Medicare Advantage and Medicaid plans.

Banner Health's mission is: "Making healthcare easier, so life can be better." The mission recognizes the need to take access and care delivery from complex to easy, from costly to affordable and from unpredictable to reliable.

Meyer Consulting has been retained to conduct this search. Applications, referrals, and requests for additional information can be sent in confidence to BMDACC's search consultants, Mike Meyer and Ryan Hubbs, via email at rhubbs@meyerconsultinginc.com. We can be reached via phone at **509/415.5209 (Hubbs)** and **602/321.0753 (Meyer)**.

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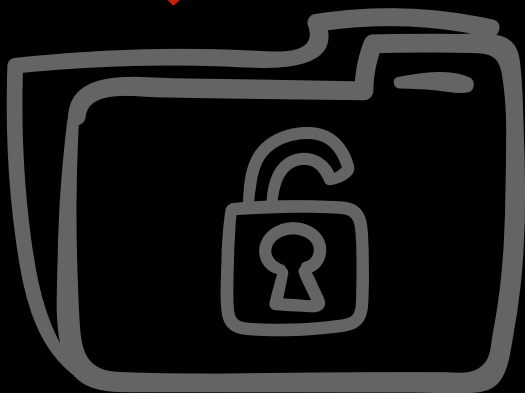
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MD ANDERSON RESEARCHERS OUSTED AS NIH AND FBI TARGET DIVERSION OF INTELLECTUAL PROPERTY

By Paul Goldberg



**HOW R01 APPLICATIONS ENDED UP EMAILED TO CHINA,
SECRET PROFESSORSHIPS, AND OTHER TALES OF CORRUPTION**



Three faculty members at MD Anderson Cancer Center were sanctioned for failure to ensure confidentiality of review of NIH grants. The scientists also failed to disclose outside funding, academic appointments, and roles in laboratories outside the U.S.

As a result of this probe, two of these faculty members have resigned, and dismissal proceedings against the third are ongoing.

Altogether, NIH and MD Anderson have examined five cases, and investigation documents reviewed by The Cancer Letter allege brazen and egregious abuses of the NIH peer review system.

These include sharing confidential information obtained through participation in NIH study sections, sometimes bouncing confidential information to unauthorized individuals down the hall, and sometimes sending it to colleagues half-way around the world, with the instruction to “keep this confidential.”

Also, the MD Anderson researchers failed to disclose ties to laboratories, faculty appointments, and financial support from the People’s Republic of China, including the Thousand Talents program and its equivalents in that country’s provinces.

Exhibiting another form of misbehavior, one MD Anderson faculty member took part in evaluation of NIH grant applications by his intimate partners.

The impetus for the inquiry at MD Anderson came from NIH and the Federal Bureau of Investigation. Late last year, NIH officials sent MD Anderson five letters containing allegations against the five researchers.

“After in-depth investigations that were performed by the University of Texas System and MD Anderson officials, violations of NIH and MD Anderson rules and policies and documentation of illegal activities led to the initiation of the termination process of three faculty members out of the five,” MD Anderson President Peter WT Pisters said to The Cancer Letter earlier this week.

“Two of the faculty members involved elected to resign in the early stages of the process. One process is just in the

very early stages of initiation,” Pisters said. “For an additional researcher—that would be a fourth researcher—the investigation revealed noncompliance, but did not reach a level of gravity to meet our threshold to begin the termination process. For the fifth case, the investigation is ongoing.

“It’s important to remember that at MD Anderson this is a tiny fraction of our 1,750 faculty members—the overwhelming majority of whom abide by our code of conduct and adhere to our core value of integrity,” Pisters said.

A conversation with Pisters is posted on [page 10](#).

The story of the investigations at MD Anderson was first reported by [Science](#) and the [Houston Chronicle](#). The Cancer Letter has reviewed the five letters mentioned by Pisters as well as reports of four completed internal investigations. The announcement of sanctions against the MD Anderson faculty members is part of an NIH-wide review of undisclosed research collaborations and their role in diverting intellectual property and undermining the NIH peer review system.

While MD Anderson is the first institution to take action in these cases, it’s a safe guess that similar actions will be taken by other institutions. In testimony before the Senate Committee on Appropriations, NIH Director Francis Collins said NIH has identified 55 grantee institutions that now face questions concerning undisclosed collaborations.

“We have had multiple opportunities to interact with the FBI, who have been investigating this vigorously,” Collins said at the NIH appropriations hearing April 11. “Some of this is classified information, some of it’s not, and as a result of that, have uncovered what has now led to more than 55 investigations that are ongoing of institutions where we believe there may be investigators who are double-dipping, receiving foreign gov-

ernment money without disclosing it or, in some instances, diverting intellectual property that was rightly the property of the institution where they are working to China or, may be most egregious of all, because it violates such an important principle for us, taking grants that they are asked to review as part of the peer-review process, and distributing those to another country, even before those grants have gone through the full review process, giving, therefore, an opportunity for somebody else’s ideas to be stolen.”

An excerpt from Collins’s testimony is posted on [page 22](#) and a video is posted [here](#).

How NIH identifies potential problems

“There are three ways in which we have identified potential problems. One is by working in consort with federal law enforcement agencies, including the FBI. The second is, we have sometimes received anonymous complaints. And the third is by the stewardship of our program staff,” said Michael Lauer, NIH deputy director for extramural research and director of the NIH Office of Extramural Research.

“As part of our routine work—this is something we do normally—we receive progress reports from awardees every year,” Lauer said to The Cancer Letter. “In those progress reports, we ask the awardee to list the publications that have come out as the consequence of NIH funding. So, what our program staff do is they will look at those publications, in part because they want to see how well the project is progressing. Sometimes some of our program staff notice things on the publications that don’t seem to match the information that we are receiving.

“For example, they may see that a project is not only being funded by

the NIH, but is also being funded by a grant coming from a foreign country. Or they may see that a large number of the authors on a grant are coming from a foreign country, or they'll just see a scientist whom we are funding, or whom we are supporting, also lists a foreign affiliation.

"Now, all that may be perfectly fine, but what has happened is that our staff look at our documentation, documentation which has been provided to us by the institution, and doesn't see any of that, and so that raises questions."

A conversation with Lauer is posted on [page 18](#).

Acknowledging that cancer research is an international enterprise, NIH officials are searching for the boundary that delineates legitimate cooperation from theft of intellectual property.

One concept that has emerged in the process of the NIH and FBI investigations is "shadow laboratories," laboratories where work being done at a U.S. institution is being duplicated, enhanced, and potentially diverted.

Researchers who are running undisclosed labs outside the U.S. are at an unfair advantage against scientists who are vying for NIH grants without such support.

Moreover, participation in the NIH Study Section system of peer review gives rogue scientists access to work by other unsuspecting researchers.

The first public indication of Collins's concern about the threat to the integrity of U.S. research enterprise came last August, when the NIH director issued a [statement](#) and sent out a [letter](#) to 10,000 research institutions.

Collins's areas of concern included:

- Failure by some researchers at NIH-funded institutions to disclose

substantial contributions of resources from other organizations, including foreign governments, which threatens to distort decisions about the appropriate use of NIH funds;

- Diversion of intellectual property in grant applications or produced by NIH-supported biomedical research to other entities, including other countries; and
- Sharing of confidential information by peer reviewers with others, including in some instances with foreign entities, or otherwise attempting to influence funding decisions.

Last December, a [working group of the Advisory Committee to the Director](#) made recommendations to NIH on approaches to deal with this issue.

Last August, FBI held an unprecedented meeting with Texas university officials to warn them about theft of intellectual property.

Many institutions have since sent letters to the faculty and some have set up educational resources, including websites. One such [website](#), set up by Penn State University, is open-access. MD Anderson's resource is available on the institution's intranet.

The MD Anderson cases

The letters from NIH officials as well as internal investigations by MD Anderson make extensive use of emails that had been obtained from the cancer center.

Asked by The Cancer Letter, Pisters said the emails were provided in response to a grand jury subpoena and upon request from FBI.

"MD Anderson provided email account contents for a number of employees during a requested period of time rather than giving them direct access to our network," Pisters said. "Real-time over-

sight was granted for one employee as part of a criminal investigation."

Prior to releasing the investigation documents under Texas Public Information Act, MD Anderson redacted the names of the researchers.

"We purposefully redacted any identifying information," Pisters said. "Our goal in telling this story was to make it about the national issue that the NIH and academia is facing and not about the people involved. Additionally, as with any personnel matter, we typically do not share names or details of affected individuals."

The investigation memoranda, labeled "Privileged and Confidential," were written by Max C. Weber, MD Anderson vice president and chief compliance and ethics officer, and addressed to Pisters.

Case 1: Unauthorized sharing of confidential material and failure to disclose affiliations in China

Weber's investigation found that one MD Anderson scientist had violated NIH peer review and confidentiality rules by sharing material made available to her by NIH for the purposes of peer review.

The materials were shared with five individuals who were not cleared to see them.

The scientist in question admitted using employees to "assist with administrative aspects of the review process such as downloading and printing grants and typing and editing drafts."

However, Weber wrote that this assistance was "more substantive than administrative in nature."

Weber also found "compelling evidence" that the researcher was receiving an equivalent of \$4,332 in monthly subsidies from a university in China and appeared to have applied for the Thou-

sand Talents program, but subsequently withdrew the application.

On top of that, Weber wrote that he believes that the researcher also held a compensated position—paying \$44,300 a year—as a “scholar and chaired professor” at Cancer Hospital of the Chinese Academy of Medical Sciences.

None of this was reported on the researcher’s R01 application. Though the researcher was a PI on an NIH grant, her grant application didn’t disclose her presumed international co-authors, whose names appeared on her published works, the report states.

The researcher opted not to appear at an interview with MD Anderson investigators.

Case 2: Failure to disclose personal relationships with PIs and academic appointments in People’s Republic of China

Here, a researcher had violated NIH rules governing peer review and “twice failed to disclose intimate, perhaps romantic, relationships with Principal Investigators (PIs) whose grant applications [he] was scoring. In one of these instances, he assisted the PI with [the] application.”

Sometime before assessing the application for NIH, the researcher wrote the following email to the applicant for the R01 grant:

The time I stood by Gate [redacted] had to be the fastest burned 20 minutes in life. Wish there were just two more minutes for me to give you a hug and say good-bye while looking into your eyes. I wasn’t firm enough to dissuade you from dashing over and I shouldn’t have let you acted [sic] like a little [redacted]. This one charge to my account for it was me

who installed the idea of a brushing by at the airport.

Comforting at last—I watched from afar the [redacted] sliding across terminals, like a movie playing out in real life. I am grateful that I got to see you and wave at you on the last second. To me, loss of a precious moment, like what took place at the airport today, serves as a sorrowful yet beautiful reminder of how life unfolds on its own terms.

While it’s permissible for NIH grantees to look into each other’s eyes, reviewing each other’s grant applications afterwards is problematic.

The researcher was also accused of “quid pro-quo exchanges of personal and professional benefits in pursuit of foreign ‘Talents Program’ membership,” Weber’s report alleges.

In the process, he “delivered know-how, data, and samples” to an entity in China. This appears to include primers designed and sequenced by his post-doc at MD Anderson. “Legal Services does not find any documentation showing any approved Material Transfer Agreements” associated with that delivery, the report states.

MD Anderson investigators recommended referring the case to state law enforcement authorities for “possible criminal prosecution.”

Case 3: “Keep this confidential.”

This MD Anderson researcher was alleged to have “emailed an NIH grant application to a scientist based in the People’s Republic of China.”

According to Weber’s report, the researcher “also may have sent at least two NIH grant applications to U.S.-based scientists who were not designated by the NIH to review the material.”

“

After in-depth investigations that were performed by the University of Texas System and MD Anderson officials, violations of NIH and MD Anderson rules and policies and documentation of illegal activities led to the initiation of the termination process of three faculty members out of the five.

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— Peter Pisters



There are three ways in which we have identified potential problems. One is by working in consort with federal law enforcement agencies, including the FBI. The second is, we have sometimes received anonymous complaints. And the third is by the stewardship of our program staff.

– Michael Lauer



In one instance, the researcher instructed the recipient of the information to “keep it to yourself.”

In another instance, the accompanying note read, “Here is bone and meet [sic] you need.”

On yet another occasion, the researcher sent an NIH grant application to a department within the National Cancer Center/Cancer Hospital Chinese academy of Medical Science. The transmittal email read: “Some methods you may learn from this proposal. Keep this confidential.”

The researcher received all of these applications from NIH legitimately, for the purposes of conducting peer review.

Like others, this researcher hadn’t disclosed relationships with institutions in China. For example, the researcher “denied having any active National Natural Science Foundation grants, though he admitted his name may be on grant applications,” Weber wrote. “When I showed him an email in which he stated that he had two active NSFC grants, [the researcher] explained that [redacted] lied in the email and that there were, in fact, no active grants. I do not find [the researcher’s] explanation to be credible.”

Case 4: Ameliorating factors

In this case, NIH found that the researcher had violated the rules governing peer review by discussing the content of a grant proposal with the submitting PI. However, MD Anderson’s Weber was unable to substantiate this allegation, he wrote.

The relationship between the reviewer and the PI didn’t meet the bar for disqualification. However, Weber found “potential conflicts of interest and commitment to foreign entities” that

the researcher had failed to disclose to the institution.

Weber recommended that the cancer center consider “several ameliorating factors.” The researcher “was forthright, cooperative and contrite” and had “volunteered information that I would not otherwise have discovered,” Weber wrote. “I believe that any corrective action should account for these factors.”

Moreover, the researcher’s relationships didn’t appear to be deep and compensation seemed to be “insubstantial.” The researcher has acknowledged sharing a reagent with a foreign colleague. “I recommend seeking guidance from the NIH on whether the supplying of reagents to a collaborator with a foreign site under the circumstances above constitutes a ‘foreign component’ within the meaning of the NIH rules,” Weber writes. “I also recommend that the CAO, CSO, and my office develop a clear communications plan concerning the disclosure of such collaborations (that is, collaborations likely to result in publication) on RPPRs and Biosketches.”

In a conversation with The Cancer Letter, Pisters said that “the investigation revealed noncompliance, but did not reach a level of gravity to meet our threshold to begin the termination process.

“We have worked with the individual and his or her supervisor to educate on our compliance procedures and on the structures for compliance moving forward,” Pisters said. “This individual’s report has been filed with the NIH, as requested, and we’re awaiting response. If the NIH and HHS were to move forward with penalties, such as debarment or suspension, MD Anderson and the UT System might revisit the status of that individual.”

Claire Dietz contributed to this story.

Q

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Pisters spoke with
Paul Goldberg, editor and
publisher of The Cancer Letter.

A



CONVERSATION WITH
THE CANCER LETTER

Pisters: “Trust is broken when a grant reviewer decides that an idea should be better done elsewhere”

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Our goal has been to raise awareness, to provide information and educational resources, and to help our faculty continue to do the right thing as we work together to accomplish our mission.

”



Peter WT Pisters
President, MD Anderson Cancer Center

As MD Anderson investigates reports of wrongdoing by its faculty members, it does so with full understanding that the stakes are as high as it gets: the integrity of the NIH peer review system, MD Anderson's good name, and the future of cancer research.

"We have had a very thoughtful, very deliberate, and collaborative process involving the UT System in order to ensure that we follow our policies and procedures and that we do so with the utmost concern for doing the right thing for our faculty, for our institutional reputation, and for our NIH funding," MD Anderson President Peter WT Pisters said to *The Cancer Letter*.

Pisters spoke with Paul Goldberg, editor and publisher of The Cancer Letter:

Paul Goldberg: MD Anderson has taken administrative action against several faculty members. Can you tell me where this matter currently stands?

Peter Pisters: As you know, NIH Director Francis Collins sent a letter to over 10,000 institutions in August of 2018 outlining the NIH's concerns regarding the threat of foreign influence, and conveying concerns about the integrity of the peer review process.

Pursuant to that letter, MD Anderson received five letters that outlined serious allegations about individual faculty researchers here at MD Anderson. And, it's important to remember that at MD Anderson this is a tiny fraction of our 1,750 faculty members—the overwhelming majority of whom abide by our code of conduct and adhere to our core value of integrity.

As I'm sure you can understand, as the recipient of significant NIH funding, we

have a responsibility and an obligation to follow-up on specific serious concerns embedded in the NIH request for investigation. Organizations that cannot or will not follow through on concerns raised by the NIH may be at risk of losing federal funding.

And after in-depth investigations that were performed by the University of Texas System and MD Anderson officials, violations of NIH and MD Anderson rules and policies and documentation of illegal activities led to the initiation of the termination process of three faculty members out of the five.

As you may know, the termination process for tenured faculty members includes constitutional due process protections.

In our organization, it entails a hearing in front of a panel of peer faculty members and ultimately requires review and final decision by the UT System Board of Regents in Austin.

Two of the faculty members involved elected to resign in the early stages of the process. One process is just in the very early stages of initiation.

For an additional researcher—that would be a fourth researcher—the investigation revealed noncompliance, but did not reach a level of gravity to meet our threshold to begin the termination process. We have worked with the individual and his or her supervisor to educate on our compliance procedures and on the structures for compliance moving forward.

This individual's report has been filed with the NIH, as requested, and we're awaiting response. If the NIH and HHS were to move forward with penalties, such as debarment or suspension, MD Anderson and the UT System might revisit the status of that individual.

For the fifth case, the investigation is ongoing.

It's important to note that immediately upon receipt of Dr. Collins's "Dear Colleagues" letter, MD Anderson made efforts to educate our faculty on NIH rules and our compliance requirements.

We shared the NIH letter with our faculty, and we hosted town halls and Q&A sessions to help answer their questions about the areas of focus for the NIH.

We also worked to create an internal website designed to disseminate information, tools, case studies, and scenarios, to help to simplify and to clarify the requirements for faculty—particularly those who are NIH investigators. Our goal has been to raise awareness, to provide information and educational resources, and to help our faculty continue to do the right thing as we work together to accomplish our mission.

We've also initiated a comprehensive approach to enterprise risk management with a state-of-the-art process to manage a variety of risks across the organization, including data security and intellectual property loss.

So, I think you can see that we have had a very thoughtful, very deliberate, and collaborative process involving the UT System in order to ensure that we follow our policies and procedures and that we do so with the utmost concern for doing the right thing for our faculty, for our institutional reputation, and for our NIH funding.

The documents pertaining to NIH investigations make extensive use of MD Anderson emails. Were these documents produced under a subpoena and did third parties—such as law enforcement agencies and NIH have access to the MD Anderson servers?

PP: In response to a federal grand jury subpoena as well as requests from the FBI, MD Anderson provided email account contents for a number of employees during a requested period of time rather than giving them direct access to our network. Real-time oversight was granted for one employee as part of a criminal investigation.

Is it fair to say that MD Anderson decided to make this matter public?

PP: MD Anderson was receiving Texas Public Information Act requests regarding this matter.

This is a complex story, and we were concerned that if articles were published that were based upon the limited information released pursuant to such requests, the articles could be incomplete and inaccurate.

Consequently, we believed it was in the public interest to tell our comprehensive story to our local newspaper's health care reporter.

The NIH investigation documents that I have here are redacted. Did MD Anderson redact them? What was your rationale for not disclosing the names of the individuals involved?

PP: Yes, we purposefully redacted any identifying information.

Our goal in telling this story was to make it about the national issue that the NIH and academia is facing and not about the people involved.

Additionally, as with any personnel matter, we typically do not share names or details of affected individuals.

To the best of your knowledge, is there more to come? Or does this close all the ongoing investigations of faculty members?

PP: The NIH is in the midst of a national plan to address the issues that are raised in Dr. Collins's letter of August 20. From what Dr. Collins shared last week in his Senate Appropriations Committee testimony, currently 55 institutions are impacted nationwide and that number is expected to rise.

The fact that the Senate Appropriation Committee is looking into this insinuates the risk to NIH funding, and emphasizes the responsibility that sits with academia to appropriately manage these matters.

MD Anderson has received just these five letters from the NIH. I can't speculate on what's to come in the future, but I can tell you that we've learned a lot through this initial process, and, should we receive additional letters, we will again go through a very thorough, independent investigation aided by UT System officials, following our core values, and working once again to ensure due process, and protect the integrity of the peer review system and our reputation.

I see in the NIH documents that at least some of these individuals have maintained contact with institutions in mainland China. How would you describe this matter and these associations—is this about China? Is this more than China? What is it?

PP: As directed by the NIH, we've looked into some of the relationships, and I'm sure that you saw in the reports that many of those relationships were not disclosed to the institution, even after the individuals were asked directly.

Although there has been focus nationally on China, our experience has been that this is not restricted to one country alone.

We've made it a priority to work with our faculty to clarify NIH rules as well as the policies that are in place for MD Anderson and the UT System. I can certainly promise to you that MD Anderson is committed to collaboration.

We just need to make sure that those relationships are fully disclosed and approved by the institution, and that legal agreements are in place to ensure that we're doing everything possible to protect the outstanding work of our faculty. We want to protect the culture of collaboration that fosters discovery.

We know that ending cancer can really only happen if we do it together, and it doesn't matter what country you come from—in fact, we have relationships with institutions around the globe, from Brazil to Spain, Turkey and China.

Also, as part of our Global Academic Program, we have over 20 Sister Institution relationships in countries around the world, including five in China. We're actively pursuing business relationships in China, and we recognize that our global relationships are very important, strong, and fundamental to our mission.

Well, science, of course, is an international enterprise. Hence, much of the collaboration is entirely appropriate and desirable. How are these cases different? What makes these relationships inappropriate?

PP: We completely agree that discovery in today's world of global research talent requires collaboration between individual researchers and institutions. Here in the United States, the NIH and academic institutions require that these relationships, along with other research funding sources and personal compensation, be disclosed to the NIH and to their home institutions.

What we're seeing now is that failure of NIH-funded investigators to disclose alternative sources of research funding corrupts the NIH peer review funding decision, and disadvantages the national research community.

For example, if the NIH knew that institution A already had partial or complete funding for a grant application, then taxpayer resources could be redirected to institution B, which has another meritorious project.

We support the fundamental principles of trust, ethics, and integrity, which underpin the NIH peer review system.

Are there rules of thumb that might help us distinguish appropriate scientific collaboration from those that raise ethical questions, or may even be illegal? I guess disclosure is one, disclosure of funding is another. Are there any rules of thumb that you can think of?

PP: Yes, the NIH and individual universities have specific policies around research collaborations, material transfer agreements, and data sharing agreements. The best guidance that we can provide is for institutions to provide clear, easily navigable education materials that individual investigators can understand, and that their best approach is always to err on the side of disclosure and transparency.

It's imperative that peer reviewers and NIH grant recipients familiarize themselves with, and strictly abide by, the NIH rules and policies.

Here at MD Anderson we have a team of experts ready, willing, and able to support our researchers with any questions they have regarding research collaboration, or any research compliance matter.

We've worked to make these resources available whenever needed, and we are working to make them more user-friendly.

We are in the process of developing educational resources, like a matrix that provides a high-level overview of what needs to be disclosed and what doesn't, in a variety of categories, and an internal website that has all the relevant resources in one location.

We're messaging to our faculty that we're here to help, and that we're committed to do whatever is needed to make possible the opportunities afforded by international collaborative relationships.

One of these cases seems particularly egregious. It seemed that way, because here's a researcher who gets an application as part of NIH peer review and shoots it over to another institution in another country. That's a rule of thumb—don't do it.

PP: You're right, and that really addresses the fundamental trust that's inherent in the peer review system.

When a gifted and talented and innovative researcher has an idea, and those ideas are put into a grant application, and submitted to the NIH, implicit in

that process is a fundamental underpinning of trust, and that trust is broken when a grant reviewer decides that that idea should be better done elsewhere, and exports the intellectual property of another researcher to an outside environment, where that work is then carried out.

Our system is based on trust, integrity, and merit, and we need to work together as a national academic community to support these principles in order to maintain the finest national biomedical research enterprise in the world.

How would you evaluate the level of harm that might have been done to MD Anderson and to science overall?

PP: We need to understand that this is a national issue, as Dr. Collins has outlined on a number of occasions. What's at stake is the integrity of the peer review system and the intellectual property that's been created by U.S.-based investigators, with the support of taxpayers, private donors, and the industry partners.

Our reputation is based on public trust and that trust is enhanced when the public sees us taking actions that are anchored in core values and fundamental ethical principles.

MD Anderson is the first institution to publicly share the actions that we have taken in what will likely be a series of actions across the country.

PP: I expect what will come from this is a sharpened focus on ethics and integrity, along with enhanced educational

materials and collaboration solutions at universities across our country. It goes without saying that this needs to be accompanied by enhanced approaches to data protection and physical security at academic medical centers and universities.

Do you—personally—know about the existence of any shadow labs that directly involve MD Anderson research?

PP: Through our investigations we became aware of what appeared to be shadow labs in other countries. We made it clear that, without institutional review and approval, our faculty investigators may not conduct overseas research for or on behalf of another entity, or operate a lab or research facility outside MD Anderson.

MD Anderson faculty who wish to engage in or oversee research outside of the UT System must receive advance approval by the institution.

Relatedly, work for any laboratory or hospital owned by a foreign government requires a contract that, at a minimum, is subject to approval by the Office of General Counsel of UT System and in some cases must be approved by our UT System Board of Regents based in Austin, Texas.

Are you personally aware of any links between MD Anderson researchers and the so called “Thousand Talents” program of the People’s Republic of China?

PP: We believe that only a very small number of our faculty have been ap-

proached to participate in these programs. We also know that these programs are not confined to one country.

Our policies don’t specifically prohibit this, but we discourage participation in what we see as predatory programs that recruit individuals, and we caution faculty not to participate in, or explore illegal programs that are setup with quid pro quo arrangements that require data or intellectual property transfer.

We’re more interested in helping faculty to set up fully-disclosed, well-documented, collaborative research relationships that work to advance our mission and to enhance the pace of discovery.

How and when was this brought to your attention? What was the mechanism for learning this? How did this story get into public view as well?

PP: We were officially notified by the NIH in August of 2018, and we began receiving letters from NIH in the fall of 2018.

These letters outline significant concerns that the NIH had about failure of NIH grant recipients to disclose significant alternative sources of research funding, the sharing of confidential materials contained in grant applications by NIH peer reviewers with others, including foreign governments, and the diversion of intellectual property and grant applications that were produced by NIH supported researchers to other entities including other countries.

As you know, the issues of foreign influence are impacting multiple sectors of the U.S. economy, including telecommunications, aerospace, semiconductor, and defense. Attention is now gradually and surely turning to academia.

How do you keep this matter from feeding into xenophobia or ethnic bias?

PP: This is fundamentally about ethics and integrity, it’s not about ethnicity. At MD Anderson, we’re justifiably proud of our international workforce and our remarkable track record of diversity and inclusion.

We’ve been recognized for our diversity commitment by the AAMC, Forbes, and the National Diversity Council. Our work force, Paul, has exceptional diversity, reflecting the diversity of Houston, which is America’s most diverse city. We are 21,000 strong, and 30% White, 29% Asian, 23% Black, and 17% Hispanic. Our employees know that we do not discriminate on the basis of age, gender, race, sexual orientation, or ethnicity.

We also have a very prestigious Visiting Scientist Program that welcomes scientists from around the world, including a majority from China. These realities about our commitment to diversity, inclusion, and collaboration reflect our belief that we can meet our mission goals optimally through robust international collaborations.

Could MD Anderson have handled this matter better than you did? Was there a way to know this earlier?

PP: We believe that we’ve acted in accordance with our core values throughout this process, and we’ve done all that we can with the information available to us at the time. As a nation, we’re grappling with the complex challenge that requires us to very carefully balance the longstanding commitment to an open and collaborative academic environ-

ment, while at the same time protecting the integrity of the peer-review system, our intellectual property, and our commercial interest.

As far as MD Anderson's approach, we've partnered with the NIH, the UT System, and our internal stakeholders, including our academic leaders and faculty senate.

This has brought us closer together around a unified commitment, anchored in our core values, and designed to ensure that MD Anderson works together with our federal partners to promote the highest levels of scientific integrity, public accountability, and social responsibility in the conduct of science.

We do so with an unending focus on ethics, core value of integrity, and a shared commitment to maintain the extraordinary levels of public trust in MD Anderson.

I was noticing a subplot within the reports that NIH sent you that there could be some liability on the part of MD Anderson, both in terms of NIH rules and state rules. Is this over? Or do you see a potential for some sanctions against the institution?

PP: That's hard to predict, because to some extent we're in uncharted waters. But as reflected by the appreciative comments of Dr. Collins, we've acted promptly, diligently, and cooperatively with the NIH in responding to its allegations.

And I'm confident that our institution has acted in the interest of protecting our faculty's work, our reputation, and the public trust in MD Anderson, as well as doing our part to protect the integrity

of the peer-review system that underpins America's leadership position in biomedical science.

This problem is by no means MD Anderson; MD Anderson is where it became visible. But it is 55 institutions, potentially, based on what Dr. Collins said, and, really, the problem has to be worldwide.

PP: Yes, based on Dr. Collins' letter it's clear that this is a national issue, and from what I've read and heard this is indeed a global problem. Colleagues in Europe, the UK, Canada, and Australia are navigating the same challenges as we are.

What steps have you taken to keep this from occurring again?

PP: NIH Director Francis Collins also has created an Advisory Committee to the Director (ACD) on the topic of foreign influence. University presidents, chancellors and academic medical center CEOs participated in formulating a series of recommendations.

The ACD [white paper](#) and [slide deck](#) provide excellent resources and will be a source for the Director in considering the possibility of future changes designed to protect the nation against these risks.

At MD Anderson, we are taking a comprehensive approach to look at risk at MD Anderson by setting up a sophisticated enterprise risk management program, which is being dovetailed with our strategic planning process. We've

set an aspirational goal to ensure that our approach to enterprise risk management is best-in-class for academia, and that it enables us to look strategically at enterprise risks, risk velocity, mitigation strategies, and to dovetail risk with strategy, operations, and audit.

For the internal community that we serve, it will create transparency with dashboards, heat maps, and risk appetite statements, and this, I believe, will position us to optimally address a myriad of risks in a holistic, best-in-class manner.

Is there anything we have missed?

PP: We've talked about an array of complex issues that really impact the fundamental tenants of biomedical science in America. Our internationally acclaimed system, revered around the world, has been built from a shared commitment on a national level, to the core values of trust, integrity, and merit. We're committed to those values that stand for everything that's great about America.

It's important for all of us to recognize the importance of a balanced approach to these complex issues. We certainly support the extraordinary opportunity that we have to eliminate cancer through research collaborations. These collaborations are designed to accelerate our path to discovery, to enhance economic opportunity, and to benefit humanity.

Thank you very much.

PP: This has been a great discussion, Paul.



Accelerating Anticancer Agent
Development and Validation

16th Annual Accelerating Anticancer Agent Development and Validation (AAADV) Workshop

May 8-10, 2019,
North Bethesda, Maryland

ABOUT THE AAADV WORKSHOP

Leaders in clinical and translational cancer research from academia, industry, government and nonprofit advocacy sectors convene each spring in North Bethesda, Maryland, for the AAADV Workshop, a unique forum designed to speed cancer treatments to patients.

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Participants gain valuable insights on negotiating the spectrum of successful drug development and hone their strategic planning skills with a focus on target validation and pathway identification.

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<https://aaadv.org/>

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Lauer spoke with
Paul Goldberg, editor and
publisher of The Cancer Letter.

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CONVERSATION WITH
THE CANCER LETTER

NIH's Lauer: "We have contacted over 55 institutions"

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This is taxpayer money, which is being used to conduct what we hope will be the highest quality science. And it is critically important that the decisions that all federal agencies make about spending limited taxpayer funds be made in a way that is fair and as unbiased as possible.

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Michael Lauer

*Deputy director for extramural research, NIH
Director, NIH Office of Extramural Research*

MD Anderson is the first institution to address the interrelated problems of theft of intellectual property, violation of ethics of NIH peer review, and researchers' failure to disclose foreign affiliations and sources of funding.

"MD Anderson is ahead of the game at this point, but this is a problem that transcends MD Anderson," Michael Lauer, NIH deputy director for extramural research and director of the NIH Office of Extramural Research, said to *The Cancer Letter*. "It involves institutions all around the country. We have contacted over 55 institutions for whom we have found problems."

Lauer spoke with Paul Goldberg, editor and publisher of The Cancer Letter:

Paul Goldberg: Could you tell me how NIH is proceeding with this investigation? Dr. Collins mentioned this at the appropriations hearing in part, or is there more to be said?

Michael Lauer: So, as Dr. Collins did say at the appropriations hearing, and also as he mentioned in the letter that was sent out last August, we are reaching out to all NIH grantee and applicant institutions. We are reaching out to institutional officials when we identify potential problems. We are working in partnership with institutions to look into problems and then deal with them as appropriate.

How do you identify that?

ML: There are three ways in which we have identified potential problems. One is by working in consort with federal law enforcement agencies, including the

FBI. The second is we have sometimes received anonymous complaints. And the third is by the stewardship of our program staff.

As part of our routine work—this is something we do normally—we receive progress reports from awardees every year. In those progress reports, we ask the awardee to list the publications that have come out as the consequence of NIH funding. So, what our program staff do is they will look at those publications, in part because they want to see how well the project is progressing. Sometimes some of our program staff notice things on the publications that don't seem to match the information that we are receiving.

For example, they may see that a project is not only being funded by the NIH, but is also being funded by a grant coming from a foreign country. Or they may see that a large number of the authors on a grant are coming from a foreign country, or they'll just see a scientist whom we are funding, or whom we are supporting, also lists a foreign affiliation.

Now, all that may be perfectly fine, but what has happened is that our staff look at our documentation, documentation which has been provided to us by the institution, and doesn't see any of that, and so that raises questions.

Has this actually happened, that you've found another source of support that wasn't mentioned before?

ML: Yes.

Or another set of authors that you didn't know about?

ML: Yes. Yes.

All of that has happened?

ML: Yes.

So that would be in that list of 55 that Dr. Collins mentioned, right?

ML: Yes. So, this is an important point here, this is not something which is a problem that is unique to MD Anderson. MD Anderson is ahead of the game at this point, but this is a problem that transcends MD Anderson. It involves institutions all around the country. We have contacted over 55 institutions for whom we have found problems.

And this actually transcends the NIH, this is not something which is unique to biomedical science, and, as you may or may not know, the Department of Energy and the National Science Foundation have also, in public fora, voiced their concerns.

Well, you mentioned that MD Anderson is ahead of the game, could you explain?

ML: MD Anderson has taken a very proactive approach in figuring out what was going on, and doing everything they possibly can to ensure the integrity of their research operation. So, they discovered this earlier than other institutions have, and we really commend them for what they are doing, because they have been particularly proactive in trying to find out what has been going

on, and what they can potentially do to enhance their security.

I believe Dr. Pisters may have spoken with you—

He has.

ML: The various security measures that they have taken there, are, I think, exemplary, and will be something that we can all learn from. And I think that the MD Anderson experience is something that we hope many institutions will learn from.

As far as the MD Anderson experience, so you found the potential problems, or did they find the potential problems? Because I'm looking at the letters from you, and they seem to suggest that you already have the names. Is there, how did you get the emails? Was it under a federal subpoena, FBI subpoena, or how—

ML: I can't talk about specific cases.

Maybe I should just rephrase it; then if you still can't talk, you can't talk. But as I look at those [internal] emails that you mention, you must have gotten them under a subpoena; or how did that happen?

ML: So, Paul, I'm sorry, I can't talk about specific cases.

Okay. Is this [problem] limited to China, or is it other countries?

ML: We have seen cases that have involved other countries; most of what we have seen does involve China. But we have seen other countries as well.

Also, with the 55 as the number that Dr. Collins mentions in his testimony, 55, some of them could actually turn out to be innocent; right? It's just something that has been flagged through the analysis you've just mentioned?

ML: Right. So, we do an analysis on our end to see whether or not there is a reason for potential concern. And, basically, our reason for potential concern is that there may have been an undisclosed foreign components or undisclosed other support that we did not know about. And under those circumstances, we then contact the institutions, and we work with them to try to learn more about what's going on.

These cases are now in progress. They're at various stages of progress, and how this is all going to pan out is something that still, time will tell.

How was the decision to make this public made? The current version of it, the MD Anderson part?

ML: That was entirely an MD Anderson decision.

And they were the ones who redacted the material, right?

ML: Right, we did not, the FOIA request went through MD Anderson, not to us.

Is there anything you can tell me, what's the next stage? Is there any sort of rule of thumb that you could suggest, that other institutions could use, to find out what's reasonable, what's not?

ML: There are a few things that I can mention, all of this is already publicly known. One is that when, if NIH discovers, or working through the institutions we discover that there are potentially serious problems; that for example, scientists have received extensive funding from other sources that were never disclosed to us, we can then refer those cases to the Office of the Inspector General, within the Department of Health and Human Services. And we have done that, and that's something which is already publicly known.

The second is that, a number of institutions beyond MD Anderson have taken a very proactive approach. If you haven't already, I would encourage you to look at the website at Pennsylvania State University, at Penn State, I don't know if you've seen it. It's really good.

Yeah. It's really good, it has a number of things. First of all, it demonstrates how the university is taking the problem seriously.

Second, it reflects, they are reflecting the concerns that they are hearing from government agencies, not just the NIH, but also other funding agencies that

are important to them, such as the Department of Energy and the National Science Foundation.

The third is that, if you look at the bottom of that webpage, they have a whole bunch of links to interesting sources that they feel are important for their staff to be aware of, and some of those I think you'll find interesting as well.

Did that happen in consultation with you, or—

ML: No.

Did they have a case to worry about, or—

ML: Well, again, I'm not going to comment on specific cases, but you might want to talk with them about their perspectives of how they put that website together.

What is next, what happens next? Is there another case being made public at some point, somewhere else? Do you know?

ML: What's next is we're working our way through, at this point we have as Francis mentioned, over 55 active inquiries going on, at over 55 different institutions. And these all take time, and that's where we are right now. Some of them have already yielded referrals to the Office of the Inspector General. That's already a publicly known fact, and I'm anticipating that there will be more.

You mentioned in your letters to MD Anderson that there could be other problems for MD Anderson in terms of getting continuing support from NIH, and so forth. I'm going by memory... I don't think I misread it. There's also some violation of state laws, potentially.

ML: Well, the general rule of thumb: it is important for institutions to be compliant with federal laws, rules, and regulations governing grant support. This is taxpayer money, which is being used to conduct what we hope will be the highest quality science. And it is critically important that the decisions that all federal agencies make about spending limited taxpayer funds be made in a way that is fair and as unbiased as possible.

So, if we have violations of our peer review rules, or if we are effectively funding research that's already being funded by somebody else elsewhere, then our ability to fund in a way that is as fair, unbiased, and appropriate as possible is compromised.

So, we work closely with universities, we see this as a partnership, and I think the relationship we've had with MD Anderson is an exemplary partnership, we see this as a partnership to make sure that things are done right, and that the public is best served, so that we can fund the best science.

It's also up to an institution to ensure ethics of the faculty, so it totally makes sense; right?

ML: Yeah. And, you know, this is serious business. So, if an institution is non-compliant, and we're unable to come up with a satisfactory resolution of the problem, they can lose the grant. The grant can be terminated, it can be suspended, a scientist can be taken off grants. We have a number of remedies that are available to us, and you know, it's all in the spirit of making sure that we are together, the federal government along with universities and institutions, are working together to be the best possible stewards of taxpayer funds.

Is there anything we've missed, anything you'd like to add?

ML: I think we've pretty much covered it.

Cool. Thank you so much.

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If we have violations of our peer review rules, or if we are effectively funding research that's already being funded by somebody else elsewhere, then our ability to fund in a way that is as fair, unbiased, and appropriate as possible is compromised.

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Collins: “Not every one of these investigations is going to reveal something bad, but some of them will”

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There are instances, egregious instances, where our funding of grants in this country is being taken advantage of by individuals who are not following the appropriate rules. This is utterly unacceptable.

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Francis Collins
Director, NIH

Stealing data obtained through the NIH peer review process is the most egregious of the cluster of rogue behaviors revealed through ongoing investigations of diversion of intellectual property, NIH Director Francis Collins said in testimony before the Senate Appropriations Committee April 11.

“Diverting intellectual property that was rightly the property of the institution where [the researchers] are working to China, may be most egregious of all, because it violates such an important principle for us, taking grants that they are asked to review as part of the peer-review process, and distributing those to another country, even before those grants have gone through the full review process, giving, therefore, an opportunity for somebody else’s ideas to be stolen.”

The exchange between Collins and Sen. Roy Blunt (R-MO) follows:

Sen. Roy Blunt (R-MO): Thank you, Dr. Collins. Why don’t we talk a little bit about the efforts you’ve made on the concern about foreign involvement, about duplicate labs in other countries, and information being shared that shouldn’t be, and then what we’re going to do about it.

Francis Collins: I’d be glad to do that. We are deeply concerned about the evidence, which has been growing and which we’ve become increasingly aware of over the course of more than a year, that there are instances, egregious instances, where our funding of grants in this country is being taken advantage of by individuals who are not following the appropriate rules. This is utterly unacceptable.

We have had multiple opportunities to interact with the FBI, who have been investigating this vigorously.

Some of this is classified information, some of it’s not, and as a result of that, have uncovered what has now led to more than 55 investigations that are ongoing of institutions where we believe there may be investigators who are double-dipping, receiving foreign government money without disclosing it or, in some instances, diverting intellectual property that was rightly the property of the institution where they are working to China or, may be most egregious of all, because it violates such an important principle for us, taking grants that they are asked to review as part of the peer-review process, and distributing those to another country, even before those grants have gone through the full review process, giving, therefore, an opportunity for somebody else’s ideas to be stolen.

Knowing the seriousness of this, I did something unprecedented and wrote, first time since I’ve been NIH director, to every one of our grantee institutions, and that’s more than 10,000, a very strongly worded letter, saying this is an issue they all need to take with great seriousness, and if they’re not aware of what their own faculty are doing in terms of these kinds of relationships, need to begin to find that out.

I think there was initially some surprise and maybe even denial that that could be happening in these institutions. I think we are past that now, and we are now seeing statements from some of those institutions, very strongly worded, to their own faculty, saying, “We realize we have a problem too.”

There are increasing instances where faculty members have been fired, have been asked to leave the institution, many of them then returning back to their previous foreign base, and I should say, while China has certainly been mentioned a lot, this is not only China.

So, actions are being taken, and you will see more evidence of that in the press, particularly in the coming week or two, to show just what is now necessary in order to respond to this.

We will not rest until we’ve looked at every possible example. We have to depend on the universities as our partners in this, but we are driving this process as vigorously as we can.

Blunt: In those 55 instances, how many different institutions would that involve, or—

Collins: That’s 55 institutions.

Blunt: 55 different grantee institutions?

Collins: Yes. And, basically, we are triggered by noting in a grantee that there is a publication that comes out that seems to involve a lot of authors and a lot of other institutions that were not mentioned in their grant application.

Now, maybe that’s an appropriate collaboration. I’m not going to tell you that every one of these investigations is going to reveal something bad happened, but some of them will.

Blunt: Well, we clearly benefit from having people from other countries here, to have their skill level here. Frankly, I think we benefit to have them if they want to stay here—

Collins: Absolutely.



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Texas House of Representatives approves two CPRIT measures

By Claire Dietz

The Texas House of Representatives approved two measures that would give the Cancer Prevention and Research Institute of Texas an additional \$3 billion to continue operations, and allow the institute to continue funding grants beyond fiscal year 2023.

The measures approved earlier this month are:

- **House Joint Resolution 12**, which authorizes \$3 billion in new bond funding, known as General Obligation Bonds, and
- **House Bill 39**, which remove a restriction against new grant awards beyond CPRIT's initial sunset date in 2023.

"It's very gratifying to hear from the state leadership, both the recognition of what CPRIT has accomplished and, in addition, the understanding of what's ahead of us in terms of continued opportunity to make an impact in cancer in Texas," James Willson, CPRIT chief scientific officer, said to The Cancer Letter (The Cancer Letter, [March 22](#)).

"And that leads us to be quite optimistic about the future continuation of this investment."

"We are encouraged by the House's overwhelmingly positive vote in support of

the continuation of CPRIT," said Peter WT Pisters, president of The University of Texas MD Anderson Cancer Center. "It's clear that the tremendous impact of CPRIT has been recognized, and we remain committed to this vital and unique resource that establishes Texas as a world leader in cancer research, prevention and commercialization of discovery."

"While This is very good news these are the first step as the reauthorization bill is now being considered by the Texas Senate and the bridge funding for the next 2 years goes to a joint conference committee. We should show the final outcome in May."

Founded in 2007, Texas voters initially authorized CPRIT \$3 billion in bonds to be put towards funding research and prevention programs throughout the state. Since its formation, CPRIT has awarded more than \$2.26 billion in grants to Texas researchers, institutions, non-profit organizations and businesses (The Cancer Letter, [March 22](#)).

The measures now await approval from the Texas State Senate.

If approved, the passage of HJR 12 means that CPRIT will have received a total of \$6 billion in bond funding since its founding. As was the case in 2007, CPRIT will have to be put to the ballot, and voters will be asked to approve a constitutional amendment, which is a requirement for reauthorizing the institute. The vote is slated for Nov. 5.

The CPRIT measures in the House are led by Texas Rep. John Zerwas. In the Senate, Sen. Jane Nelson has introduced [Senate Bill 438](#), the equivalent of HB 39. SB 438 was unanimously approved by the Texas Senate committee on Health & Human Services.

The Texas legislature recognizes CPRIT's role in accelerating innovation, said James Gray, managing director of the South Region of the American Cancer Society Cancer Action Network.

"Today's vote clearly communicates that the House is committed to Texas remaining a leader in cancer research and prevention," Gray said in a statement.

IN BRIEF



\$15.1M awarded to Rutgers Cancer Institute of New Jersey for redesignation as Comprehensive Cancer Center

Rutgers Cancer Institute of New Jersey has been awarded a \$15.1 million grant (P30CA072720) as part of its successful 2019 redesignation as a Comprehensive Cancer Center.

In its comprehensive on-site review of Rutgers Cancer Institute programs, NCI recognized the Institute's treatment, prevention, education and outreach efforts as well as acknowledged its value as a collaborative matrix/consortium cancer center between Rutgers, The State University of New Jersey and Princeton University.

Rutgers Cancer Institute collaborates with Princeton University as part of a research consortium.

This partnership provides continued opportunities for scientific collaboration and cooperative use of state-of-the-art shared resources. As a result of this rela-

tionship, scientific advances in the areas of cancer metabolism, metastasis, and genomics have contributed to impactful clinical progress in areas such as precision medicine and immunotherapy.

As an NCI-approved consortium partner, Princeton is considered part of the Rutgers Cancer Institute.

In this latest review, the NCI affirmed the entire state of New Jersey as Rutgers Cancer Institute's catchment area.

Also highlighted were efforts by Rutgers Cancer Institute research members in examining tobacco regulation and the impact on tobacco control policies, as well as the support of public health initiatives—including the recently developed ScreenNJ initiative with the New Jersey Department of Health to enhance cancer screening, prevention and education activity.

Inova dedicates Inova Schar Cancer Institute; John Deeken named president

The Inova Schar Cancer Institute will open its doors to patients on May 13. The center, which is a part of the Inova Health System and Inova Fairfax Hospital, offers multi-disciplinary, patient-centric cancer care.

The center was dedicated in a ceremony April 24.

In 2017, The Cancer Letter published a series of stories about the making of The Cancer Center and the community and business leaders who raised money for developing it (The Cancer Letter, [Dec. 8](#), [Nov. 17](#), [Nov. 10](#), 2017).

The center is named after developer and philanthropist Dwight Schar and his wife Martha, who made a lead gift of \$50 million to the center.

In conjunction with the dedication, John Deeken was named president of the Inova Schar Cancer Institute. Deeken, medical director for the Inova Schar Head and Neck Cancer Program, had been serving as acting president of Inova Schar.

Deeken replaces Donald "Skip" Trump, who retired from the job late last year.

In the past, Deeken served as the cancer center's chief medical officer and CEO of the Inova Translational Medicine Institute.

"When it comes to cancer, personalized care should not just mean taking care of a patient's medical problems, but treating the whole person, and that's what we do at Inova Schar," Deeken said in a statement. "That's why we've put everything in one state-of-the-art building, bringing doctors and the entire care team to the patients, not the other way around."

Letter urges exempting FDA rules from review by Congress and the president

Twenty-five health groups signed on to a letter to the Trump administration, urging that FDA be exempted from the requirement to submit proposed rules for review by Congress and the administration.

The Congressional Review Act, a law reaffirmed in a recent [memorandum](#) by the Office of Management and Budget, allows Congress to vacate agency rules by passing a joint resolutions of the House and Senate and obtaining the signature of the president.

The text of the letter follows:

Dear Mr. President, Secretary Azar, Mr. Mulvaney, Mr. Vought, and Mr. Grogan;

The undersigned organizations, representing millions of patients, advocates, caregivers, and health-care professionals strongly urge the Administration to reconsider the enactment of the memorandum issued on April 11, 2019, regarding “Guidance on Compliance with the Congressional Review Act.”

We strongly believe that if applied to the U.S. Food and Drug Administration (FDA), the public health, safety, and future well-being of the American people will be put at risk.

The FDA is unique from most all other agencies regarding the guidance process. The agency currently has a vigorous process for issuing and reviewing potential guidance, including a robust public vetting of draft guidance that are noticed and open for public comment and input long before they are finalized.

For decades, through this process, the FDA has put forth some of its most innovative and important pathways for how new therapies will be reviewed and how they can most safely and efficiently reach patients. With the current pace of scientific discovery unfolding at an unprecedented pace, the FDA needs to be able to effectively communicate with the biomedical research community without delay.

We respectfully ask that the Administration exempt the FDA to avoid the serious unintended consequences that delaying or impeding science would have on millions of patients and their families.

We welcome a future productive dialogue with the Administration surrounding the importance and rigor of the FDA guidance process and any other policy proposals that impact patients’ lives.

Sincerely,

Alliance for Aging Research
 American Academy of Pediatrics
 American Association of Colleges of Pharmacy
 American Society of Clinical Oncology
 American Society of Hematology
 Association of Clinical Research Organizations
 CancerCare
 Children’s Cause for Cancer Advocacy
 Fight Colorectal Cancer
 Friends of Cancer Research
 GO2 Foundation for Lung Cancer
 LUNgevity Foundation
 Melanoma Research Alliance
 Melanoma Research Foundation (MRF)
 National Alliance on Mental Illness
 National Coalition for Cancer Survivorship
 National Organization for Rare Disorders (NORD)
 National Osteoporosis Foundation
 National Patient Advocate Foundation
 Ovarian Cancer Research Alliance
 Prevent Cancer Foundation
 Research!America
 Solving Kids’ Cancer
 St. Baldrick’s Foundation
 Stand Up To Cancer
 The Leukemia & Lymphoma Society

UPMC Hillman Cancer Center joins Beat AML Master Clinical Trial

UPMC Hillman Cancer Center has become one of the 15 sites nationwide to offer a collaborative clinical trial for acute myeloid leukemia.

The Beat AML Master Clinical Trial, led by the Leukemia & Lymphoma Society, will test multiple targeted therapies for patients with AML (The Cancer Letter, [July 27, 2018](#)).

The standard therapy for AML has remained virtually unchanged for decades—a combination of chemotherapy and, for some patients, a stem cell transplant. Many patients, particularly those over the age of 60, cannot tolerate this harsh regimen. The Beat AML trial aims to change that with a precision medicine approach.

“AML is extremely aggressive, and clinical decisions on the appropriate therapies need to be made quickly,” Stanley Marks, chairman of UPMC Hillman Cancer Center, said in a statement. “To provide individualized treatment for each patient based on their genetic makeup will help us select the approach that gives the patient the best chance for a cure.”

The Beat AML trial uses sophisticated genomic technology to identify the genetic drivers of the patient’s AML to match them with an appropriate targeted therapy. More than 490 patients have been screened to date.

The Beat AML trial at UPMC Hillman Cancer Center will be led by Michael Boyiadzis, co-director of the acute leukemia program at UPMC Hillman.

“AML is not a uniform or a single disease,” Mounzer Agha, director of the Mario Lemieux Center for Blood Cancers at UPMC Hillman said. “It encompasses wide genetic variations that we will now be able to specifically target for each patient. It gives us a whole new approach to the way we currently treat AML.”

The LLS and its collaborators recently presented the first data from this trial at the 60th American Society of Hematology Annual Meeting.

The data showed that the trial already has met the primary endpoint, proving that with genomic technology, clinicians can identify the genetic mutations of AML patients to make a treatment decision within an unprecedented seven days. This was achieved for 95% of patients in the trial.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP



Inivata shows positive clinical validation results and real-world utility for its InVisionFirst-Lung liquid biopsy test

Inivata conducted two prospective, multi-center studies in collaboration with 41 key institutions across the United States. The data, published in *JCO Precision Oncology*, highlights the potential of Inivata's first Medicare-reimbursed commercial test to improve delivery of comprehensive tumor genomic profiling.

The publication follows the presentation of these data at the World Conference on Lung Cancer in September 2018.

The studies recruited 264 advanced NSCLC patients and compared the genomic profiling performance of InVi-

sionFirst-Lung versus standard-of-care tissue testing.

The studies showed that Inivata's liquid biopsy test demonstrated excellent concordance with tissue profiling, with a high level of sensitivity and specificity. Notably, the InVisionFirst-Lung liquid biopsy test was able to detect 26% more actionable alterations versus standard-of-care tissue testing. More comprehensive testing with InVisionFirst-Lung could lead to more accurate patient stratification and potentially to improved outcomes based on more personalized therapy.

Two prospective multi-center clinical validation and utility studies were conducted enrolling 264 advanced untreated NSCLC patients.

Tumor tissue-based genotyping was available in 178 patients for comparison to plasma profiling. The remaining 86 patients were included to compare ctDNA profiles across patients with and without tissue for profiling.

Considering specific alterations in the eight clinically relevant genes that most influence patient management in advanced NSCLC, sensitivity was 73.9% with 99.8% specificity; 97.8% PPV and 97.1% NPV.

Overall concordance of InVisionFirst-Lung with matched tissue profiling was 97.8%, 70.6% sensitivity and 99.2% specificity with 82.9% PPV, 98.5% NPV.

The studies support the hypothesis that InVisionFirst-Lung has clinical utility in over 50% of patients in untreated advanced stage NSCLC, based on detec-

tion of clinically relevant mutations in 53.8% of the enrolled patients.

Across the enrolled population, 48 patients with actionable alterations were identified by ctDNA testing compared to only 38 by tissue testing; InVisionFirst-Lung identified 26% more actionable alterations.

Trial suggests that treatment de-escalation in HER2-positive breast cancer needs to be personalized

De-escalation approaches in the treatment of women with HER2-positive breast cancer need to be personalized, according to Carmen Criscitiello at the European Institute of Oncology. Her comments will be included in a presentation of updated research results at the inaugural ESMO Breast Cancer Congress 2019, May 2-4, in Berlin.

"The introduction of anti-HER2 therapies has brought a huge survival benefit in early and advanced HER2-positive breast cancer, thus there is now a need for reducing the intensity and side effects of the treatment administered," Criscitiello said in a statement. "However, the priority is to identify which patients might be spared some toxic therapies without worsening the survival benefit."

A de-escalation strategy that omits chemotherapy in the first line treatment of

HER2-positive metastatic breast cancer was attempted in the PERNETTA trial. As previously reported, the strategy does not worsen two-year overall survival but significantly shortens progression-free survival.

The phase II trial randomly allocated 210 patients to trastuzumab plus pertuzumab alone vs. trastuzumab plus pertuzumab combined with chemotherapy until progression. After progression, both groups received T-DM1 as second line therapy.

The primary endpoint of overall survival at two years was reached by 77% of patients receiving antibodies alone and 76% of those who also had chemotherapy. Progression-free survival after first line therapy was 8.4 months with antibodies alone and 23.3 months with antibodies plus chemotherapy group.

New findings revealed today at the ESMO Breast Cancer Congress 2019 show that the results were similar regardless of hormone receptor status, and overall quality of life was also similar between groups during first line treatment. But according to analyses of adverse events and patient reported symptoms, those receiving antibodies alone had less hair loss, mouth sores, nausea, and fatigue.

The difference in PFS between groups has prompted the investigators to look for predictive factors to identify patients who could receive targeted therapy alone with little or no detriment in PFS. They are using the PAM50 test to profile tumours of all patients in the trial.

“Trials of HER2-positive breast cancer in the neoadjuvant setting have shown that the HER2 enriched subtype is the most sensitive to anti-HER2 therapy,” Jens Huober, first author, said in a statement. “Our hypothesis is that this also applies to the metastatic setting.

If the PFS difference is smaller in this subtype, then omitting chemotherapy in the first line may be a good option for these patients.”

Huober said the trial was conducted to discover if it is safe to omit chemotherapy from first line treatment of patients with HER2-positive metastatic breast cancer who receive dual anti-HER2 therapy followed by T-DM1.

“We looked at two-year OS because physicians are afraid they will lose patients early if they don’t give the maximum treatment,” Huober said. “PFS was shorter but did not seem to affect overall survival in the long run.”

“Omitting chemotherapy in the first line could be discussed as an option with patients who have a low to intermediate tumour burden. However, a phase III trial is needed for definitive proof that patients are not at risk of early death if they start with antibodies alone.”

ESMO spokesperson Criscitiello said it is important for studies in this field to select a specific population in which to attempt treatment intensity optimisation and agreed that using the PAM50 test to select patients with the HER2 enrichment subtype may be an effective approach.

“There was no biological selection of patients in the PERNETTA trial,” said Criscitiello, who also highlighted the choice of primary endpoint. “Here we have a PFS that is almost two times less than that achieved with chemotherapy.”

“The short OS endpoint did not capture if denying a treatment which is demonstrated to be meaningfully most effective impacts on long-term survival. In addition, the sample size is very small to detect a difference in OS. Avoiding chemotherapy in HER2-positive disease is appealing for patients and investigators, but it has to be done safely.”

Academic trials are now crucial in breast cancer, Criscitiello said.

“The prognosis of patients with breast cancer has dramatically improved thanks to several new available treatments; we might see a reduced interest from industry to further invest in this disease, especially in trials designed with de-escalation attempts,” Criscitiello said. “Independent academic supported trials are very important to investigate research questions which are relevant for patients and doctors, like de-escalation to less toxic and demanding treatments and the identification of patients who may benefit the most from such an approach.”

Genetic testing in women diagnosed with breast cancer decreases cost of care nationwide

A new study suggests Oncotype DX-guided treatment could reduce the cost for the first year of breast cancer care in the U.S. by about \$50 million—about 2% of the overall costs in the first year. The study, conducted by Georgetown Lombardi Comprehensive Cancer Center and NCI researchers, was published in JNCI.

The landmark TAILORx (Trial Assigning Individualized Options for Treatment) trial results suggested that use of the Oncotype DX gene test can offer women valuable information about treatment options, potentially sparing 70% of women from needing chemotherapy if they are newly diagnosed with the most common subtype of breast cancer. The information only applied to women with early-stage breast cancer that is hormone positive, HER2neu negative, and has not spread to the lymph nodes.

The projected cost savings in the new study are based on two factors: about a 50% increased cost in gene testing assuming that it will be done for all newly diagnosed women, which would be offset by an approximately 8% expected drop in the overall cost of chemotherapy due to fewer women being recommended this form of treatment. Chemotherapy is considerably more expensive than gene testing, hence the 8% reduction in its cost is greater, dollar-wise, than the 50% increase in cost for gene testing.

“Individual women’s decisions should not be about dollars and cents, but what is right for them based on consideration of the best evidence and personal preferences,” said Jeanne S. Mandelblatt, professor of oncology and medicine at Georgetown Lombardi.

Mandelblatt and her colleagues examined the monetary impact in the U.S. of providing care based on evidence from TAILORx. The researchers looked at statistics on gene testing and chemotherapy use in NCI and Medicare databases, before and after the TAILORx trial results were announced in 2018.

The periods during which costs accrue are usually grouped into three timeframes: initial costs, terminal costs, and continuing care costs. This study only estimated initial costs.

The estimated individual Oncotype DX test costs in this analysis were about \$3,400 and based on Medicare reimbursement rates. Many insurers, including Medicare, cover the cost for most women diagnosed with early-stage breast cancer. Another gene test that is used less often in the U.S., called MammaPrint, has similar costs.

The investigators estimated that, prior to 2018, the mean initial costs of healthcare nationwide for newly diagnosed women with breast cancer, which were fairly stable for a number of years, in-

cluded two components: chemotherapy costs of \$2.701 billion and Oncotype DX testing costs estimated to be \$115 million, for a total healthcare cost of \$2.816 billion in the first year after diagnosis. The researchers estimated that only 34.8 to 57.2% of women were receiving the Oncotype DX testing in this period as the clinical application of such tests was still uncertain.

In 2018, the TAILORx findings showed no benefit from chemotherapy for women whose tumors had lower risks for recurrence based on Oncotype DX scores. For their modeling, the researchers projected that all women with scores of 0-25 (low to intermediate risk) would forgo chemotherapy starting in 2018, so those treatment costs would go down by 8%, saving \$338 million in initial chemotherapy costs.

The researchers also assumed 100% of women would get Oncotype DX testing, raising those costs by \$116 million (from \$115 to \$231 million). The total initial costs for this period were therefore projected to be \$2.766 billion.

Comparing the two initial 12-month costs of care for the pre-2018 and 2018 and after periods, the researchers projected that the combined treatment and testing costs would decrease from \$2.816 to \$2.766 billion, for a net savings of about \$50 million (1.8% decrease).

“This study only answers the question about whether, in the first 12 months after diagnosis, costs of gene testing are likely to be offset by savings in avoided costs of chemotherapy—and the answer is yes. We did not estimate how the trial results could diffuse into medical practice, since those data will not be available for several years,” Mandelblatt said in a statement.

“The gene tests are not perfect predictors of who will ultimately have a recurrence of breast cancer, so it will be important to model the long-term

outcomes and costs from diagnosis to death.”

NCI’s Angela Mariotto was the first author on the paper. Additional authors from NCI include Valentina Petkov, Lindsey Enewold, Kathy J. Helzlsouer, and Eric Feuer. Additional authors include Jinani Jayasekera, of Georgetown and Clyde Schechter, of Albert Einstein College of Medicine.

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The authors report no relationships or conflicts of interest to disclose relevant to this study.

DRUGS & TARGETS



FDA approves pembrolizumab plus axitinib for advanced RCC

FDA approved pembrolizumab plus axitinib (Keytruda) for the first-line treatment of patients with advanced renal cell carcinoma.

Keytruda is sponsored by Merck.

Approval was based on KEYNOTE-426 (NCT02853331), a randomized, multi-center, open-label trial conducted in 861 patients who had not received systemic therapy for advanced RCC. Patients were enrolled regardless of PD-L1 tumor expression status and were randomly allocated to receive either pembrolizumab 200 mg intravenously every 3 weeks in combination with axitinib 5 mg orally twice daily, or sunitinib 50 mg orally once daily for 4 weeks and then off treatment for 2 weeks.

Treatment was continued until confirmed disease progression or unacceptable toxicity. Pembrolizumab was received for a maximum of 24 months.

The main efficacy measures were overall survival and progression-free survival, assessed by blinded independent central review (RECIST 1.1.) The trial demonstrated a statistically significant improvement in OS in a pre-specified interim analysis for patients on the pembrolizumab plus axitinib arm (HR 0.53; 95% CI: 0.38, 0.74; $p < 0.0001$).

With deaths reported in 18% of patients, the median OS was not reached in either arm. The 12-month OS rate was 90% in the pembrolizumab plus axitinib arm and 78% for those treated with sunitinib. The trial also demonstrated a PFS improvement for patients receiving pembrolizumab plus axitinib (HR 0.69; 95% CI: 0.57, 0.84; $p = 0.0001$). Median PFS was 15.1 and 11.1 months for those receiving pembrolizumab plus axitinib vs. sunitinib, respectively.

The recommended pembrolizumab dose for this indication is 200 mg every 3 weeks with axitinib 5 mg orally twice daily.

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