THE CANCER LETTER

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*A Misdirected Email*

## CPRIT Official Speaks of "New Regime" As Institute Denies Deepening Crisis

*By Paul Goldberg*

The board chairman of the Texas cancer institute has something to say to America's premier scientists who are resigning from his organization's peer review committees: Good riddance.

"Better to get them all out of the way now," wrote Jimmy Mansour, chairman of the Oversight Committee of the Cancer Prevention and Research Institute of Texas. "Gives us the prime opportunity to announce a new regime."

Mansour, a telecommunications entrepreneur, composed this memo for CPRIT executive director Bill Gimson and oversight board chairman Joseph Bailes, but had mistakenly hit the Reply All button, sending the nasty epistle to a resigning scientist.

The document, which came into public view because of Mansour's sloppiness at the keyboard, belittles scientists and the peer review process, and inadvertently provides evidence for the case that troubles in Texas are first and foremost about peer-reviewed science.

(Continued to page 2)

*Guest Editorial*

## Nobel Laureates Offer Simple Formula To Save CPRIT From "Infamy and Irrelevance"

*By Alfred Gilman and Phillip Sharp*

The citizens of Texas were wise to contribute $3 billion to the fight against cancer.

Legislation and an amendment to the state Constitution created the Cancer Prevention and Research Institute of Texas (CPRIT), enabling a 10-year program in cancer research and community-based prevention activities.

(Continued to page 11)

*In Appreciation*

## Sen. Arlen Specter Remembered as Champion Of Federal Biomedical Resesarch Funding

**Arlen Specter**, senator from Pennsylvania from 1981 to 2011, died Oct. 14, from complications of non-Hodgkin's lymphoma. He was 82.

NIH Director Francis Collins described Specter as a "towering champion for biomedical research and the mission of the National Institutes of Health."

"His favorite saying, which we all heard many times over the years, was that NIH was the crown jewel of the federal government," said Collins.

(Continued to page 13)

# CPRIT Mulls "Future Directions" As Scientists Quit in Protest

(Continued from page 1)

According to former reviewers who are continuing to submit letters of resignation, CPRIT has moved away from reliance on peer review and into the territory mainstream scientists classify as the wilderness.

Mansour's email is also remarkable because it illustrates the reluctance on the part of CPRIT officials to recognize that the institute that distributes $300 million a year in state funds is, in fact, in the midst of a crisis.

The new "regime" would be run by "Dubois and his new Chair of the Scientific review Panel," Mansour wrote.

The "Dubois" in the memo is none other than Raymond DuBois, the former provost of MD Anderson Cancer Center, who is reportedly being courted to accept the challenge of righting CPRIT, while scientists resign from its review committees and cite the state agency's disregard for the principles of reliance on peer review.

At the time Mansour wrote the email—Oct. 14—DuBois hadn't accepted the job. In fact, he still hasn't—and after the email came out, Bailes said that no formal offer was made. DuBois was recently named executive director of the Biodesign Institute at Arizona State University, which means that if he takes the CPRIT job, he would be have to do it part time.

CPRIT's previous chief scientific officer, Alfred Gilman, and the former head of Scientific Council, Phillip Sharp, resigned last week, triggering the exodus of other members and reviewers (The Cancer Letter, Oct. 12).

In a guest editorial that appears on page 1, Gilman and Sharp, both Nobel laureates, offer advice for the future of CPRIT. Changes on the CPRIT staff and its oversight board would be required for the institute to regain relevance, they argue.

By trying to recruit DuBois, CPRIT would seize control of events prior to the 2012 annual conference, which will be held in Austin Oct. 24-26, wrote Mansour in his email.

"The headline at the conference will automatically migrate to the new direction for research," he wrote. "Gilman and Sharp and the other resignations will not dominate our conference.

"The excitement surrounding the potential for a new panel will be the topic, if we properly highlight that at the conference. Gilman is gone and so is his influence."

In-fighting between Texas institutions would work in CPRIT's favor, Mansour wrote.

"There will be a number of Texas institutions who will be ecstatic including TAM, Methodist, TTU and others," he wrote. "We need to take advantage of this opportunity to put a stake in the heart of the past news. The message of a positive conference will be heard around the State and many will realize we are moving forward.

"Gilman and the regime of the old guard (of research) will get the message as well."

**Mansour, Bailes Explain**

"The message I am getting is that they no longer want to be constricted by rigorous scientific review," Gilman said to The Cancer Letter. "They want freedom to follow the path of increased commercialization, whether or not they get meritorious proposals."

CPRIT will not be able to solve its problems by issuing a call for new scientific reviewers, as no responsible scientist would join the organization without clear evidence that CPRIT has addressed the causes of its current problems, Gilman said.

"They need to clean house and they don't seem to want to clean house," he said.

Responding to questions from reporters, Mansour said he didn't intend to be disrespectful: "My comment was referring to getting the resignations out of the way, not the reviewers.

"I felt that rather than having them trickle in over time, it was better to have them come in all at once and get them out of the way. I have tremendous

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respect for our peer reviewers and have a deep appreciation for the work they do for CPRIT. It is understandable that peer reviewers would leave when Drs. Gilman and Sharp leave—and make way for a new Chief Scientific Officer."

What was the message Mansour intended for "Gilman and the regime of the old guard (of research)"?

"CPRIT is evolving," Mansour explained. "Dr. Gilman is gone and we're moving ahead. Getting products to patients in Texas quickly is why CPRIT was created. With only seven years left, we believe a healthy balance of research and commercialization grants is the best way to make a serious impact on cancer. We're looking for a new Chief Scientific Officer and peer reviewers who embrace this full mission of the Institute."

What might the new direction be?

"My reference to 'new direction' was referring to the natural change that will be taking place with a new Chief Scientific Officer coming on board," Mansour said. "There have been a number of discussions as part of the Future Directions initiative about potential shifts in funding, but none of these decisions have been made."

**From:** Jimmy Mansour <jimmym@3000partners.com>
**To:** [redacted], bgimson@cprit.state.tx.us
**Cc:** jsbailes@gmail.com
**Subject:** RE: Resignation from CPRIT Basic Science Cancer Research Committee-3A (BCRC-3A)

Better to get them all out of the way now. Gives us the prime opportunity to announce a new regime under Dubois and his new Chair of the Scientific review Panel. The headline at the Conference will automatically migrate to the new direction for research. Gilman and Sharp and the other resignations will not dominate our conference. The excitement surrounding the potential for a new panel will be the topic if we properly highlight that at the conference. Gilman is gone and so is his influence. There will be a number of Texas Institutions who will be ecstatic including TAM, Methodist, TTU and others.

We need to take advantage of this opportunity to put a stake in the heart of the past news. The message of a positive conference will be heard around the State and many will realize we are moving forward. Gilman and the regime of the old guard (of research) will get the message as well.

Jimmy

**The hazards of hitting Reply All**: Mansour provides an inside perspective on resignations—confidentially, he thinks.

The claim that "there will be a number of Texas institutions who will be ecstatic" referred to the fact that Gilman's office was located on the UTSW campus, "a fact that and many people across the state had expressed concerns about." Mansour explained.

And another thing: the "Dubois" in the email was cited symbolically and didn't necessarily refer to *Raymond* DuBois. Someone who resembles him would fit the bill.

"Obviously, this was meant to be an internal email only, so you can understand that my reference to Ray was to express that someone like him would be ideal," Mansour wrote. "I do not serve on the search committee and therefore have no role in the selection. The search committee is made up of a diverse group of individuals in the Texas cancer community and my understanding is that no decision has been made."

Speaking for that committee, Bailes added another bit of clarification:

"As chairman of the 15-member CPRIT Chief Scientific Officer search committee, I want to state for the record that we are in the middle of the search process and absolutely no decision has been made. CPRIT Oversight Committee Chairman Jimmy Mansour is not a member of the search committee and has no role in the process. CPRIT will announce the new CSO once the remaining candidates have all been interviewed and fully evaluated. We expect that to happen soon."

This isn't the first Mansour email to attack Gilman and peer-reviewed research.

In an earlier email, Mansour said Gilman's opposition to funding a commercialization grant was motivated by a power grab.

"I believe Al is upset because he wants these [incubator] proposals to come as [multi-institutional research grants] proposals so that he has control over it... If this is accurate, then once again Al is operating from improper motives," he wrote in a March 22 email to Bailes, which was obtained by The Cancer Letter, (The Cancer Letter, Sept. 28).

Troubles at CPRIT were triggered by the institute's handling of a proposal for an $18 million biotechnology incubator led by Lynda Chin, a senior scientist at MD Anderson Cancer Center (The Cancer Letter, May 25).

Chin is married to MD Anderson's president, Ronald DePinho.

**Crisis Recognition**

Over the past week, an advisory panel of academics from around the state has been urging CPRIT officials to start using the word "crisis" to describe their current situation.

Earlier this week, CPRIT staff asked a committee of 15 Texans involved in cancer research, care and advocacy to conduct a series of meetings to set "future directions" for the institute.

The committee was asked to comment on a four-page document describing a vision for post-Gilman CPRIT.

In emails that circulated within the committee and obtained by The Cancer Letter, the members blackballed the plan, urging the institute to seek outside help to restore its credibility.

In an email sent out to committee members Oct. 17, Leonard Zwelling, professor of medicine and pharmacology at MD Anderson, said CPRIT cannot plan for the future until it addresses its current crisis.

"I believe that the CPRIT administration has the cart before the horse," Zwelling wrote, calling for independent review of the situation. A careful, unbiased assessment of the CPRIT mission, vision, strategy and tactics by outside experts in cancer research, prevention, clinical trials, commercialization and research administration would seem to be the next best step prior to establishing any specific new goals or distribution of grant funds to various categories.

"If this takes a few months, so be it. At least we will have the possibility of regaining the scientific and ethical high ground that will be needed to convince the people of Texas and their elected representatives that the trust they put in us with their tax dollars is under good stewardship."

Another committee member, John Minna, a lung cancer expert at UT Southwestern, agreed.

"The reality of the situation is that CPRIT is in a crisis and in danger of total collapse," Minna wrote in the same exchange. "We need to acknowledge this (at least among ourselves). To overcome this, we need to have the careful unbiased outside assessment of 'all things CPRIT,' including the peer review process as well as what the goals and metrics should be.

"Our current, in-state, focus groups have a lot of potential to do both harm and good based on our own individual (parochial) interests. We can only go forward with unbiased expert opinion from outside. Because of the exodus of our prior world-class expert reviewers this kind of advice is going to be hard to come by, but we must obtain it."

Without peer review, CPRIT is rudderless, Minna wrote.

Consider cancer prevention and survivorship programs:

"Quite frankly, I am all for prevention services and survivorship, but the reality is these are more part of the cost of health care delivery," Minna wrote. "I was one that spoke up for the need of prevention research coupled to the prevention services as an untapped CPRIT opportunity. But prevention research needs to be well thought out and undergo peer review. This was not a call by me to 'spend more on prevention research,' but to make sure prevention research can be included in the total research portfolio.

"Likewise, a lot of the basic research discoveries can be translated through prevention research activities in populations—but this needs to be planned and done by people who are expert in this area. We need to see if the required multi disciplinary teams for this type of research can be formed in Texas or whether we have to recruit in new talent. Likewise, if we are going to 'study survivorship,' we need to see novel research plans and have the expertise to do this.

"I am all for a healthy lifestyle—no smoking, better diet, no obesity and all the 'right stuff.' However, this is part of health care delivery and not part of CPRIT's main research mission—fine if it is part of the 10 percent of prevention services effort. However, to do this right for Texas would take many times the total CPRIT available funds and clearly this was not what was approved by the people or the enacting legislation."

Commercialization efforts require peer review, too.

"The key for successful commercialization will be to have a well trained workforce, great new basic research findings for which Texas has the IP, academic clinicians and scientists working with cancer doctors in private practice working together, and patient populations and mechanisms to test these in," Minna wrote. "These will come from CPRIT-sponsored infrastructure investments, basic research discoveries, CTNet, and the types of MIRAs and multi disciplinary teams CPRIT sponsored research is generating. In my opinion it would be a disaster of the first order to start pouring CPRIT funding into 'commercialization efforts,' which are not ready for 'prime time.'

"I think you would find that savvy venture capitalists using their own money (and not our Texas citizen's money) for these gambles would feel the same way."

**Letters Keep Arriving**

Meanwhile, reviewers keep sending in their letters of resignation.

The most recent member to quit formally was Everett Vokes, the John E. Ultmann Professor, chairman of the department of medicine, and physician-in-chief at the University of Chicago Medical Center.

Vokes's letter of resignation reads:

"This note is to indicate my intention to resign from my position as co-chair of the Translational and Clinical Review Committee 1A/2A of the Cancer Prevention and Research Institute of Texas effective immediately.

"CPRIT has been a powerful and highly impactful institution that has succeeded at funding innovative research and attracting scientific leaders in cancer research to the state of Texas.

"I have been highly honored to be a member of this process and to serve under the scientific leadership of Drs. Al Gilman and Phillip Sharp and work with the many exceptional reviewers on our committee.

"CPRIT is in a state of transition following the events of the last several months. I hope that the disruption and distraction that has resulted from this transition can soon be ended and that new credible leadership be appointed. Should at that time my services be of interest, I would be willing to consider future interactions."

Only one member of the council—Richard Kolodner, professor of medicine and member of the Ludwig Institute for Cancer Research at the University of California, San Diego—isn't known to have resigned.

In addition to Sharp and Vokes, other committee members who have resigned are:

• **Tyler Jacks,** the David H. Koch Professor in the department of biology and director of MIT's Koch Institute for Integrative Cancer Research.

• **William Kaelin,** professor of medicine in the department of medical oncology at Harvard University and the Dana-Farber Cancer Institute.

• **Charles Sherr,** chair of tumor cell biology, co-director of the Molecular Oncology Program, and Herrick Foundation Chair at St. Jude Children's Research Hospital.

• **Sanjiv Sam Gambhir,** the Virginia and D.K. Ludwig Professor in the department of radiology and bioengineering, chair of the department of radiology, director of the Molecular Imaging Program, and director of the Canary Center for Cancer Early Detection at Stanford University.

• **Clara Bloomfield,** the William G. Pace III Professor of Cancer Research at Ohio State University.

The stature of rank-and-file reviewers is perhaps the most remarkable aspect of the peer review structure Gilman constructed. Now, these reviewers are sending in their letters of resignation.

*Several of these letters follow:*

## Brian Dynlacht

*Professor of pathology, New York University School of Medicine*

I am writing to formally resign my position as a scientific reviewer for the CPRIT Basic Science Cancer Research Committee-3, BCRC-3, effective immediately.

By way of introduction, I have been a scientific reviewer for the CPRIT BCRC-3 committee under the chairmanship of Dr. Charles Sherr. I have followed with much interest and, I must admit, substantial consternation, the series of events that have transpired at CPRIT over the past six months.

I am extremely disappointed by what I have heard, and especially upset by both accusations against Al Gilman and the direction of CPRIT leadership has chosen, which is apparently to promote commercialization at the expense of rigorous scientific review.

In all of my years in academia, I have never encountered two more honest, intellectually rigorous scientists than Al Gilman and Charles Sherr. I can say with complete certainty that their motives are, and always have been, completely free of bias.

They are the absolute cream of the crop. I wholeheartedly agree with their stance on matters that have recently surfaced at CPRIT, in particular, those matters stipulated in Dr. Sherr's resignation letter, which I will not reiterate here. On that basis, I must follow them by submitting my resignation. I anticipate that you will be receiving an onslaught of letters similar in content and sentiment to my letter.

In addition, I will forward this letter to Dr. Sherr, CPRIT review Council members, and, in all likelihood, The Cancer Letter and The Houston Chronicle.

I have served on many federal and private scientific review committees, and I have *never* served with such an accomplished and outstanding group of scientists. The elite panel assembled by Dr. Sherr was intellectually rigorous, honest, and conscientious. Al Gilman oversaw each meeting with professionalism beyond reproach. You will not find a better group of human beings or scientists no matter how hard you search. Let me repeat that: Drs. Gilman and Sherr have done something remarkable here, by assembling this group, and it is unlikely that

you will be able to reproduce their accomplishments without them no matter how hard you try.

You may find that it was not worth subverting the entire scientific enterprise—and my understanding was that the intended goal of CPRIT was to fund the best cancer research in Texas—on account of this ostensibly new, politically-driven, commercialization-based mission. Indeed, I am of the opinion that such a policy—wherein science that is judged meritorious by a highly esteemed group of scientists is discounted at the expense of science that has not been methodically reviewed--will not only fail to recognize and extract the best possible science from your state, but it will in fact succumb to mediocrity and systematic abuses.

It has been an honor to serve on this esteemed committee. It is a shame that it will be completely dismantled. While it was challenging and arduous work, it was indeed a genuine pleasure to work with this group of enlightened and brilliant scientists. It is extremely unlikely that I will serve with a better group of scientists in the future.

## Monica Bertagnolli

*Professor of surgery, Harvard Medical School, chief, DF/BWCC Division of Surgical Oncology, Group Chair, Alliance for Clinical Trials in Oncology*

I am writing to inform you of my decision to resign from my position on the CPRIT scientific review panel led by William Kaelin, MD, effective Oct. 12, 2012. I do so with regret, as my work on the panel provided me with tremendous professional satisfaction.

It was a great honor to work under the direction of Dr. Kaelin, whose grasp of basic and translational cancer research is truly remarkable. He led the committee to recognize and reward excellence where it was demonstrated, and to provide constructive feedback and encouragement to researchers whose proposals were not recommended for funding.

Working with Dr. Al Gilman was one of the highlights of my professional career. His is not only one of the greatest scientists of our age, he also is one of the rare individuals who understand the real world strategies that must be employed to achieve success. In their service to CPRIT, both Dr. Kaelin and Dr. Gilman demonstrated the highest professional and ethical standards without exception, and their single goal was to serve the citizens of Texas by promoting cancer research of the best possible scientific quality and integrity.

The implication that reviews were biased toward or against a particular awardee institution is simply ridiculous. In fact, the committee ignored mention of the institution unless there was a specific reason to consider it, e.g., if the research required access to a specific resource that was only available in a particular location. It is similarly outrageous to consider that many detailed applications so painstakingly prepared by Texas researchers could be reviewed and approved for funding in good faith, only to have this review negated by diverting funding to a briefly outlined "commercialization" proposal from MD Anderson/Rice.

This shows an appalling lack of respect for the applicants as well as the reviewers. Finally, in awarding funding, I believe that it is critically important for commercialization potential to be secondary at all times to scientific quality. Many projects that have significant commercialization potential in the short term also lack scientific validity.

Without placing scientific rigor above all else, the citizens of Texas risk supporting investments that ultimately prove wasteful, while diverting resources from important work that can improve the lives of cancer patients.

My experience on the committee was one of hard work, thoughtful deliberation, and respect for the goals set forth by CPRIT. Our committee reviewed a large number of outstanding proposals from Texas cancer researchers, and I am confident that those recommended for funding will benefit the state by achieving significant advances in the battle against cancer. Unfortunately, given the events of the past several months, I can no longer be certain that this will be the case going forward. I therefore respectfully submit my resignation.

## John Cleveland

*Professor and chair, Department of Cancer Biology, The Scripps Research Institute, Scripps Florida*

I hereby tender my resignation as a Member of the CPRIT BCRC-3A Review Panel. This decision in based on the recent events that have unfolded at CPRIT, which appear to have driven by very misguided perceptions, special interests and agendas of the Oversight Committee that, very sadly, undermined the principles of grant peer-review.

I assure you that, under the leadership of our esteemed Chair, Dr. Charles Sherr, and that of Dr. Al Gilman, the very highest principles and standards were applied to the review of all IIRA, HIHR and MIRA grants, and that all funding decisions were made purely

on the basis of the merit of the proposed science, and on their importance to the stated mission of CPRIT. Indeed, the rigor of these reviews, and the incredible group of scientists that were recruited by Dr. Sherr, made the CPRIT BCRC-3 Review Panel truly exceptional.

It was a true honor and privilege to serve on the CPRIT BCRC-3A Review Panel, and to provide these important services to the citizens of the great state of Texas for such a worthy cause. However, given the actions of the Oversight Committee I cannot in good conscience continue to serve as a reviewer for CPRIT. I sincerely hope that in some way this action prompts the Oversight Committee to reconsider their current direction and restore sanctity to the proper review of CPRIT applications.

## William Hahn

*Deputy chief scientific officer and chief of the division of molecular & cellular oncology, Dana-Farber Cancer Institute*

I write to inform you that I am resigning from the BCRC-1A Review Panel of the Cancer Prevention and Research Institute of Texas (CPRIT) effective immediately.

When I was asked to join this committee three years ago, I did so with enthusiasm for a program that I believed had real potential to accelerate cancer research and to eventually bring new treatments to patients. The citizens and legislature of Texas are to be applauded for their foresight and generosity to establish CPRIT as a bold statement of what can be done to improve the lives of patients affected by cancer.

For the past three years, I thoroughly enjoyed working with top cancer scientists from around the country to provide CPRIT with rigorous and impartial review to ensure that these public funds would be allocated to those projects most likely to impact the prevention, diagnosis and/or treatment of cancer.

These deliberations occurred in an environment created by Dr. Al Gilman and the chairs of the CPRIT review panels that was entirely free of political influence or institutional bias. I have served on numerous international and national study sections and can say with confidence that these CPRIT panels were models for high quality, unbiased review.

Unfortunately, recent actions of the CPRIT Oversight Committee now undermine the basic tenets of this process. The accusation that applications were ranked by institutional bias rather than scientific merit is simply not correct and is an affront to all of us who participated in these reviews. At the same time, delaying the funding of highly ranked applications to fund incubator projects without scientific review emasculates the credibility of CPRIT and the entire review process.

Moreover, I am troubled by the Oversight Committee's recent request that those of us that participated in the scientific review of commercialization applications reconsider our scoring in the absence of any additional substantive information or progress by the applicants to strengthen what were wholly naïve and underdeveloped applications.

These actions make it clear that the CPRIT Oversight Committee has elected to disregard scientific review to pursue a different agenda.

Under these circumstances, I cannot continue to serve on this panel. The Texans who made CPRIT possible deserve an unbiased process that ensures that these funds are allocated based on merit. I still believe in the potential of CPRIT and would consider serving again in the future but only if the CPRIT Oversight Committee commits to the principles of scientific rigor, intellectual integrity and impartiality that formed the basis of these original peer review panels. If CPRIT Oversight Committee elects to bypass peer review, I fear that this will not only damage CPRIT's reputation but may also erode the public's confidence in cancer research.

## J. Wade Harper

*Vallee Professor of Molecular Pathology, Harvard Medical School Department of Cell Biology*

This letter is written to tender my resignation as a member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

Having spent 15 years as a faculty member at Baylor College of Medicine and a resident of Houston, I was very excited to be asked by Dr. Sherr to participate in his review panel. This was especially the case because I have admired Dr. Sherr's science and intellect for more than 2 decades. Recognizing that Texas institutions have significant promise, I felt that the CPRIT model and the funds available would truly be transformative, but only if the best science was funded.

I was strengthened in this feeling of promise upon the first meeting of the BCRC-3 study section, where I discovered just how scientifically stellar the BCRC-3 study section actually was. Through Dr. Sherr's vision, he was able to establish a national panel of experts who judged each application based solely on the science and

the ability of that science to transform cancer treatment in Texas.

I have served on numerous other study sections, including NIH. The BCRC-3 study section was by far the most rigorous and fair study section I have ever been associated with. This is due in no small part to Dr. Sherr's efforts in bringing this incredible group together and keeping us together for 3 years.

Having talked to members of the other scientific review panels, I believe that they all feel this way about their individual groups. Prior to joining CPRIT's review panel, I had not had the pleasure of knowing Dr. Gilman. Through the 3 years I have known him, I have NEVER heard him say anything that would sway reviewers in either direction toward ANY grant. I have never seen him display favoritism in any form.

Thus, one of the most depressing things about the last 6 months has been the extent to which Dr. Gilman's integrity has been challenged. He has my utmost respect. Also, I must say that the new policy of having a monitor present during our discussions is one of the most insulting things that have happened to me in my professional career.

In my view, the direction that CPRIT is going—putting commercialization schemes in place at the expense of well-grounded scientific studies—will ultimately degrade the process that CPRIT originally intended. Without appropriate and rigorous scientific review, those with the greatest hype, rather than the greatest science, will likely receive the lion's share of the funding, often I fear, with an outcome that is not in the best interest of the residents of Texas.

There is much more of a chance, using this mechanism, for favoritism to be given, and for politics to be inserted into the process. I am very much afraid that the enormous efforts that all of the study sections have given to the review process with the hope of transforming cancer research in Texas during the last three years will possibly be for naught if strict and rigorous scientific review is not maintained. Given the dramatic changes in the approach being taken by CPRIT, I am unable to continue my support for this endeavor.



## Kurt Zinn

*Professor, Departments of Radiology, Medicine, and Pathology, director, Division of Advanced Medical Imaging Research, the University of Alabama at Birmingham*

Thank you for the opportunity to serve as an external reviewer for the CPRIT program. I now inform you of my resignation as reviewer for the Interfaces Review Committee. I fully support Dr. Gilman and Dr. Gambhir in the positions they have taken against those in the CPRIT organization that decided to bypass scientific peer review for certain commercialization projects. Commercialization projects should be scientifically sound if they are to be funded, and how would that be determined if the projects are steered to bypass the peer review mechanism?

As you know, I was one of the reviewers that you specifically requested for a "second look" for a commercialization project that I scored not fundable on the original review. You did not inform me that Dr. Gilman had rejected your idea to contact reviewers for a "second look." My "second look" showed the project was not different from my first review, and therefore my score was not changed.

However, upon further reflection, I think it was inappropriate for you to request a "second look" when Dr. Gilman rejected your plan. I think your style of making "on the fly" decisions during the review process is not transparent or fair to all applicants.

## Eric Fearon

*The Emanuel N. Maisel Professor of Oncology, professor, Departments of Internal Medicine, Human Genetics and Pathology, associate director for basic science, deputy director, University of Michigan Comprehensive Cancer Center, chief, Division of Molecular Medicine & Genetics, Department of Internal Medicine*

I am writing to offer my resignation as a member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

The citizens of Texas and the Texas legislature are to be congratulated for their wisdom in supporting innovative cancer research and prevention efforts via the founding and funding of CPRIT. It was a great honor and privilege to serve over the past three years as a member of the BCRC-3 panel, in a scientific review process conceived by outstanding leaders such as Al Gilman, Phil Sharp, and the Cancer Research

Committee chairs, alongside truly outstanding and committed cancer researchers from outside the state of Texas.

Our panel evaluated and discussed all scientific applications before the Committee without any bias or conflict of interest, with the singular goal of identifying only the most promising, innovative, and high impact cancer research proposals.

Having participated as a panel member and/or chair at numerous scientific review committees at the NIH and multiple foundations over the past two decades, the quality of the scientific review process at the BCRC-3 panel was the most outstanding of any such evaluative process that I can recall.

Based on my reading of news articles over the past few months in various forums (e.g., Houston Chronicle, Dallas Morning News) and opinion pieces (e.g., the June 29, 2012 Houston Chronicle piece from Charles W Tate, chairman and founding partner of Capital Royalty LP, a leading investment firm focused on providing growth capital to the biopharma industry and a member of CPRIT's Oversight Committee, who chairs its Economic Development and Commercialization Subcommittee) discussing CPRIT's likely intentions going forward, I am left with the impression that "grand" science and "commercialization" projects may represent much of the future for CPRIT.

As a result, I am uncertain that the robust scientific review process for CPRIT applications of all types that was conceived by Drs. Gilman, Sharp and the other review panel chairs, and executed by the varied review panels will be needed going forward. Indeed, I found the press release from CPRIT on their website (Sept. 21, 2012) stating that "we look forward to continuing and expanding our support for MD Anderson's prevention, research and commercialization projects, particularly the multidisciplinary groups of researchers and clinicians that are mounting comprehensive attacks on the eight target cancers" to be a most remarkable statement, especially so, in light of the fact that the statement is a forward-looking one.

To me, the CPRIT press release seems to imply that certain, yet-to-be-submitted MD Anderson applications to CPRIT have already been judged to be sufficiently meritorious to deserve CPRIT support, even though the hypothetical applications have presumably not yet been fully conceived or submitted in final version to CPRIT by MD Anderson scientists and clinicians, nor have the hypothetical applications been subjected to full scientific evaluation by outside, independent review panels.

Perhaps for some in the cancer research field such as myself, the CPRIT press release statement on their website could be seen as consistent with the view that unencumbered and unbiased expert peer-review of cancer research applications submitted to CPRIT might simply be a quaint relic of the past.

## Scott Kern

*Associate professor of oncology and pathology, Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center*

It is ironic that I again find myself in the undesirable position of resigning from a hard-working and highest-quality scientific study section. As Twain noted, history does not repeat itself, but it does rhyme.

Ten years ago, I served on the scientific review board of a private philanthropic organization. In an unusual development, I was asked to review two special grant applications that had arrived out-of-cycle. After my review, I was informed by the organization that they had beforehand decided to fund the two grants, a decision made prior to obtaining the reviews from the scientific board.

They had in this instance perhaps operated as a direct money conduit and not as a peer review-guided granting operation. Owing to the deprecated role of scientific review under such procedures, I regretfully resigned from their board. To my knowledge, subsequently they adhered tightly to the procedures established in their founding document, pursued a stellar and constructive path, and remain a healthy organization.

I now find that a somewhat similar situation exists at CPRIT.

The irony is as follows. The PI of a grant receiving questionable dispensation ten years ago, and a PI of a grant recently under critical scrutiny for improper dispensation at CPRIT, were the identical person.

For history to rhyme,

I must resign.

I wish CPRIT well.

## Gregory Longmore

*Director, Section of Molecular Oncology, Washington University in St. Louis*

I am writing to inform you that I am resigning my position as member of the CPRIT Basic Science Cancer Research Committee-3 (BCRC-3), effective immediately.

It was a pleasure to be part of an outstanding group of scientists that strived, without prejudice or conflict of interest, to support only the very best cancer biology in Texas. I believe the events of the past few months have tarnished what was at the outset a wonderful program that thoughtfully and fairly funded outstanding cancer research in the state of Texas.

This initiative and program was something that the people of Texas could be proud of, and I have no doubt would have served the state of Texas and the U.S. in years to come. In my opinion actions by the oversight committee have significantly compromised and tarnished the initial mission of CPRIT. For the sake of cancer research and cancer patients in the state of Texas I hope that CPRIT will be able to get back to whence it began.

Under the current circumstances and perceived new direction of how CPRIT funds will be allocated, I feel that I cannot continue in my role.

## Carolyn Anderson

*Professor of radiology and pharmacology & chemical biology, director, Molecular Imaging Laboratory, University of Pittsburgh*

This e-mail is to inform you of my resignation, effective immediately, as a reviewer for CPRIT Interfaces Review Committee.

I thoroughly enjoyed working with outstanding scientists on the review panel, as well as our esteemed chair, Dr. Gambhir.

I am also privileged to have had the opportunity to work with Dr. Al Gilman, who was incredibly supportive of the peer review process and of all the reviewers, which lead to the funding of outstanding cancer research in the state of Texas.

Working with consummate professionals such as JoAnn Eckert and the SRA staff, especially Rajan Munshi, made the experience of reviewing for CPRIT feel a pleasure more than hard work.

I sincerely hope that the unfortunate circumstances that have led to the numerous resignations of the council leaders and reviewers can be rectified.

CPRIT has done the field of cancer research and cancer patients in Texas a tremendous service, and hopefully this can continue in an honorable fashion that abides by the principles of scientific peer review.



*Guest Editorial*

# CPRIT Of Old Never Promised More Than It Could Deliver

(Continued from page 1)

In three years, CPRIT has funded hundreds of excellent research programs at many Texas institutions, recruited roughly 50 outstanding scientists to Texas, established a statewide clinical trials network and helped companies develop ways to help patients.

Recent controversies at CPRIT caused us to resign as the institute's chief scientific officer and chairman of its scientific review council. Leaving, we pause to review lessons from CPRIT's past and offer advice for its future.

We have been guided by a few simple principles:

We were truthful about the complexity of cancer. To find cures, we must ponder dynamic cellular systems containing huge numbers of parts whose behaviors are governed by rules that have evolved over millions of years. We don't understand these systems in nearly enough detail to explain why and how they become dysfunctional. Progress in treating cancer requires rare and penetrating insights into deep pools of ignorance and translation of these insights into new therapies. It's pointless to push money at a problem—no matter how important it may be—if you lack insight for finding a solution.

Money entrusted to CPRIT financed the best ideas—period. Texans deserve the best cancer research, the best scientists, the best clinicians. Quotas based on geography, favoritism, type of cancer, or type of patient drain resources.

Funding decisions were based on the best possible advice from the finest experts, free of conflicts of interest. CPRIT's research peer review committees have been chaired by some of the best cancer biologists and physicians in the country. All work and reside outside Texas. The chairs chose more than 100 committee members—again paying attention to expertise and lack of conflicts. These recruits to the Texas war on cancer joined because they recognized a unique opportunity to make an impact. We used their time efficiently and treated them and their recommendations with respect.

CPRIT selected the best efforts from the best people who were willing to risk failure to make major strides. Peer review systems can be too conservative, searching for sure bets, where experiments are easy to execute but only buy minor increments in knowledge.

Missed are the opportunities to take great leaps. Yet great leaps are exactly what's required, and we looked for them.

Science must come first; commercialization is essential but comes second. Businesses hunger for great insights to turn into great products. We see this in the thriving biotech corridors of Boston and San Francisco.

The past eight months were difficult. Controversy flared when several well-regarded, multi-investigator, multi-institutional collaborative research projects were put in the freezer for months—not brought to the Oversight Committee for funding after strong recommendation by the Scientific Review Council.

This delay was at least partially based on the concern that several of these projects came from one institution. CPRIT's executive director has offered different and conflicting explanations for this action.

Simultaneously, an expensive "commercialization" proposal, constructed and submitted in unorthodox ways that circumvented CPRIT's rules, was rushed to the Oversight Committee and approved for $20 million for its initial year of operations, despite the absence of description or scientific review of its drug development program. This was ultimately corrected, albeit with great effort. Writing in the Chronicle, Todd Ackerman and Eric Berger reported on various individual relationships that might have motivated these events.

How can CPRIT once again become a program respected by scientists across the U.S. and the world?

A commission should be appointed to determine whether individuals tried to violate the public trust in the actions described above. If so, they should be removed from their positions.

CPRIT's governing board should have sufficient expertise to do its job. Only one member of this 11-person Oversight Committee has any direct knowledge of cancer, medical practice or research. The Oversight Committee should promote policy, provide broad oversight of personnel and operations, and ensure legal and ethical behavior. Members who meddle in day-to-day operations of the organization to further their own interests should be removed.

Texans deserve to hear the truth about cancer. They must understand that miracles will not happen in a short time. Progress will not be made by those who simply proclaim without explanation that they can do better than hundreds of skillfully staffed and well-financed pharmaceutical and biotechnology companies. Real progress requires the concerted high-quality efforts of basic, translational and clinical investigators from the academic community collaborating with counterparts from the private sector when appropriate. There is no single "cure" for cancer. Cancer is hundreds of diseases, and victories will come one or a few at a time. CPRIT will have an enormously positive impact on society over time, both in terms of the health of its citizens and its economy. Texans must understand this and demand that CPRIT continues to adhere to its core principles.

Academic institutions and for-profit companies have very different cultures, and these differences must be respected. Academics strive to develop new knowledge and, usually, disseminate it widely (i.e., by teaching, broadly defined, and publishing). Companies operate much more competitively and in many cases in secret, with the goal of providing financial returns to investors by bringing useful products to society. There can and should be synergy between the two types of institutions, with academic knowledge being used to further the commercial activities of companies, and there can be links between the two. But the relationship shouldn't be excessively intimate. Secretive behavior impedes education and research training and therefore doesn't belong in academia. There are also questions of compensation, ownership, neglect of academic responsibilities, etc. CPRIT needs to understand this as it strives to facilitate commercialization of its research activities.

Reliance on peer review to identify the best science must continue to guide CPRIT in the future. Of course, there are other ways to distribute public funds, but they are worse. Their side effects include infamy and they end in irrelevance.

*Gilman is professor emeritus of pharmacology at the University of Texas Southwestern Medical Center. Sharp is an institute professor at the Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology. Sharp won a Nobel Prize in Physiology or Medicine in 1993, while Gilman won the same Nobel Prize in 1994. This editorial was originally published in The Houston Chronicle and is reprinted with permission.*

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*In Appreciation*

## Specter Pushed For Doubling Of NIH Budget Over Five Years

(Continued from page 1)

Specter helped accomplish the five-year doubling of the NIH budget, which was completed in 2003. In addition, his support of an amendment to the American Recovery and Reinvestment Act in 2008 led to an additional $10.4 billion to support the work of the NIH and NCI.

During his tenure in the Senate, Specter served on the Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, which is the subcommittee responsible for allocating funding for the NIH. He served as chairman for 10 years.

Specter was awarded the American Association for Cancer Research Centennial Award for Distinguished Public Service at the AACR 100th Annual Meeting in 2009, and the AACR praised him for his leadership and support of increased federal funding for cancer research following the passage of the American Recovery and Investment Act of 2009.

"With his passing, the cancer research and biomedical science community lost one of its greatest supporters and promoters," said a statement published by the AACR.

In 2005, the AACR honored him with its Public Service Award, and in 2007, recognized his efforts at the AACR's Centennial Dinner. Also in 2007, Specter received the Public Service Award from the American Society of Clinical Oncology.

"For years, Specter was one of the most ardent advocates for increased spending for the National Institutes of Health," said AACR CEO Margaret Foti.

"Senator Specter demonstrated exemplary leadership in advocating for federal funding to support a national biomedical research enterprise that brings critical laboratory and clinical research discoveries to millions of Americans with cancer," said ASCO President Sandra Swain.

*The entirety of Collins' statement follows:*

I am greatly saddened by the death of former Senator Arlen Specter, who over the course of his illustrious career served as a towering champion for biomedical research and the mission of the National Institutes of Health. Our thoughts are with Arlen's wife Joan, his children, grandchildren, and the many others who worked with him over the years and knew of his passion and extraordinary vision.

Arlen served as a forceful advocate for the millions of Americans eagerly awaiting new cures and treatments. His favorite saying, which we all heard many times over the years, was that NIH was the crown jewel of the federal government.

I particularly appreciated Arlen's direct, no-nonsense approach, which he used so effectively to advance biomedical research in ways that some thought impossible. His legendary accomplishments on behalf of biomedical research include: recognizing the potential of stem cells and holding hearing after hearing to bring to the forefront the importance of federal funding to support this research; doubling of the NIH budget between FY 1998-2003; the establishment of an NIH Office of Emergency Medicine; the creation of the Cures Acceleration Network; and securing $10 billion in the Recovery Act to provide an immediate infusion of new research dollars for the NIH in 2009.

The distinguished Senator from Pennsylvania also gave of himself in a much more personal way. When he was diagnosed with heart disease and several different types of cancer, the Senator not only refused to give up, he took his battles public and, in the process, inspired countless other patients striving to live full lives in the face of very tough odds. A fighter to the end, Arlen taught us all some valuable lessons about the power of perseverance.

As NIH Director, I truly miss Arlen's steady hand and vision for our agency, which is the world's largest supporter of biomedical research. Arlen was the epitome of a public servant, and the American people were extremely well served by his wisdom and vigilance. His expectations of the NIH were as high as his confidence in NIH. To pay tribute to the Senator's legacy, we at NIH will work harder than ever to meet those high expectations and to carry out our mission of turning scientific discoveries into better health for all.

*FDA Approvals*

# FDA Approves Abraxane And Alimta for NSCLC

**FDA approved a new use of Alimta**, adding the continuation maintenance setting for locally advanced or metastatic nonsquamous non-small cell lung cancer, following first-line Alimta plus cisplatin.

FDA approved the label inclusion of Phase III data that demonstrated progression-free and overall survival advantages in the continuation maintenance setting for these patients.

Alimta (pemetrexed for injection) is indicated for the maintenance treatment of patients with locally advanced or metastatic NS NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. Alimta is not indicated for patients with squamous-cell NSCLC.

Approvals were based on results from the PARAMOUNT trial, the final results of which were shared in an oral presentation at the American Society of Clinical Oncology annual meeting June 4, 2012. PARAMOUNT was the first study to evaluate the first-line use of Alimta plus cisplatin therapy followed immediately by the use of Alimta as a single-agent in the continuation maintenance setting.

A total of 939 patients with advanced nonsquamous NSCLC were enrolled in the study and received Alimta in combination with cisplatin induction therapy. All patients received vitamin B12, folic acid and dexamethasone. Patients whose disease had not progressed during the Alimta plus cisplatin induction and who had an ECOG performance status of 0-1 (n=539) were randomized two-to-one to receive Alimta maintenance (500 mg/m2 on day one of a 21-day cycle) plus best supportive care (n=359) or placebo plus best supportive care (n=180) until disease progression.

Of the patients whose disease had not progressed during Alimta plus cisplatin induction therapy and who were randomized to receive maintenance therapy, 44 percent versus 42 percent achieved a complete or partial response to induction therapy and 53 percent versus 53 percent had stable disease after induction treatment in the Alimta and placebo arms, respectively.

Final results of the trial demonstrated a 22 percent reduction in the risk of death (HR=0.78; 95% CI: 0.64–0.96; p=0.02) with Alimta, compared to placebo. This reduction in the risk of death resulted in an improved median overall survival from the time patients were randomized of 13.9 months median for patients receiving Alimta, com- pared to 11.0 months median for patients on the placebo arm.

Median progression-free survival measured from randomization was 4.1 months on the Alimta arm as compared to 2.8 months on the placebo arm with a hazard ratio of 0.62.

The grade 3-4 adverse reactions with Alimta as a single agent for patients in the maintenance setting were anemia, neutropenia and fatigue

**FDA approved Abraxane** for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.

The approval is based upon the results of CA-031, a phase III, multi-center, randomized open-label trial where patients with advanced NSCLC received either Abraxane (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) plus carboplatin (n=521) or paclitaxel plus carboplatin (n=531).

The trial demonstrated a higher overall response rate for patients in the Abraxane arm compared to those in the paclitaxel arm (33 percent vs 25 percent).

Abraxane demonstrated a higher overall response rate as compared to paclitaxel for squamous cell carcinoma (41 percent vs. 24 percent) and large cell carcinoma (33 percent vs. 15 percent). Abraxane achieved a similar overall response rate to paclitaxel in patients with carcinoma/adenocarcinoma (26 percent vs. 27 percent).

The most common adverse reactions of Abraxane in combination with carboplatin for NSCLC are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue.

This is the second indication for Abraxane in the U.S. Abraxane was first approved in 2005 for the treatment of metastatic breast cancer after failure of combination chemotherapy.

Abraxane for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.

Abraxane is indicated for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.