THE CANCER LETTER

Vol. 38 No. 21
May 25, 2012

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

Cancer Centers: Permanent Reinvention

Standard Procedures Discarded in Review Of $20 Million in Texas Funds For Project Led by Wife of MD Anderson President

By Paul Goldberg

Top-level scientists whose involvement lent credibility to an effort to invest $3 billion in Texas taxpayers' money in cancer research are saying that the state program departed from peer review procedures when it awarded its largest grant ever—to a technology incubator co-directed by the wife of the president of MD Anderson Cancer Center.

Earlier this month, the highly respected chief scientific officer of the Cancer Prevention & Research Institute of Texas resigned in protest over the decision to award as much as $20 million to a technology "incubator" co-directed by Lynda Chin, professor and chair of MD Anderson's Department of Genomic Medicine, who is married to the institution's president Ronald DePinho.

Chin's grant, the largest one-year expenditure in CPRIT's history, didn't go through the same peer review machinery to which standard research grants are subjected. Instead, the six-and-a-half-page proposal sailed rapidly through a commercialization review panel over less than three weeks.

(Continued to page 2)

Q&A with The Cancer Letter

MD Anderson Provost Had No Say

A controversial $20 million project that lists the wife of MD Anderson Cancer Center as the leading investigator didn't go through review by that institution's provost, The Cancer Letter has learned.

In an interview arranged by his institution's press relations staff, Raymond DuBois, MD Anderson provost and executive vice president, revealed that his office wasn't asked to review the proposal.

The proposal may have been reviewed by the provost at Rice University, which is slated to receive $2 million—only 10 percent—of the commercialization grant from the Cancer Prevention and Research Institute of Texas, DuBois said.

However, officials at Rice said that institution's provost didn't review the MD Anderson portion of the proposal, which means that it wasn't reviewed by any provost.

(Continued to page 14)

Follow us on Twitter: @TheCancerLetter

Permanent Reinvention
A $3 Billion Initiative
. . . Page 5

The Moon Shot
And Commercialization
. . . Page 5

Letters of Resignation
And Support
. . . Page 7

Protest from Sharp
And the Review Council
. . . Page 9

Houston Chronicle Asks
"Unsettling Questions"
. . . Page 10

MD Anderson and CPRIT
Defend the Grant
. . . Page 11

DePinho's Response
. . . Page 12

Nobel Laureate Gilman Resigns in Protest

(Continued from page 1)

In his letter of resignation, Alfred Gilman, a Nobel laureate, said that the $20 million joint project of MD Anderson and Rice University was, at its core, a scientific program, which needed to be subjected to scientific review.

The Cancer Letter has established that standard procedures were not followed either at MD Anderson or at CPRIT in the handling of the application.

• In a departure from standard procedures, the proposal didn't go through review by the MD Anderson provost. Raymond DuBois, the provost, said he wasn't asked to conduct a review. (See the Q&A on page 1.) Provosts manage the academic mission of their institutions, looking out for potential ethical pitfalls, which can occur when a husband and wife team holds key positions in an institution. The MD Anderson proposal includes expanding the capacity to conduct phase I trials, opening the potential for ethical problems to spill over into the clinic.

• The MD Anderson proposal was, in fact, submitted without review by any provost. Officials at Rice said that they reviewed only their own portion of the proposal. Rice officials said they "saw" the MD Anderson portion of the proposal after it was first submitted to the state funding agency.

• After bypassing standard institutional review, the MD Anderson portion of the proposal was submitted to CPRIT in a way that bypassed the procedures specified in the state agency's request for proposals. The proposal was submitted by an official of Chin's unit of MD Anderson directly to CPRIT chief commercialization officer via email.

• The CPRIT official then turned around and, bypassing the electronic filing procedures, forwarded the email over to the contractor that manages grant awards for the state agency, knowledgeable sources said. The contractor then forwarded the application to the reviewers.

• In another departure from rules, a meeting of outside advisors who reviewed the commercialization proposal was convened by the CPRIT general counsel, rather than the contractor, sources said.

• At that meeting, which was held March 21, a reviewer who recused himself—citing his role on the board of directors of a company founded by Chin and DePinho—was nonetheless invited to address the committee and describe the track record of the individuals involved.

• The chair of the five-member review committee and one member of the board figured on the Rice portion of the application, which had been reviewed earlier. The committee's chair didn't cast a vote, but the conflicted committee member voted on the MD Anderson portion of the application, state officials confirmed.

This Texas drama has been escalating in recent weeks.

Following Gilman's resignation from his position as CPRIT chief scientific officer, the members of the institute's Scientific Review Council, which conducts peer review and lends academic credibility to the state effort, wrote a letter to the CPRIT's state-appointed Oversight Committee.

The six-and-a-half-pager submitted by MD Anderson should have been subjected to scientific review, even though "it contained essentially no scientific detail," wrote Phillip Sharp, chair of the institute's Scientific Review Council, in a May 14 email and co-signed by the council as a whole.

Sharp, also a Nobel laureate, is a professor at the David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology.

In their letter, Sharp and other council members quoted the incubator's goals:

• Expand current target biology and small molecule discovery efforts

• Fund counter-screens against related protein family members

• Expand pipeline to include biologics

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

Editor & Publisher: Paul Goldberg
Associate Editor: Conor Hale

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.


iPad
Saturday, June 02, 2012 at 7:00am
100%
Top Charts
Velos Aversi for iPad
Velos, Inc.
Velos Aversi for iPad
Developer Page >
Tell a Friend >
velos
Adverse Event and GVHD
FREE
Category: Medical
Version: 1.0
Seller: Velos, Inc.
Description
Come learn more about Velos Aversi, a mobile device application developed in collaboration with MD Anderson and Stanford that captures:
• Adverse Events (using NCI CTCAE)
• Acute GVHD (Seattle criteria)
• Chronic GVHD (NIH consensus criteria)
• Immunosuppressant Dosage Summary
Requirements:
Compatible with iPad.
Using a Mobile App to Capture AEs and GVHD at Point-of-Care
WHEN: Saturday, June 02, 2012, 7:00am – 8:00am
WHERE: Hyatt Regency McCormick Place – Chicago, IL
ROOM: CC10AB
Breakfast will be included!
For more information about Velos Aversi, contact us at aversiapp@velos.com.
To learn more about Velos and our medical informatics solutions, visit us at www.velos.com!
Can't make the session? Visit us at Booth 19118 June 2-4 during the 2012 ASCO Annual Meeting!
Customer Ratings
Current Version
All Versions
Tap to rate
It's great!
Featured
Genius
Top Charts
Categories
Purchased
Updates
empowering clinical innovation
Not an official event of the 2012 ASCO Annual Meeting. Not sponsored or endorsed by ASCO or The ASCO Cancer Foundation.

• Invest in efforts to develop novel chemistry platforms to address traditionally undruggable protein targets.

This list prompts critics to ask: what is development of chemistry platforms for hitting "traditionally undruggable proteins" if it isn't research?

"Although the brief document was strikingly lacking in specific research plans, we would characterize these activities as research," Sharp, et al., wrote in the email sent to the CPRIT Oversight Committee. "Apparently, the absence of a specific research plan was taken by CPRIT leadership as justification for bypassing and review by CPRIT's panel of reviewers.

"As we understand it, CPRIT leadership determined that incubator proposals were to be considered under the category of commercialization, not research," the letter stated. "However, no products are mentioned in the IACS proposals, nor is a company involved."

DePinho was initially silent regarding the controversy, but after the Houston Chronicle published a hard-hitting editorial that laid out a series of questions about the grant, he responded with a letter that portrayed the central question in the controversy as a "difference of opinions."

"Some may choose to call our proposal 'research,'" he wrote in a letter submitted to the newspaper. "We call it business, and we are confident Texans will be the beneficiaries in the future.

"As one who has worked in the laboratory and the clinic and founded multiple biotechnology companies, I have learned that academic discoveries will only benefit patients if they are converted into approved commercial products. The current output of the IACS pipeline will prove its commercial impact in the near future."

MD Anderson Provost Didn't Review the Proposal

In an interview arranged by the MD Anderson press relations staff, Raymond DuBois, the institution's provost and executive vice president, confirmed that "a decision was made" for the proposal not to go through his office, which would have been a requirement for standard research grants.

DuBois said he surmised that the proposal went through the Rice University provost, but said he hadn't checked whether this was the case.

An estimated $18 million of the $20 million grant will be spent at MD Anderson, and an appendix to the application contained budgets and projections, which are usually of intense interest to provosts.

Rice officials told The Cancer Letter that their institution's provost didn't review the MD Anderson proposal. "Cindy Farach-Carson, Rice's vice provost for translational bioscience and PI for the Rice portion of the proposal, said she saw the document from MDACC in March," the institution's spokesman said in an email.

CPRIT Executive Director William Gimson told The Cancer Letter that the Rice provost "was involved" in submitting the documents.

"SRA [International, a contractor that manages peer review] received the proposals and distributed to [Commercialization Review Council] reviewers," he said in an email.

"The IACS business plan was initially submitted to [Chief Commercialization Officer] Jerry Cobbs and he immediately turned around and sent it to SRA. SRA sent it to the peer review members," wrote Gimson.

The MD Anderson application was submitted to Cobbs by Eric Devroe, the IACS executive director for strategic alliances, state officials confirmed.

Meanwhile, the Rice portion of the application was forwarded to SRA in a manner specified in the RFA, Gimson confirmed. Not only is MD Anderson getting most of the money, but the CPRIT website lists Chin as the "primary investigator/program director" on the grant: http://www.cprit.state.tx.us/funded-grants/

Bypassing the provost of your own institution is puzzling and unusual in the extreme, grant administrators and ethicists say. A provost is the chief academic officer responsible for managing the institution's academic integrity.

"If a provost has heartburn about something, you want to hear it," said Arthur Caplan, the Sidney D. Caplan Professor of Medical Ethics in the Department of Medical Ethics and Health Policy at the University of Pennsylvania. "If you have animal experimentation or phase I research, you need to involve all the university and hospital officials that need to be aware be aware.

"You put the institution at risk when you go off course in terms of regular review procedures."

In a situation where a husband and wife team is employed in key positions at the same institution, the provost should play a more significant role, especially when research on human subjects and animals is involved.

A situation where a nepotism issues can arise requires more scrutiny rather than less scrutiny. "You can say, we would normally take it though the provost, but we are going to do something extraordinary because of a concern about a nepotism issue," Caplan said.

Additional review is needed in case a provost is unable to say No to the president. "In any case, it's a

mistake not to let the provost sign off on the institution's portfolio," Caplan said. "If they want to have a special committee look into conflicts of interest, I have no issue with that, but they should not reach out of the standard pattern," Caplan said.

"That creates the worst appearance."

Is it reasonable for an institution to rely on a provost of another institution to review a research project?

"It's not possible to outsource an institution's academic mission," Caplan said. "I have never heard of such a thing. It seems strained and strange. It also feels like a unilateral action by someone in the administration. It would be hard to imagine a faculty senate approve something like this."

A $3 Billion Initiative

Vast sums of money and stellar reputations are at stake in this controversy. In 2007, Texas voters approved the largest investment in cancer research outside the federal government: $3 billion, to be spent over 10 years. So far, the program has spent over $670.7 million on research within the state and on helping recruit scientists from the outside. Altogether, $489.6 million went to research, $111.4 went to commercialization, and $69.7 went to prevention.

A program to fund research can be only as good as the peer review system that oversees it, and the CPRIT's scientific peer review has been one of the best.

Scientists involved in reviewing grants said they were involved in part because they realized that 70-year-old Gilman, who shared the 1994 Nobel Prize in Physiology or Medicine with Martin Rodbell for discoveries involving G-proteins, ran a clean operation that was devoid of conflicts of interest.

Both Gilman, professor emeritus at UT Southwestern, and the reviewers see this matter as something other than a difference of opinion. Letters from Gilman and Sharp, et al., point to matters of principle, which is what scientists do before they leave and slam the door behind them.

Gilman did. The letter from Sharp, et al., suggests that others very well may follow.

The review board members write that Gilman's "reputation for integrity and high standards of scientific leadership is what attracted us to serve as chairs and panelists in the peer review process for CPRIT." Should these academics find something else to do with their free time, it's not clear how CPRIT could recover.

Gilman and other scientists fear that technology incubators that can be described without any scientific detail would allow research proposals to slip through without scrutiny.

In the resignation letter, dated May 8, Gilman wrote that he wanted to stay through October to shepherd through some unfinished business, which included making certain that the Oversight Board approves investigator-initiated grants that had gone through peer review and to stand in the way of "further award of vast funds for research programs ostensibly within incubators that were not described and therefore could not have been reviewed."

In their letter, which has been distributed to all members of peer review committees, the Scientific Review Council members said that incubators are an affront to the process.

"We are surprised and disappointed by the failure of proposals of this sort to receive scientific (research) peer review," Sharp and other members of the Scientific Review Council wrote. "The $20M one-year award is by far the biggest that CPRIT has ever made. As members of the body that has been authorized to pass judgment on the merits of scientific proposals made to CPRIT, we will be viewed to have approved this award, and the failure to include us in the process calls into question our roles and the integrity of the review program in general.

"More importantly, this bypass is inherently unfair to every scientist in Texas who participates in the CPRIT program. Over this past two years, we have reviewed proposals from many Institutions in Texas that include one or more of the four scientific objectives listed above. These scientists have played by the rules that we understood were established by CPRIT's Oversight Committee and publically stated in the announcements of the program."

The Moon Shot and Commercialization

This drama appears to be closely linked to changes DePinho is making at MD Anderson.

He has created an Institute for Applied Cancer Science, which will receive most of the money given by CPRIT and, separately, has initiated a project described as "the moonshot," in which MD Anderson faculty committee would identify five major cancers and develop plans to cure them within five years.

Twelve teams are now working competitively to come up with plans for these five cures. The results will be announced in September. Next, $3 billion would have to be raised for the cures.

The drug discovery program launched by DePinho and Chin is not so much a creation of academic medicine as a hybrid of academia and industry. This approached

emerged when the couple ran the Belfer Institute for Applied Cancer Science at the Dana-Farber Cancer Institute. More than 50 people followed DePinho and Chin from Belfer to MD Anderson.

"Belfer was an organization that was within an academic environment, but was successful in spinning out entrepreneurial-based companies, some of which have become successful," said Robert Young, who first became aware of the couple when he was the chair of the scientific advisory board at Dana-Farber.

Young, former director of Fox Chase Cancer Center, now serves on the board of directors of AVEO Oncology, a company that DePinho and Chin founded, and is a member of CPRIT's five-member Commercialization Review Council.

At the IACS, Chin and colleagues say they want to have the freedom to initiate (or kill) projects rapidly with the goal of producing compounds, as opposed to papers in top-tier journals.

One striking example of a more corporate MD Anderson is a video describing this initiative and featuring Chin and Giulio Draetta, professor in the Department of Genomic Medicine and director of IACS: http://www.mdanderson.org/publications/conquest/issues/2012-spring/drug-development-cancer-research.html

According to the proposal, MD Anderson plans to invest $75 million of its own funds in IACS projects.

In his letter to the Houston Chronicle, DePinho described the genesis of the incubator application. The brief proposal took three months to prepare and didn't include science because it wasn't presented as a research project.

"That Rice and MD Anderson received a $20 million award from CPRIT speaks to the quality of the business plan we submitted with Rice and coincides with MD Anderson's new capabilities," he wrote.

"Last fall, we learned that a CPRIT commercialization review found that no incubator proposals were worthy of funding, but that a proposal from Rice had significant merit, if a pipeline for producing drugs/agents could be identified as a partner. With this knowledge, the scientists at IACS began a three-month process of writing a top-flight business plan to pair with Rice's ideas.

"MD Anderson and Rice applied for the grant based on a request for proposals issued by CPRIT. Our final proposal presented a solid business strategy to enhance drug development and new company formation. The proposal received four outstanding reviews from knowledgeable individuals outside Texas. Because it is not a research project, no in-depth science was included."

The MD Anderson portion of the incubator proposal and a 10-page supplement, which includes the biographies of key staff members and budget projections, are both posted at: http://www.cancerletter.com/categories/documents.

IACS appears to be a component of DePinho's focus on curing five cancers. He unabashedly uses the words "cure" and "moonshot," portraying cancer as an engineering problem that can be solved by teams of scientists.

Last October, in a speech to the MD Anderson Board of Visitors, DePinho quoted John F. Kennedy's "moon speech," delivered at Rice University a half a century earlier:

"We choose to go to the moon. We choose to go to the moon in this decade and do the other things, not because they are easy, but because they are hard, because that goal will serve to organize and measure the best of our energies and skills, because that challenge is one that we are willing to accept, one we are unwilling to postpone, and one which we intend to win."

Then, like so many cancer program leaders before him, DePinho drew the parallel between the moonshot and the disease:

"So, what will our cancer moon shot look like?

"In this decade, the cancer genome atlas will provide scientists with the list of genes that are mutated in cancer.

"With the complete list of mutated genes in hand, we will make use of our newfound ability in functional genomics to silence specific genes at will. We can see if the extinction of a mutated gene causes the cancer cell to die. We anticipate that there will be several hundred genes playing critical roles in cancer and our goal will be to identify every one of these rogue genes.

"It is important to appreciate that going after a single target will not lead to cure. Cancer DNA is highly unstable, allowing for emergence of resistance. Thus, the key to success will be to determine which combination

of targets will need to be co-extinguished in order to elicit durable responses, i.e., cure. This is key—there is no single magic bullet.

"With that list of key drivers, we can genetically engineer perfect models of human cancer. Test drug and drug combinations. Needed are combination strategies—designed to co-extinguish multiple cooperative targets as well as harness the power of the immune system to eliminate every last cancer cell in the body.

"Once drugs are in hand, we need sophisticated mouse model systems to enable testing of combinations prior to clinical testing, and we need a clinical trial design that incorporates the genotyping to select tumors with those targets.

"This is the future of treatment at MD Anderson."

DePinho's speech is posted at: http://www.cancerletter.com/categories/documents.

DePinho isn't the first cancer politician to promise the cure. The most recent predecessor was fellow Texan and former top-level MD Anderson official Andrew von Eschenbach, who structured his tenure as NCI director around the goal to "eliminate suffering and death due to cancer" by the year 2015.

"Ron does have a somewhat different view of how to go about impacting cancer than someone from classic academia," said Young. "He is intensely interested in taking world-class science and moving it much more rapidly into clinical application."

Does Young cringe when he hears the words 'moon shot,' which have been uttered in the context of cancer so many times in the past?

"Having been around this a long time, I think it gets a little bit overblown," he said. "I think he really does believe that the targeted approach to cancer, the knowledge base that's emerging about the specific defects associated with particular cancers, is going to transform the field.

"I certainly hope that's true," Young said. "I am not quite as convinced that this whole thing is going to break open tomorrow morning.

"I hope I am wrong."

Letters of Resignation, Support

For now, MD Anderson and state officials in Texas will need to contend with terrestrial problems.

It's not clear what role the state funds will play in fueling the DePinho vision, especially if the peer review system Gilman built falls by the wayside.

Earlier this week, the Houston Chronicle published a story in which it said that two members of CPRIT's five-member Commercialization Review Council that recommended approval of the incubator had ties with the project.

According to the Chronicle, the CPRIT Commercialization Review Council chair Robert Ulrich, general partner in Vanguard Ventures, figured in the proposal as a "distinguished member," and another member of the Commercialization Review Council, Jack Geltosky, managing director of JEG and Associates LLC, was listed on the Rice proposal's "strategic investment committee."

The Chronicle story is posted at: http://www.chron.com/default/article/Conflicts-of-interest-possible-in-Houston-cancer-3578293.php.

Another member of the five-member council, Young, serves on the board of directors of AVEO Oncology, a company founded by DePinho and Chin.

CPRIT officials said that Ulrich, being the chair of the panel, didn't vote on the matter and Geltosky voted on the MD Anderson portion of the application, recusing himself from the Rice portion. (This raises questions of whether it was possible to separate two portions of what appears to be a single application, several insiders said.) Young, too, recused himself.

CPRIT Executive Director Gimson said all procedures were followed. His email blast accused the Houston Chronicle of being unbalanced and "inflammatory," to which the reporters responded with a blog post: http://blog.chron.com/sciguy/2012/05/cancer-research-group-objects-to-the-chronicles-inflammatory-story/#comments.

In an interview with The Cancer Letter, Young confirmed that he recused himself from voting on the proposal, but said that Jerry Cobbs, CPRIT's chief commercialization officer, had invited him to discuss DePinho's and Chin's track record in commercialization of drugs and his long-running professional association with the couple. Young spoke prior to discussion of the proposal.

"The committee asked me was what was my experience with Belfer and AVEO," Young said.

Though Young's role on the company, by anyone's standards, constitutes a conflict, it provided Young with information that the committee wanted. "One of the things I learned about the way they go about evaluating potential new opportunities is whether or not the model has been used and whether it's successful," he said.

Gimson said that the comments were provided to the group "with the understanding that Dr. Young had recused himself from the deliberations—and our policies allow for this kind of interaction in special cases."

Young said his role in the review points to the

differences between the classical model of grant review, as opposed to review of commercialization projects.

"There is a philosophical difference and the set-of-criteria are different for the evaluation of classical grant review and reviews of potential commercialization programs," Young said.

"I spent most of my life in the other side of the forest, on classical grant review. It's only later on in my life that I got involved with the other role and began to look at how experts evaluate the potential for success in emerging biotechnology opportunities. And one of the things that I learned from venture capitalists and other people who do this for a living is how much weight they place on the leadership team and how much weight they place on previous success with a particular business model.

"And that's the big difference in this particular situation. There will always be big differences between these two groups, because in a sense they are looking at the problem from a different vantage point."

Commercialization vs. Investigator-Initiated Grants

CPRIT can spend no more than $300 million a year for ten years, with reauthorization by the state assembly every two years.

These funds have to cover research, commercialization and prevention. Gimson said that the current controversy has prompted him to propose that the governing 11-member Oversight Committee set a distribution formula for CPRIT's future projects.

Gimson said that funding the incubator precluded him from bringing forward the proposals for seven large peer-reviewed grants for multi-investigator awards that required nearly $40 million.

"I was aware of the fact that these incubator and other company awards were coming in to the March meeting," Gimson said to The Cancer Letter.

Altogether, commercialization was projects totaled $50 million.

"Our Oversight Committee has a great interest in commercialization projects, they have been encouraging us to increase commercialization," Gimson said. "We couldn't fund both.

"So I felt, from a priority perspective, it was best to come forward with the commercialization projects, hold the seven multi-investigator awards for a few months," he said. This way, the seven grants could be funded with next year's money after the new fiscal year starts on Sept. 1.

This version of events differs substantially from one that appears in Gilman's letter of resignation and the subsequent letter from Sharp and other peer reviewers, which suggest that cross-state rivalry between academic institutions has spilled over to the Oversight Committee and CPRIT.

Reviewers had also gone through a pool of 40 proposals for multi-investigator grants, selecting seven of them.

Gimson declined to bring these projects forward to the Oversight Committee, telling Gilman that Oversight Committee members may object to having a large proportion of the grants go to UT Southwestern.

"By this action, members of the Oversight Committee essentially accused Al of somehow biasing the system," Sharp and other members of the Scientific Review Council wrote. "Such an accusation of bias implies further that we and the members of our review committees participated in the scheme, a point that we vigorously deny.

"We judge the review system managed by Al Gilman and led by us to not have been biased in any way relative to any institute or individual. At every point in this process, we have attempted to select the best cancer research and cancer scientists in the service of the citizens of Texas."

The text of Gilman's letter of resignation follows:

The purpose of this letter is to indicate my Intention to resign from CPRIT, effective (with your permission) on October 12, 2012. At that time I will have worked for CPRIT for over three years—I believe longer than originally anticipated.

During that time we have launched strong programs because funding decisions have been based on high-level competitions, where the judges have been some of the best cancer researchers and physicians in the country—free of conflicts of interest and all coming from outside of Texas. It was exciting to launch this program, to design effective requests for applications, and to oversee the peer review process.

The program is now essentially at a steady state. Research activities that are yielding exciting results should be continued, and new applications should continue to be received—but some programs will perhaps need to be constrained or curtailed because of the desire to fund competitive renewals and expand commercialization activities. I doubt it will be possible to launch new Initiatives at this point.

The job of Chief Scientific Officer has become routine. You no longer require a full-time person. Your most critical concern will be to keep the external peer review system intact—retaining as many of the current committee chairs as possible. Your ability to

do so will be critically dependent on the attitudes of CPRIT leadership, especially including the Oversight Committee.

I have chosen the resignation date of October 12 for a few specific reasons:

• The next Scientific Review Council meeting that is scheduled to approve a slate of recommended research grants is October 5th. I will stay until then to be certain that those who are preparing applications to be submitted by May 31 will still encounter a functional peer review system.

• Major decisions about research funding will be made by the Oversight Committee in July. I will attend that meeting to champion the research slate and to make it clear to the Committee that negative decisions about it would have a fatal impact on CPRIT's peer review system. Negative actions would In addition be extremely harmful to the research community's view of science in Texas, and thus on the ability to recruit scientists to the state (or, for that matter, the ability to attract capital for commercialization efforts). The MIRA grants to be presented to the Oversight Committee in July should have been funded In March; further delay simply must not happen. Also, July will see a large number of recommended recruitment applications. The relevant institutions are already engaged in attempts to secure commitments from these excellent candidates; some have already succeeded.

• If additional incubator grants are to be approved at the July meeting of the Oversight Committee, I will be there to hope that the rules governing review and funding of incubators have been revised to prevent further award of vast funds for research programs ostensibly within incubators that were not described and therefore could not have been reviewed.

• A delay of my resignation until October provides you with an extended opportunity to find someone new to fill my position.

• I ask for one additional week after the October 5th meeting of the Scientific Review Council to complete my affairs, dispose of professional books and papers, vacate my office, etc. I will be ending my career during its 42nd year.

Protest from Sharp and the Review Council

The text of the email from the Scientific Review Council members follows:

Date: Mon, May 14, 2012 at 9:11 AM
To: Members of CPRIT's Oversight Committee (James Mansour, Joseph Bailes, and William Gimson)
From: CPRIT's Scientific Review Council (Phillip Sharp, Clara Bloomfield, Sam Gambhir, Tyler Jacks, William Kaelin, Richard Kolodner, Charles Sherr, Everett Vokes)

We received the letter (on May 11) from James Mansour, Joseph Bailes, and William Gimson proclaiming their faith in the peer review system established under the initiative of Al Gilman for CPRIT: "complete trust in the gold standard process that CPRIT has established". Further, "we know that the Oversight Committee wholly supports, and will continue to support, this process and will expect the Institute to maintain the high level of integrity and excellence that has been established."

However, these statements seem inconsistent with recent actions taken by CPRIT management or its Oversight Committee, and these actions are the reasons for Al Gilman's resignation. The following is a response to these statements set in the context of the related events as we understand them.

1. The seven Multi-Investigator Research Applications that the Review Committee recommended for funding (out of the 40 that were reviewed) were never brought to the Oversight Committee for approval and funding at its March meeting. As related by Gilman, Mr. Gimson stated that the reason was that he feared they would not be approved because of opposition from certain Oversight Committee members over the fact that a substantial fraction of the funding would go to UT Southwestern. By this action, members of the Oversight Committee essentially accused Al of somehow biasing the system. Such an accusation of bias implies further that we and the members of our review committees participated in the scheme, a point that we vigorously deny. We judge the review system managed by Al Gilman and led by us to not have been biased in any way relative to any institute or individual. At every point in this process, we have attempted to select the best cancer research and cancer scientists in the service of the citizens of Texas.

2. At the same meeting of the Oversight Committee in March, 2012, a $20M award for one

year's effort was approved for an incubator at Rice University and for research at The Institute for Applied Cancer Science (IACS) at MD Anderson. Approximately $18M of that award is slated for the IACS at MD Anderson. The IACS proposal was 6.5 pages long. It was submitted just a few weeks before the Oversight Committee meeting, and it contained essentially no scientific detail. The stated intent of the IACS is to discover anti-cancer drugs. From the proposal, it appears to have been developed to:

• Expand current target biology and small molecule discovery efforts

• Fund counter-screens against related protein family members

• Expand pipeline to include biologics

• Invest in efforts to develop novel chemistry platforms to address traditionally undruggable protein targets

Although the brief document was strikingly lacking in specific research plans, we would characterize these activities as research. Apparently, the absence of a specific research plan was taken by CPRIT leadership as the justification for bypassing any review by CPRIT's panel of reviewers.

As we understand it, CPRIT leadership determined that incubator proposals were to be considered under the category of commercialization, not research. However, no product candidates are mentioned in the IACS proposal, nor is a company involved. After concluding that this proposal should be considered under the rules governing incubators, CPRIT followed the letter of their own law, in that incubator proposals were not to be reviewed for scientific content.

We are surprised and disappointed by the failure of proposals of this sort to receive scientific (research) peer review. The $20M one-year award is by far the biggest that CPRIT has ever made. As members of the body that has been authorized to pass judgment on the merits of scientific proposals made to CPRIT, we will be viewed to have approved this award, and the failure to include us in the process calls into question our roles and the integrity of the review program in general.

More importantly, this bypass is inherently unfair to every scientist in Texas who participates in the CPRIT program. Over this past two years, we have reviewed proposals from many Institutions in Texas that include one or more of the four scientific objectives listed above. These scientists have played by the rules that we understood were established by CPRIT's Oversight Committee and publically stated in the announcements of the program.

As the Oversight Committee is aware, in order to reduce possible conflict of interest, all members of the research peer-review teams are not from Texas and that we and the reviewers are excluded from discussions in which a real (or perceived) conflict of interest might arise because of a relationship with a Texas institution or investigator.

Moreover Gilman, when present at the meetings, is there as an observer and to answer procedural questions. During the review process, Gilman does not offer an opinion on the scientific merit of a proposal, investigator, or institution. In fact, Gilman's reputation for integrity and high standards of scientific leadership is what attracted us to serve as chairs and panelists in the peer review process for CPRIT.

We firmly believe that the integrity of the CPRIT review process and its proper implementation are essential for advancing cancer research and cancer care in Texas.

We would appreciate it if you would please forward this letter to the other members of CPRIT's Oversight Committee and let us know when you have done so. It is essential that all members of this group are informed about the issues that face CPRIT. We are distributing copies of this letter to all members of CPRIT's research peer review committees.

Sincerely yours,

Phillip A. Sharp [Koch Institute for Integrative Cancer Research Massachusetts Institute of Technology]

Clara Bloomfield [Ohio State University Comprehensive Cancer Center]

Sanjiv Gambhir [Stanford Cancer Institute]

Tyler Jacks [MIT Koch Institute for Integrative Cancer Research]

William George Kaelin, Jr. [Dana-Farber Cancer Institute]

Richard Kolodner [University of California San Diego]

Charles J. Sherr [St. Jude Children's Research Hospital and Howard Hughes Medical Institute]

Everett Vokes [The University of Chicago]

Houston Chronicle Asks "Unsettling Questions"

On May 20, The Houston Chronicle published an editorial titled "Cancer Grant raises troubling questions" (http://www.chron.com/opinion/editorials/article/Editorial-Cancer-grant-raises-troubling-questions-3570013.php).

The editorial states that the grant raises a series of what the paper described as "unsettling questions,"

which include:

• Why is CPRIT even funding commercial enterprises? Didn't voters expect the bond money to support research?

• What exactly does CPRIT require of a research incubator? MD Anderson, which will receive the bulk of the $20 million grant, submitted a proposal only six and a half pages long. When millions of taxpayer dollars are on the table, we expect more explanation.

• Why did CPRIT consider this a business incubator grant—the first that the institute has ever awarded—instead of a scientific proposal? The proposal doesn't mention any products or businesses. And according to Gilman, it involves "early-stage, pre-clinical drug discovery." Isn't that research?

• Why are considerations behind the grant still not thoroughly public? CPRIT officials told the Dallas Morning News that the proposal was more thorough and involved than is publicly known. But if that's true, why not divulge those details to the taxpayers footing the bill?

• Did CPRIT properly weigh the possibility of a conflict of interest? The incubator's head, Dr. Lynda Chin, is married to MD Anderson president Dr. Ronald DePinho. But the reviewers didn't seem troubled by anything in the proposal: It whizzed to approval in three weeks, without even an in-person presentation.

• Was that grant fair to other Texas scientists who proposed similar research, applying for CPRIT money through the regular scientific-review process but not marketing their labs as business incubators? CPRIT's panel of reviewers says no, and we agree.

• Will the eminent scientists who serve on CPRIT's review panel resign? We hope not. But as Phillip Sharp, the panel's chairman, told Chronicle medical reporter Todd Ackerman, their decisions depend on CPRIT's future actions: "We'll have to wait and see."

• Will this mess hurt Texas' scientific credibility? And will future research grants seem just as questionable?

• Why did CPRIT consider this a business incubator grant—the first that the institute has ever awarded—instead of a scientific proposal?

MD Anderson, CPRIT Defending the Grant

The following day, MD Anderson Provost and Executive Vice President Raymond DuBois sent out an email to the institution's "faculty and administrative leaders."

The communication, which addresses some of the questions, reads:

Yesterday's Houston Chronicle carried an inflammatory editorial concerning the CPRIT incubator grant recently awarded to Rice University and our Institute for Applied Cancer Science (IACS)...

As many of you already are aware, a $20 million CPRIT commercialization grant awarded to Rice University and MD Anderson is at the heart of the controversy. Some said the grant proposal should have been evaluated as "research," following one set of CPRIT guidelines. Others on the CPRIT board and staff accepted the proposal for what it is—a business plan to "commercialize" research findings—so it was evaluated using a different set of CPRIT rules.

At first, we viewed this debate as a difference of opinion between Dr. Alfred Gilman and others on the CPRIT board and staff. We have remained silent out of respect for both Dr. Gilman and the agency leaders. With the latest accusations in the Chronicle, it is clear that we need to speak up and provide information to explain the award and the process taken to receive it.

Since the institute was first announced last fall, IACS has consistently been presented as a professional drug development enterprise designed to generate mature assets for commercialization via co-development alliances or new company formation. With its team of industry-seasoned professional staff, it definitely is ***not*** a typical academic research program. No one at MD Anderson or Rice has ever portrayed it that way.

IACS and Rice joined forces because, together, we knew we could create a powerfully transformational incubator for the emerging life sciences industry in Houston.

MD Anderson and Rice did nothing "wrong" in applying for the grant based on an RFP issued by CPRIT.

Following the RFP, the IACS and Rice teams worked together for more than three months, with guidance from CPRIT, to develop the business plan. The final proposal presented a solid business strategy to enhance drug development and generate IP that could be used to establish new companies. Because this process is not a typical research project, no science was presented.

The IACS professional team is committed to science-driven drug discovery and development, but as its name indicates, it is APPLIED, not DISCOVERY science that it will perform. No targets or programs were presented in the proposal because it described a business plan for drug development.

The Rice-MD Anderson joint proposal was submitted to CPRIT as a venture in commercialization. The proposal was reviewed by CPRIT's Commercialization Review Committee and received four enthusiastic recommendations for funding from knowledgeable individuals outside the state of Texas. The CPRIT Board then met and approved the funding.

Basic discovery research is important, but without its application patients will not benefit in the long run. This joint venture will enable not only development of new drugs to benefit cancer patients worldwide, but also enhance the formation of sustainable biotech companies in Texas to create jobs and further economic growth. We are proud and excited to work together with our colleagues at Rice in this endeavor. With the support of CPRIT, I am confident that the Institute for Applied Cancer Science will prove itself worthy of this valuable funding.

Those who know the IACS understand what it is and what it is not. We will extend invitations for an on-site visit to CPRIT science reviewers and staff to obtain an accurate view of this truly game-changing institute.

DePinho's Response

DePinho, too, responded in a letter to the editor.

The text of the letter, as submitted to the newspaper, follows:

The debate over the CPRIT grant to Rice University and The University of Texas MD Anderson Cancer Center has little to do with either the rigor of the CPRIT grant review process or the quality of the proposal we submitted.

I believe it boils down to a difference of opinion. Rice and MD Anderson developed a strategy to *commercialize* research in Texas and responded to a CPRIT request for proposals. Some others think our business plan should have been evaluated as a research project, which it is not.

At first, we at MD Anderson viewed this as a debate between the CPRIT board and staff and Dr. Alfred Gilman. We remained silent out of respect for both Dr. Gilman and the CPRIT leaders. With the questions raised in Sunday's Houston Chronicle editorial, it's clear we need to state MD Anderson's position.

Commercialization is a relatively new venture for us. MD Anderson has not previously submitted a commercialization proposal anywhere near this magnitude to CPRIT because, quite frankly, prior to the creation last fall of our Institute for Applied Cancer Science, we did not have the capability to compete in that arena. IACS is a game-changer—not a traditional research undertaking—that provides a robust pipeline for successful drug development.

We already have earned $125 million in research, recruitment and technology awards from CPRIT, offering our research ideas for scrutiny under CPRIT's rigorous review process and high standards. (MD Anderson also holds more competitive research grants and more grant dollars from the National Cancer Institute than any other U.S. institution, another measure of our own high standards for research.)

That Rice and MD Anderson received a $20 million award from CPRIT speaks to the quality of the business plan we submitted with Rice and coincides with MD Anderson's new capabilities.

Last fall, we learned that a CPRIT commercialization review found that no incubator proposals were worthy of funding, but that a proposal from Rice had significant merit, if a pipeline for producing drugs/agents could be identified as a partner. With this knowledge, the scientists at IACS began a three-month process of writing a top-flight business plan to pair with Rice's ideas.

MD Anderson and Rice applied for the grant based on a request for proposals issued by CPRIT. Our final proposal presented a solid business strategy to enhance drug development and new company formation. The proposal received four outstanding reviews from knowledgeable individuals outside Texas. Because it is not a research project, no in-depth science was included.

Historically, academic medicine has relied on the pharmaceutical industry to bring new drugs to patients. However, that industry is struggling with shrinking research and development budgets, poor success rates and challenges with dismantling the traditional and more profitable "blockbuster" based business models in order to deliver personalized cancer care. The current academic-biotech-pharma ecosystem experiences a 95% failure rate for drugs entering into clinical trials.

Under the direction of Dr. Giulio Draetta, former worldwide head of oncology drug development at Merck, the IACS is a new hybrid model that blends the best features of academia and industry into a cohesive organization. With its industry-seasoned professional staff numbering 56, the IACS conducts rigorous, goal-oriented, milestone-driven activities with sufficient resources allocated toward programs with the highest degree of long-term success in the clinic.

Some may choose to call our proposal "research."

We call it business, and we are confident Texans will be the beneficiaries in the future. As one who has worked in the laboratory and the clinic and founded multiple biotechnology companies, I have learned that academic discoveries will only benefit patients if they are converted into approved commercial products. The current output of the IACS pipeline will prove its commercial impact in the near future.

CPRIT Official Offers Explanation

CPRIT Executive Director Bill Gimson also issued a response to the editorial:

The Cancer Prevention and Research Institute of Texas (CPRIT) has one goal—to end cancer. We take that responsibility and the faith entrusted to us by the people of Texas very seriously. The Editorial published in this paper on May 20, 2012 did a disservice to that lofty goal and the work of the Institute by not reporting the facts accurately.

As Executive Director, I have a responsibility under the law that established the Institute to "give priority to....expedite innovation and commercialization." One may ask why the Legislature placed an emphasis on anything other than basic research. The reason is that while $500 million invested to date by the Institute supports research in academic settings, we know that to actually deliver lifesaving products to cancer patients, this research must be taken out of the lab and made into drugs for patients—a process that is often referred to as commercialization.

Our mandate includes prevention, research, and commercialization of cancer research. It is important to note that our nation funds tens of billions of dollars in research, much of it basic research through the National Institutes of Health.

Academic research is critical to our success; however, we at CPRIT are also mindful that Texans did not want to merely duplicate or replace federal funding for cancer but rather wanted us to invest in areas with promise that have not been fully resourced.

The Rice and MD Anderson Incubator is the very first of its type funded by CPRIT. The single purpose of this enterprise is to participate in the early and very difficult phase of transforming discoveries from those academic labs and others into the drugs that ultimately save the lives of cancer patients.

The Institute's governing body, the Oversight Committee, directed CPRIT to develop incubator requests for application more than a year ago and to have them reviewed through the commercial process, as that is where the appropriate expertise lies to review such grants.

The Rice/MD Anderson Incubator was peer reviewed, just as the Oversight Committee directed, by experts and scientists with relevant commercial experience.

The Institute has three distinct areas – prevention, research and commercialization—each with its own group of reviewers with relevant subject matter experience. Importantly, all of these reviewers live and work outside of Texas to avoid conflicts.

We did indeed move quickly with the review of the collaboration between Rice and MD Anderson, just as we have fast tracked other very exciting and potentially lifesaving commercial ventures and research recruitment awards—which can be approved in as little as a couple of weeks.

The combined Rice and MD Anderson applications were nearly ninety pages (including a seventeen page business plan from MD Anderson) and the review process began with the review of the Rice portion in the last quarter of 2011. Dr. Lynda Chin, an extraordinary scientist, was recruited from Harvard to MD Anderson.

Dr. Chin's skills were considered so important to the State that she was selected as a "CPRIT Scholar" by our scientific peer review chairs and funding help with her recruitment was provided by our Institute. You have wronged Dr. Chin by suggesting a conflict of interest.

Neither she nor Dr. DePinho served on the Scientific Review Council that designated her as a CPRIT Scholar, nor on the Commercialization Review Council that suggested funding of the incubator award.

The incubator award is intended to fund a unique drug development model under the leadership of Dr. Giulio Draetta as the director and Dr. Chin as the scientific director. It's important to note that Dr. Draetta is a veteran drug developer who has previously led oncology efforts at both Merck and Pharmacia.

I am extremely proud of the work that the small, dedicated staff of the Institute does on a day-to-day basis. I am proud of the 387 remarkable projects in prevention, research, and commercialization we have funded – all reviewed by experts in their respective fields. I am proud of the passion and volunteerism of our 11-member Oversight Committee. And in particular, I am proud of what we are accomplishing in Texas.

We promise to continue to invest in the very best projects, with the very best people, selected by the very best minds, to end cancer.

In Brief

MD Anderson Provost DuBois: It Did Not Go Through My Office

(Continued from page 1)

Bypassing review by a provost of the institution that employs the researcher seeking funds is highly unusual and problematic—especially when medical research is involved, and more so in situations where there is a potential for conflicts stemming from nepotism, experts in ethics and grant review say.

The MD Anderson proposal mentions phase I trials.

State officials confirmed to The Cancer Letter that they received the MD Anderson portion of the application from Eric Devroe, executive director of strategic alliances at the MD Anderson Institute for Applied Cancer Science. IACS, the unit that received the $18 million in state funds, is co-directed by Lynda Chin, who is married to MD Anderson President Ronald DePinho.

The Q&A with DuBois was conducted by Paul Goldberg, editor of The Cancer Letter.

PG: *I guess we should first establish whether the incubator proposal went through your office.*

RD: The incubator proposal was a joint effort with Rice [University], and my understanding is that it went through the Rice [provost's] office in terms of being submitted, along with the Rice proposal.

PG: *So it didn't go through your office?*

RD: We have an office of grant administration and an office of grants and management, and since this was a joint effort with Rice, the institute team worked directly with the provost at Rice. I assumed that it was routed through the grants office at Rice since it was a collaborative effort with them. However, I have not checked directly with Rice on this issue.

PG: *It did not go through the MD Anderson provost? That's unusual; isn't it?*

RD: We do process a lot of CPRIT grants that go to the scientific review panel. This is a new mechanism—the RFA just came out several months ago—and that was apparently the preferred mechanism. I believe the institute team had worked closely with CPRIT in formulating their application, and I think this was the preferred route.

PG: *Preferred by whom? I would have thought that because this proposal has a budget, and the budget is an MD Anderson budget, you would have been given the opportunity to review it.*

RD: Well, we do joint grants with a lot of other institutions. A lot of that comes as a subcontract. That is the mechanism used when we have multi-investigator grants that are led by some of these other institutions. You would have to ask CPRIT to understand that mechanism.

PG: *I was thinking more in terms of an MD Anderson question, I would have thought it would have gone through your office. I'm just surprised it didn't. Are you surprised it didn't?*

RD: Well, I don't know if I'm surprised, but this is the way that CPRIT and the individuals working on the incubator proposal worked it out.

PG: *I'm just trying to establish which questions you're able to answer, because if it didn't go through your office…*

RD: It really didn't go through my office. That was the route that it took. I haven't discussed that with the CPRIT individuals, or people at Rice, or others.

PG: *So I'm the first one asking. Do you know where it was submitted? Was it submitted to the [CPRIT} contractor as the RFP requires?*

RD: All I know is that it was done through the Rice University provost's office. I don't have any details of how it got routed through in terms of getting to the CPRIT office. I just don't know those details.

PG: *Well, you're the provost and it has a budget. And the budget generally should have gone through your office. It might be because it is a commercial project…*

RD: All of the CPRIT research grants that go through scientific panel review definitely go through this office. But this was co-done with Rice and I think it's basically some type of a sub-contract.

PG: *Are you comfortable talking about the project itself?*

RD: Sure.

PG: *It was only six-and-a-half pages long, and some of the very well-respected scientists, highly decorated scientists, are saying that this is actually research rather than commercialization. Where do you stand, with the caveat that this is somewhat peripheral since you didn't review it?*

RD: Well, I'm familiar with the institute and what's integral to the mission. It's a group of individuals that were participating at Dana-Farber and the Belfer Institute, which is well established there. And Dr. DePinho saw that as an advantage of trying to do drug development in an academic setting. He certainly had some projects and other things going on that seemed to be effective there. One of his visions

was to try and set that type of situation up here, and that's how the Institute for Applied Cancer Sciences was formed.

And there is a lot of information about that institute on the website and I've heard all the project leaders talk about what they're doing on their involvement with the institute. It's really clear that the main focus of that institute is for developing new targets for therapies and new drugs for cancer treatment.

It's set up to do specific projects that are doing drug target discovery and drug development—and when those projects aren't fulfilling the expected needs, they're discarded and new projects are started.

It's not really a typical basic science approach, where you just do discovery and go from one publication to another. It's really using an industry model. A lot of employees there came from positions in the pharmaceutical industry, and they're not pursuing an academic career at all…

PG: *It's a hybrid?*

RD: It's really focused on drug development.

I wish you could come and hear their presentations, because when you see the information and how people are spending their time there—I just don't think there's any question of what the purpose of that institute is.

There was a 17-page appendix that went in with the five or six page grant to try to explain some of that.

PG: *I have that, that has the names of the individuals involved, and it has the budget, and all these other things. But that didn't go through your office, so it's probably unfair to ask you much more about it.*

RD: I have copies of it, but you're right, it didn't go through my office.

PG: *I just want to be fair about this, and just wait and get an answer elsewhere, because it's an interesting question. A recent editorial in the [Houston] Chronicle asked this question, and I am going to quote it: "Did CPRIT properly weigh the possibility of a conflict of interest? The incubator's head, Dr. Lynda Chin, is married to MD Anderson president Dr. Ronald DePinho. But the reviewers didn't seem troubled by anything in the proposal: It whizzed to approval in three weeks, without even an in-person presentation."*

RD: I must say that Dr. Chin is one of the most well-respected cancer researchers in the country. She has accomplished quite a bit in her own right, doing her own cancer research, and clearly she's taken a major leadership role in the Cancer Genome Atlas project.

She has really done some really high-impact research in the area of melanoma, and I think she's quite creative and a top researcher across the nation. So I think based on her qualifications, she is someone that would be of value to any cancer center.

PG: *Oh, there is no question about it. It's just that when a problem like this occurs, whether it's a real problem or a perceived problem—and this is, me speaking by the way, not the Chronicle—but the next question is, wouldn't everyone's life be easier if she were working at, say, Baylor?*

RD: There was recognition by the University of Texas system and the executive vice chancellor, [Kenneth] Shine, when Lynda came on board of the potential conflicts of interest when you have a department chair in the institution and her husband as the president. You always worry about potential conflicts of interest, but we've tried to put things in place to alleviate those conflicts.

And Lynda actually reports directly to Dr. Ken Shine. She doesn't report to Ron or to me—it's set up so that she reports to Dr. Shine.

Obviously Dr. Shine and I confer on things and make sure that we are all on the same page. But that reporting relationship was set up from the very beginning when Ron and Lynda came on board.

PG: *This is very interesting. So you basically review everyone's conflicts except the president's. And the president's conflicts would be the same as Dr. Chin's conflicts by virtue of marriage, right? So that's why it's set up like that?*

RD: Yeah, the UT system has set up a sort of system-wide review panel made up of individuals from across the university system to look at those conflicts, to make sure that there is no problem there.

The other fact is that the CPRIT scientific review committee, which reviews all of the research applications, did award Lynda Chin a CPRIT scholarship award for $5 million. They were able to review her research and her accomplishments and they provided her with that award, and didn't say anything at that point in time about any of these conflicts.

PG: *One of the things that's also in the questions that the Chronicle asks, but I could also ask them myself—and this is more of a CPRIT question, I guess—is that if CPRIT chose not to go forward with these multi-investigator grants, and instead fund this incubator, and of course Dr. [Phillip] Sharp [of the CPRIT Scientific Review Council] and others are saying that this was unfair to people who are submitting grant applications through regular scientific peer review; that this would go so fast through a different*

channel.

So that's sort of an argument, and it feels scary to see people of this caliber saying that they may just walk away from reviewing CPRIT grants.

RD: I haven't had any communications with the review panel, so I don't know. I've seen the letter that Dr. Sharp sent, and they have voiced some concern.

But I think the issue of not funding those other grants really boils down to a budgetary issue for the institute. Clearly Dr. Gimson and the other oversight committees are the ones that deal with the CPRIT budget. And my understanding was that during that cycle there wasn't enough funding in the budget to fund all of the projects and include the incubator grant.

So they made a decision at the level of CPRIT of what they wanted to fund. My understanding is that during the next round of funding those grants will be considered, but I haven't gotten any clear information on that from the CPRIT leadership.

PG: *Let's talk about the people whose proposals go through you. Are you gauging some discontent on their part?*

RD: All the research proposals for the whole institution come through here, both at the federal level and the state level. There is a lot of unhappiness with not getting grants funded.

I think that's a natural reaction. I also have my own research funded through some of those agencies, and I don't always get things funded when I apply, and it's hard to deal with, but it's part of the disappointment of doing biomedical research.

With this particular issue, that was a decision that CPRIT made. I don't know what they were thinking specifically when they made it. But I can certainly understand why some of the other investigators are disappointed that they didn't get funded on that cycle.

PG: *Right. One other question, that I guess would fall under your purview, is, with the teams of scientists now looking for five cancers to cure, or at least make a big dent in, it feels like you can't come up with a plan like that without restructuring an entire institution. And how is that working out?*

RD: There is a lot of excitement at the institution about using that approach. Clearly that is something that Ron brought here with his vision. And I would hate to speak for him, but clearly I do represent the institution, and the idea of selecting some higher priority areas is the idea of bringing a really comprehensive, multidisciplinary team together to try to tackle some of the issues related to individual cancers.

What we've been doing so far is spending a lot of time bringing groups of MD Anderson faculty and staff together to talk about what it would take in some of these areas to really have a maximal impact.

It's a different way of thinking about tackling these problems in academic centers around the country.

We set up individual experiments to answer pretty low-level questions about different types of cancers and different issues related to cancer biology. It's a very iterative process that depends on what the individual experimental results are from point a—and then the next experiment you design is to get to point b.

This is actually taking a much broader look at these problems and trying to understand what it is about a certain type of cancer that we don't know. Something that, if we did know, we'd be able to make a transformative impact in.

It's a difficult process. Typically our faculty and others, and other cancer centers around the country, haven't thought about tackling the problem this way. So clearly we are still in the phase where we're developing our plans of attack and evaluating our strengths in different areas and in different types of cancers, and where we would be able to have the most impact in terms of the low-hanging fruit.

We are sort of in the development phase of thinking about this. We're trying to formulate these questions and we haven't really gotten to the point where we've put a whole team together or selected individual types of cancers that we want to attack.

I guess the simple answer is yes. It's a different way of thinking about things. I think it has the potential to be transformative—if we can get the right teams together and select the truly most impactful questions to answer.

It's exciting to think about a single institution having such major impact on the disease. So there is enthusiasm across the campus. Individual faculty members are becoming involved in the strategic planning sessions.

I have to be honest, we don't know exactly what to expect, because we've never done something like this before. But it could be transformative.

PG: *Well, is it still on schedule to be announced in September?*

RD: That's the goal. We've set that date and we're working really hard to meet that deadline.

It is possible that not all five things will happen at the same time, because these are massive projects. But we are doing the best we can to meet that schedule.

PG: *I find it hard not to when I hear about goals to cure cancer. It goes back to President Nixon. How*

is this going to be different?

RD: I sort of disagree, Paul, we're not really setting goals to cure cancer. I don't see it that way.

I think what we are trying to do is select out what the unknown information is about a certain type of cancer and really try to focus our energy on that particular problem.

The way that research is done even since the Nixon era is that faculty members usually have a favorite topic that they like to work on, and they sort of stick to that area for their whole lifetime. That's the way that people build their reputations and have an impact in that particular area.

This is sort of looking at it in a different way. And it's trying to really discern about what it is about a particular disease that we need to know, even though it may not be the topic that a particular investigator was studying and then to try to see if a team can be assembled that can ask those questions in a really effective and a timeline driven way.

PG: *Well, that really helps to distinguish it from the previous efforts.*

RD: It's quite different, and I can't take any credit for the idea, because it's really Ron's idea, but I think it has a lot of potential if we select the right areas and are able to formulate the most needed questions.

PG: *Thanks for your help.*

RD: There was one question [in the Chronicle editorial]: why was CPRIT funding a commercial enterprise.

PG: *I didn't think it was a question for you—I thought it was a question for CPRIT. Unless you want to tackle it.*

RD: I can tackle it easily. I'm also a citizen of the state of Texas, and I supported the enabling legislation to establish CPRIT. It's actually written into the legislation that this Cancer Prevention and Research Institute will help innovate and develop commercialization in the area of cancer research. There is language there.

PG: *Oh, absolutely, that's another reason that I didn't ask it. It's obvious that it's there; they just haven't done much of that. But it's set up for it. That actually might be a good question to ask: would it help to have the budget predetermined for commercialization versus basic science?*

RD: This is a good question. There is some set-aside for the prevention research. It was written into the statute that a certain percentage per year would go for prevention. [Rebecca] Garcia runs that program down at CPRIT, and they have applications that go in every year for those types of grants. They know what their budget is because it was set up at the beginning of the year.

This could be a good way to avoid this kind of situation in the future, by budgeting the amount in a way that was clear to everybody about what was going into research, what was going into prevention and what was going into the commercialization effort. So I haven't heard much discussion about that, but I think it would make a lot of sense.

PG: *It was a discussion that's starting and they are probably putting it into the rules at the next meeting. Or at least that's the plan, they tell me.*

RD: Well then you know more than me on that [laughter].

PG: *Well I was just talking to them. So yeah that would make sense. But also it sets up a conflict to some extent, because if you're going to have a set-aside for commercialization what about people whose proposals go through you? They will not be happy.*

RD: This particular incubator grant was definitely a new mechanism. And it went in that way. Certainly, CPRIT was involved in the formulation of the plan. You might want to ask them why it went through Rice, but I think that's just the way it happened.

PG: *Well it's just that somebody made some decisions, but we know that it didn't go through you, and that's very interesting. I really appreciate your help on this.*

In Brief

Senate Reauthorizes PDUFA, Generic User Fees Included

The Senate voted in favor of new user fee legislation that would require generic drug manufacturers to pay $299 million annually for the next five years.

The act was part of the fifth reauthorization of the Prescription Drug User Fee Act, which passed 96-1 Thursday.

If passed into law, the Generic Drug User Fee Act would go into effect October 1 of this year. The funds collected from the manufacturers of generic drugs and biosimilars would supplement the FDA's budget and would provide additional resources for the approval of generic medicines and facility inspections.

The reauthorization bill still needs to be considered by the House.

Follow us on Twitter: @TheCancerLetter