THE CANCER LETTER

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NCI Grant Funding

"Zone of Likelihood" Moves From 7 to 9 Percent

By Paul Goldberg

NCI will extend the "zone of likelihood" of grant funding from 7 percent to 9 percent, Institute Director Harold Varmus said to the National Cancer Advisory Board Nov. 29.

This change means that next year a larger number of grants will be funded based on the score they receive from the study section. Grants that fall outside this zone are subjected to an additional level of review.

"We are, at least provisionally, extending the zone of likelihood this year from the seventh percentile and better to the ninth percentile and better, with the supposition that the division will highlight for us a proposal that got a very high score that they don't want to fund, so we can at least have a very brief discussion about that," Varmus said to the board.

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Beyond Guidelines

NCCN, McKesson Form Partnership To Build Clinical Support Software

By Paul Goldberg

The National Comprehensive Cancer Network, McKesson Specialty Health and the US Oncology Network announced a collaboration to create clinical pathways and to produce software that will allow physicians to assess treatment options consistent with evidence-based standards.

The pathways and supporting software will also allow providers to consult coverage policies mandated by payers.

The system, Value Pathways Powered by NCCN, will be produced in collaboration between the NCCN guidelines panel members and the US Oncology Network physicians who develop the company's Level I Pathways.

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Turmoil in Texas

Texas Agency Funded $11 Million Grant Without Peer Review; Official Resigns

By Paul Goldberg

The Cancer Prevention & Research Institute of Texas acknowledged that two years ago it gave out an $11 million "commercialization" grant without peer review.

The grant was awarded in June 2010 to Peloton Therapeutics Inc. of Dallas.

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Success Rate: 15% For R01s, 10% for R21s in Fiscal 2012

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The shift means greater reliance on the priority scores in awarding grants. Outside the ninth percentile, the institute's decision to fund grants can be influenced by a variety of considerations.

"The policy that I've put into effect since I've been here is basically that every single grant is on the table," Varmus said. "It's really a bad idea to say we have a sharp payline at a certain percentile, because percentiles don't reflect the full value of a grant application. They are judged by a study section, competing against different grants, they don't reflect the shape of the portfolio, and in our meetings with scientific program leaders, we take into consideration the amount of effort we are making in certain areas, the importance of certain areas, the novelty of the grants—and we've learned from experience that virtually everything that has a percentile score of 7, 8, 9 or better is very likely to be funded."

Overall, in 2012, NCI's success rate for R01 grants was 15 percent—4,143 applications were received and 618 were funded. For R21 grants, the success rate was 10 percent, with 1,911 applications received and 200 funded.

At the meeting, Varmus presented graphs and tables showing the success rates by type of grant, the scores and type of investigator.

"We usually support funding with minimal or no discussion, unless the division decides to bring some application to special attention," Varmus said. "Then we have a zone that runs all the way through to percentile scores into the 20s to examine in a discussion among the scientific program leaders.

"The result has been, as you saw last year, that virtually all grants that had percentile scores of 7, 8, 9 or better are funded and then it's a decreasing likelihood of being funded as the scores get worse, then only a few of the percentile scores in the 20s are likely to be funded, and we don't consider things much below that."

Though the boundary of the zone of likelihood has shifted, last year's data showed that application in the ninth percentile or better had at least a 90 percent chance of being funded.

"I don't want to put you on the spot, but it might be helpful to have examples," said NCAB chairman Tyler Jacks, Professor of Biology at the Massachusetts Institute of Technology and director of the MIT David H. Koch Institute for Integrative Cancer Research.

"There were a few grants in the low percentile that actually were not funded, and on the other side there were grants that were not so well funded. I'm curious as to where the decisions came from, I know it's through the scientific leaders group, but if you could give us some color, without naming names, just to give us a sense of how those decisions were made."

VARMUS: "It wouldn't surprise me to find that a couple of those cases where someone with a very high score didn't get funded that there was usually some issue about the number of grants or overlap with existing grants.

"There are very few of those in total, four or five over the course of a year, so I hesitate to give any more color because it would become evident who we are talking about. And when you look out at the 20 percentile scores, what you generally find is that someone had an idea that was novel, and the review suggested that there was one naysayer that pulled down the score significantly, and this area is particularly important and underrepresented in the portfolio.

"And the other point is that these things have usually been discussed at divisional meetings, so we could not possibly do all this work at the SPL meetings. In fact, one of the things that is influencing this process is the divisional conversations, which, in my experience, have been extremely rigorous and have diminished the need for extensive discussion at the SPL meetings."

JACKS: "I think there is a concern in the community that the payline is extremely low, historically low. And these numbers do not back up this concern, they're the same this year as last."

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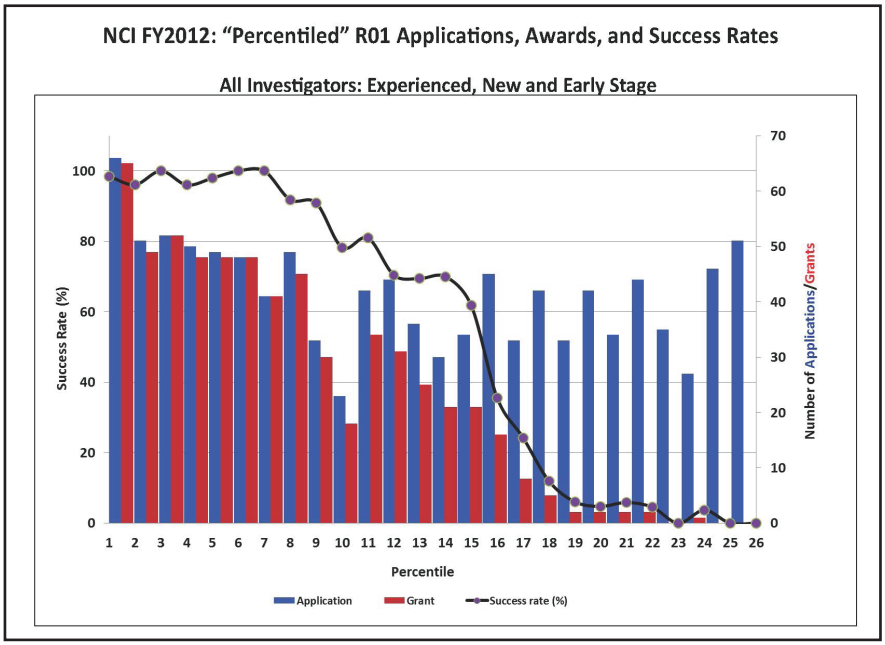
VARMUS: "Let me just interject, because you and others have alerted me to the fact that there are people going around saying that the success rate is 7 percent, and that's simply not true.

"People need to understand the difference between the percentile score you receive from a study section evaluation and this zone of high likelihood of being funded.

"The success rate is bad. I don't believe the NIH functions well, or that the scientific community functions well, with a success rate of 15 percent—but at least it's not 7 percent."



JACKS: "The fact is that if you got a score of 15, by these numbers, you have a 30 to 40 percent chance of being funded. That is not known."

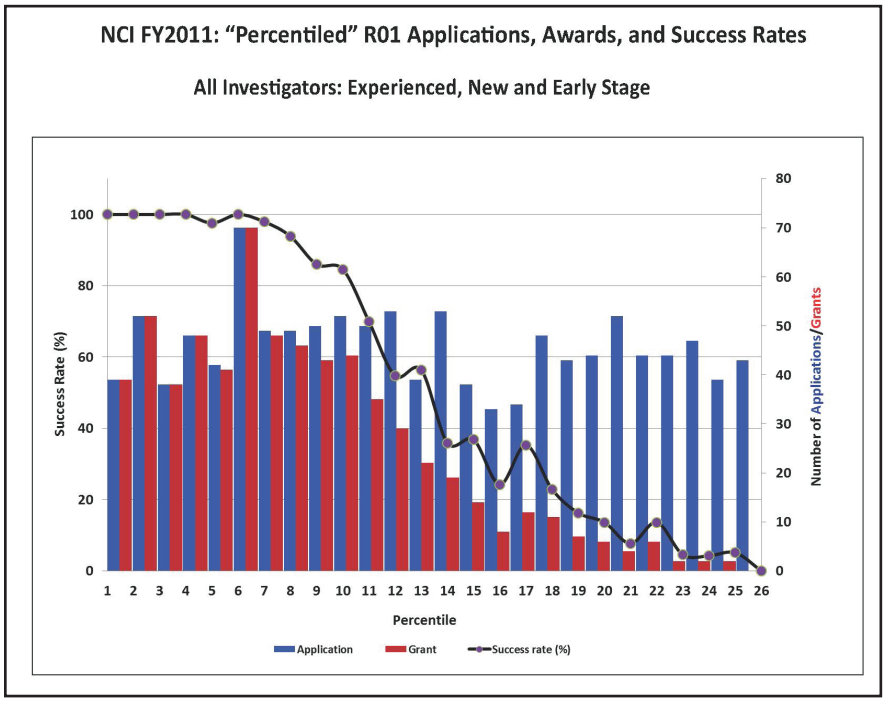
VARMUS: "Well, all I can tell you is—you've asked about your role here at NCAB—you are knowledgeable, tell your colleagues.

"These numbers were posted last year from the FY11 results, and you can see what the findings are. I don't want people to think I'm saying everything's fine; look at the numbers. Things are bad.

"But it doesn't help the effort to fix things by exaggerating erroneously what's actually happening."

OLUFUNMILAYO OLOPADE [NCAB member and professor of medicine and human genetics and director, Cancer Risk Clinic, at the University of Chicago]: "If you look at investigators who are within 10 years of taking their position, you have 564 applications, and 15 percent—so the question is how could we figure out a way to get that number—whether through targeted RFAs or new study sections—the young investigators are not moving through the pipeline, if the success rate is going to remain this low."

VARMUS: "When we review these applications at scientific program leader meetings, the [early stage investigators] are highlighted.



"One thing we could do, and it will be available on the website, is show you that those folks got funded with lower percentile scores or worse percentile scores.

"It will be on the website, it's on the website for FY11, so your chances of being funded, even though your score's not so good, are greater if you're an [early stage investigator]. Because we pull those grants up. Now are you saying we should do it more? Or have special set-asides?"

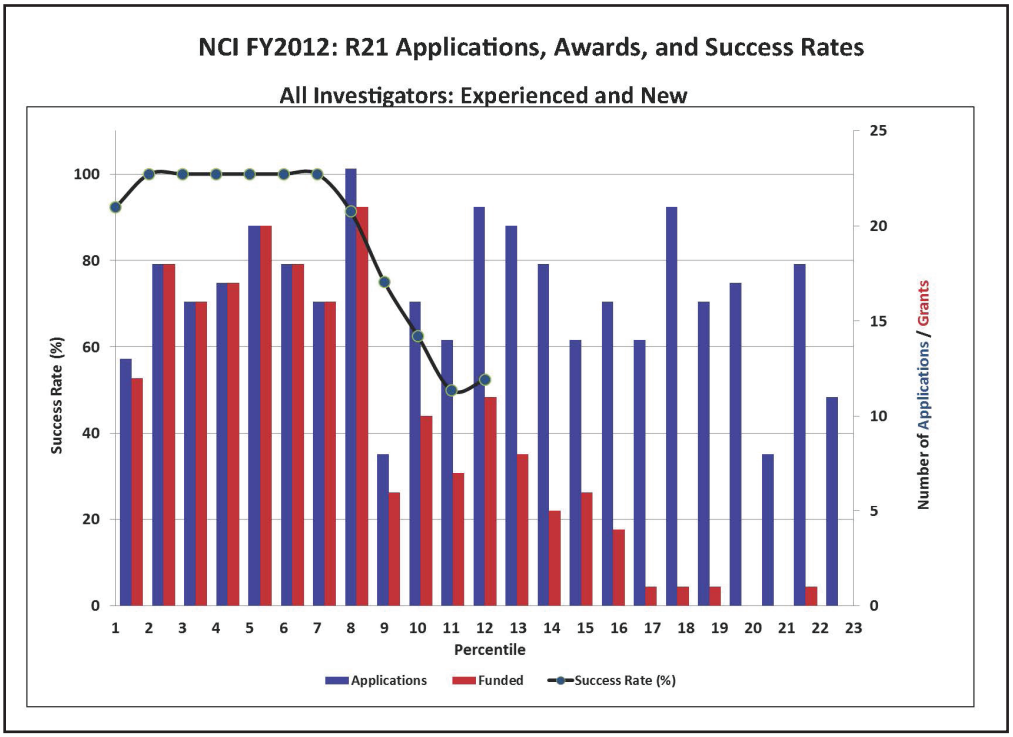
OLOPADE: "No I'm just really thinking in terms of making sure the pipeline is robust, because over the past 10 years if we only have a 15 percent of them funded, then over time, we're not going to

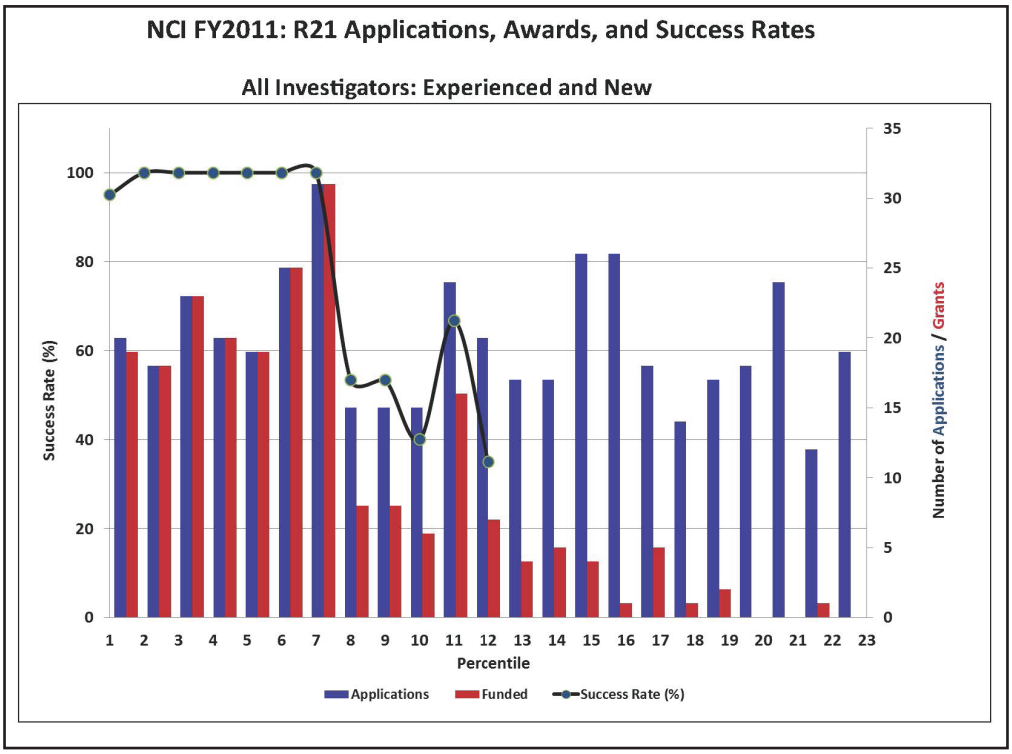
be able to replenish, so I know you pull them up but the question is what else can we do to expand that pool."

VARMUS: "Increase the budget. Give less money to your cancer center. Cut the intramural program.

"I mean, there are limited options.

"What I have to be most responsible to is the progress of cancer science. I'll be saying to somebody who has worked, effectively, for the past five years on the second renewal of their R01 that you are not going to get your grant because we need to fund a new investigator, that's a big deal."





Fiscal Year 2012: Success Rates (investigator-initiated R01's and R21's)

	Total Applications	Number With Percentiles Of 25 or better	Number With Percentiles Of 10 or better	Funded	Success Rate
R01 – All Investigators	4,143	1,029	462	618	15%
Experienced Investigators - Total	2,849	777	356	466	16%
Type 1	2,345	556	245	316	13%
Type 2	504	221	111	150	30%
New Investigators	1,294	252	106	152	12%
Early Stage Investigators	564	129	59	86	15%
R21 – All Investigators	1,911	411	165	200	10%
Experienced Investigators	751	194	73	87	12%
New Investigators	1,160	217	92	113	10%

Fiscal Year 2012 vs. 2011: All Competing Research Project Grants

	FY 2012		FY 2011	
	Funded	Success Rate	Funded	Success Rate
R01 – Unsolicited	620	15%	655	15%
R21 – Unsolicited	200	11%	223	10%
R03	101	20%	72	17%
Solicited R01/R21	88	8%	68	14%
*Other RPGs	78		88	
Total Competing RPGs:	1,085	14%	1,106	14%

*Other RPGs include R03, R15, P01, U01 and UM1.

Association of American Cancer Institutes

AACI Translational Cancer Research Fellowship Now Available

Applications are due February 1, 2013 for the AACI Translational Cancer Research Fellowship. The Association of American Cancer Institutes (AACI) is comprised of 95 leading cancer research centers in the United States. AACI's membership roster includes National Cancer Institute-designated centers and academic-based cancer research programs that receive NCI support.

The intent of the fellowship is to provide additional support to individuals who are engaged in any area of clinical and/or translational cancer research in order to further the development of their careers and enhance their future success in an academic discipline. The AACI fellowship will provide a one-year, non-renewable $50,000 grant to support post-doctoral training to individuals who have completed at least one year of training in any field of oncology and have at least one year of training remaining at an AACI member institution.

This award is designed to help ensure that qualified applicants receive research training and experience under the guidance of highly trained, well-respected researchers who have demonstrated success in their field. The goal is to assist the trainee in becoming a high-caliber, productive independent researcher with an enduring focus on the importance of translational research relevant to cancer.

One applicant per AACI member institution will be accepted for consideration.

Important Dates

Application Deadline: **February 1, 2013**
Start of Grant Term: **July 1, 2013**

Interested applicants please visit: www.aaci-cancer.org for detailed application instructions.

Beyond Guidelines

NCCN, McKesson Expand Longstanding Collaborations

(Continued from page 1)

The pathways will become available next spring, developers say. The US Oncology Network is a part of McKesson Specialty Health.

The system will initially cover 19 tumor types and will be expanded to match all of the NCCN guidelines.

The NCCN guidelines are developed by panels of clinicians and oncology researchers from the network's 21 centers. The guidelines are available on the Web for downloading at no cost. However, their commercial use must be licensed. Level I Pathways are proprietary.

"Our collaboration creates a tool that optimizes the ability to interact transparently with payers and support new conversations on quality and value," said Roy Beveridge, chief medical officer for McKesson Specialty Health and the US Oncology Network. "Value Pathways will create a single set of content that we believe will enhance national best practices for optimal patient care and value-based outcomes in a completely transparent process."

The licensing agreement between NCCN and McKesson is non-exclusive, but the collaboration is meant to drive adoption of a single set of standards in the marketplace. These standards would be based on NCCN guidelines.

The financial terms were not released.

Practices in the US Oncology Network treat about 18 percent of cancer patients in the U.S., and McKesson sells drugs to practices that treat another 20 percent. "This means that nearly 40 percent of the market could be using the same pathways," Beveridge said.

The pathways will be used at practices in the US Oncology Network and at other practices that would license it.

Also, it will be used at hospitals, where it would provide clinical decision support for oncologists employed by hospitals. McKesson's core business is supplying drugs to hospitals.

The market for clinical pathways and decision support and review systems is competitive.

Players include the P4 Pathways owned by CardinalHealth, Via Oncology Pathways, Eviti Inc., ICORE Healthcare, and others. Content libraries and software from these firms are used by a number of regional and national payers. IBM has also announced plans to develop a decision support system using the Watson technology.

The latest deal strengthens the multiple links between NCCN and McKesson.

In February, McKesson acquired assets from Proventys, a company that was working on a clinical decision support system in collaboration with NCCN.

Two years ago NCCN agreed to make its drug compendium available in two McKesson software tools through its InterQual clinical content:

• Clear Coverage, a point-of-care prior authorization, coverage determination and network compliance decision support platform that supports shared decision-making between a payer and its network providers.

• CareEnhance Review Manager, a clinical decision support criteria for reviewers which automates the care review process and enables data retrieval and aggregated reporting.

"It was a convergence of the relationship and of market forces that caused us to come together in this logical collaboration," Patricia Goldsmith, NCCN executive vice president and chief operating officer, said to The Cancer Letter.

"The collaboration combines McKesson technology and pathways expertise with the academic rigor and content expertise from NCCN to bring to market enhance access to the NCCN Guidelines and new Value Pathways."

Capitol Hill

Recalcitrant Cancer Legislation Added to Senate Defense Bill

A letter from Sen. Tom Coburn (R-Okla.) gave NIH officials an opportunity to spell out their reasons for opposing earmarks for specific diseases.

Coburn, a physician, had placed a hold on the controversial legislation in September—stalling H.R.733/S.362, or the "recalcitrant cancers" bill. The bill would mandate greater spending on pancreatic and lung cancers.

The legislation has now been added as an amendment to the Senate defense bill, the National Defense Authorization Act of 2012, which may be approved within the next week.

The measure, drafted in response to aggressive lobbying on the part of the Pancreatic Cancer Action Network, has cleared the House.

The original version of the authorizing measure limited the NCI authority in charting the course on research in pancreatic cancer (The Cancer Letter, Aug. 3, Aug. 10, Sept. 14, Nov. 16).

In a letter dated Nov. 16, NIH Director Francis Collins spelled out his reasons for opposing earmarking for specific diseases.

"Because our science often produces new and unexpected findings and because medicine is often confronted with altered or unyielding threats to public health, the NIH Institutes and Centers must constantly assess their research plans and portfolios," Collins wrote.

"For example, the National Cancer Institute recently organized a group to perform a 'horizon scan' of pancreatic ductal adenocarcinoma (PDAC) research, building on previous planning exercises in 2001 and 2008. This new group will examine current research efforts, benchmark our scientific understanding, and identify promising and possibly underexplored areas for future research in hopes of improving the still dire outcome of this dreaded disease."

The text of the letter follows:

Dear Sen. Coburn:

Thank you for your Sept. 17 letter requesting that I address four questions about how disease-specific legislation affects the ability of the National Institutes of Health (NIH) to plan and perform research.

First you asked if the NIH already has the ability to create strategic plans and working groups without a legislative mandate to do so. The Secretary of Health and Human Services and leaders of the Institutes and Centers of the NIH have the authorities needed to constitute standing advisory committees, create working groups, and develop plans for research programs; as a result, they do not need legislative mandates to take such actions.

The NIH Institutes and Centers have senior advisory councils that oversee the research portfolio of each component. Individually or in collaboration, the NIH Institutes and Centers frequently form other advisory groups charged with planning research on Institute-specific or trans-NIH subjects. These many activities, in conjunction with our peer review panels, are part of our ongoing effort to evaluate the current scientific landscape and to protect and advance our investments in research for public benefit.

Let me provide a recent example of how these planning processes work. The National Institute of Allergy and Infectious Diseases (NIAID) has used working groups to identify scientific opportunities in areas where there are pressing public health needs. One example is influenza—both seasonal influenza, which kills up to 49,000 Americans each year, as well as pandemic influenza such as the recent 2009 H1N1 pandemic. In early 2006 NIAID convened a Blue Ribbon Panel on Influenza Research to help identify areas in which progress was needed. This panel recommended eight areas in which there were opportunities for scientific advancement, including research on improved influenza vaccines. To continue and build upon these efforts, NIAID released NIAID Influenza Research: 2009 Progress Report, which identified the development of "universal" influenza vaccines as an expanding area of scientific opportunity.

Currently, the NIAID's extramural researchers are pursuing multiple vaccine strategies for the development of a universal influenza vaccine. In addition, researchers at the NIAID Vaccine Research Center are making significant progress towards the development of such a vaccine. They have tested in animals a two-step, prime-boost vaccine that generates neutralizing antibodies against many strains of influenza virus. Animal studies of this technique have proven promising, and researchers will soon study the approach in human clinical trials.

This past summer, NIAID sponsored, with the Food and Drug Administration, a scientific meeting to revisit progress and challenges with regard to the development of universal influenza vaccines. This comprehensive NIAID effort is just one example of how the NIH constantly examines scientific opportunities and conducts research evaluation and planning activities within its current statutory authority.

You next asked me to address the NIH's ability to foster ground-breaking discoveries without legislation that directs it to address a specific disease or group of diseases. While we seek always to be responsive to the concerns of the public, often expressed through "report language" in appropriations bills, the NIH has considerable statutory authority to plan and oversee the research that leads to important discoveries.

Because our science often produces new and unexpected findings and because medicine is often confronted with altered or unyielding threats to public health, the NIH Institutes and Centers must constantly assess their research plans and portfolios.

For example, the National Cancer Institute recently organized a group to perform a "horizon scan" of pancreatic ductal adenocarcinoma (PDAC) research, building on previous planning exercises in 2001 and 2008. This new group will examine current research efforts, benchmark our scientific understanding, and identify promising and possibly underexplored areas for future research in hopes of improving the still dire

outcome of this dreaded disease.

You further asked me to address the impact of disease-specific legislation on the NIH's ability to allocate resources freely and to study basic biology and mechanisms. When providing technical assistance to the Congress on possible legislation, the NIH generally suggests that Congress provide the maximum flexibility for our mission. Basic research that may lack any overt connection to specific diseases is the foundation for disease specific translational and clinical research, and it must be preserved to ensure the discoveries that later drive applied work on individual diseases.

If Congress is too proscriptive when it directs the NIH to focus on specific diseases, the agency loses its valued flexibility to allocate resources in a manner that optimizes the likelihood that the scientists we support will discover the underlying disease mechanisms that must be understood to achieve our goal of improving the health of our nation.

Let me provide an example of basic research that addresses several specific types of cancer. As early as the 1980s, cancer researchers observed mutations in a certain critical gene, the KRAS gene, in a variety of human cancers, including about a third of lung cancers, about half of colon cancers, and as many as 95 percent of PDACs. Basic research on a wide variety of cell types, from yeast to human, has taught us that the KRAS gene encodes an unusual signaling protein that acts in conjunction with other proteins as a molecular "on/off" switch for signals promoting cellular growth.

Mutations in this gene leave the switch "on", resulting in persistent cell growth and division. Despite what we know about KRAS mutations, and despite extensive efforts in both industrial and academic research sectors, we have not yet been able to counter these mutations therapeutically.

In order to treat PDAC and many other cancers exhibiting KRAS mutations, we must focus on research that increases our understanding of how such mutations drive the biological effects that cause these devastating diseases. Given what we have learned about molecular mechanisms, it would be counterproductive to limit that effort to a specific cell type. In other words, if Congress directs the NIH to study specific diseases without flexibility, it can limit our ability to follow the best leads in science and to pursue discoveries that move an entire research field forward in a way that produces maximum benefit to the public.

Finally, you asked me to address how genomics has revolutionized the study of underlying mechanisms of disease. Recent advances in genomics are transforming the way science is conducted. Our understanding of basic mechanisms has increased exponentially with the widespread adoption of high-throughput screening, genome sequencing, and advances in bioinformatics. This transformation of the biosciences is profoundly affecting the practice of medicine. Advances in the biological sciences have changed the way we view disease. We now recognize that dysfunction of specific biochemical pathways that govern cell behavior may be similar in superficially disparate diseases or quite different in patients with the same category of diagnosis.

When you and I were in medical school, all patients with cancers of a given organ were treated with the same combination of chemotherapy, radiation therapy, or surgery. With today's application of high-throughput screening and genomics, we are now shifting to treating an individual's cancer with a kind of "precision medicine" that is based upon the patient's genome and the genome of his or her individual tumor.

As an industry scientist recently told The New York Times, "[t]he old way of doing clinical trials where patients are only tied together by the organ where their cancer originated, those days are passing."

This is just one more reason why directing research resources toward a particular disease without flexibility, as defined in the pre-genomic era, can run counter to scientific opportunity. In closing, let me be clear that the NIH is not permitted to take a position on the recalcitrant cancer legislation being considered by the Congress. Such statements can only be issued by the Office of Management and Budget as a Statement of Administration Policy.

Sincerely yours with best personal regards,
Francis Collins

Turmoil in Texas

Latest Irregularity Discovered During "Compliance Review"

(Continued from page 1)

In a press release Nov. 29, CPRIT officials said they discovered the irregularity in the course of a compliance review. The state agency said it has notified Peloton and placed a hold on future funding.

CPRIT said that its compliance officer "learned that CPRIT's chief commercialization officer improperly included the Peloton proposal on a commercialization award slate presented to the Institute's Oversight Committee."

The statement said that the proposal "did not have the required formal recommendation from the commercialization or scientific research peer review committees."

The $11 million award is the latest scandal emanating from the agency that was created to spend $300 million a year over ten years on cancer-related causes in Texas. The agency's chief scientific officer, Alfred Gilman, had recently quit, citing irregularities in the handling of another commercialization grant to establish a technology incubator headed by Lynda Chin, the wife of MD Anderson President Ronald DePinho.

Concurring that review of the incubator constituted an egregious act, said the scientists who reviewed grant proposals followed Gilman out the door (The Cancer Letter, May 25, Oct. 12, Oct. 19, Oct, 26).

CPRIT officials said that its investigation revealed that Peloton was "unaware CPRIT processes had not been followed and had played no role in placement of the proposal on the award slate."

Peloton has resubmitted its proposal, which will undergo a commercialization and scientific review pursuant to CPRIT's formal process. It's not clear why Peloton received special treatment.

The company was founded by Steven McKnight, chairman of Biochemistry at the University of Texas Southwestern Medical Center. The company's investors include the Column Group and Remeditex Ventures. While it appears that CPRIT violated its own rules in awarding Peloton the agency's first "Company Creation and Recruitment Award," the company has withstood scrutiny to receive another $18 million in Series A financing.

Whatever the explanation, CPRIT officials said the compliance officer confirmed that all other commercialization awards were assigned to and reviewed by a peer review committee.

CPRIT's commercialization official, Jerald Cobbs, announced his resignation on Nov. 16, and the agency officials declined to elaborate on the departure, initially describing it as a "personnel matter."

Cobbs also oversaw the funding of Chin's incubator grant.

Less than two weeks after refusing to comment on Cobbs's resignation, CPRIT Executive Director Bill Gimson commented on the Peloton matter. "CPRIT must have the trust of our fellow Texans that we are not only doing great work, but that we are also doing everything the right way," he said in a statement Nov. 29. "We proactively initiated this comprehensive review in an effort to be transparent and ensure good stewardship."

According to CPRIT's policies, it is Gimson, not Cobbs, who is ultimately responsible for bringing projects to the oversight committee, which rules on whether they should be funded.

"The executive director is the CPRIT employee who oversees the strategy and operations of the Institute; which includes creating the list of applications recommended for funding substantially based on the list proposed by the SRC and/or PRC and submitting the list to the CPRIT Oversight Committee for final approval." The policies are posted at: http://www.cprit.state.tx.us/images/uploads/policies_and_procedures.pdf.

Gimson is also ultimately responsible for bringing the Chin incubator proposal to the committee. The decision to fund the incubator has left CPRIT with few, if any, peer reviewers.

Cobbs's letter of resignation, a copy of which was obtained by The Cancer Letter, does not refer to Peloton or any other CPRIT controversies. The official said he was leaving because had accomplished his objectives and would now move to the private sector.

"I am resigning my role as Chief Commercialization Officer of CPRIT as my objectives have been accomplished in helping Texas establish a due diligence system with a proven track record of success," Cobbs wrote.

"I look forward to seeing the outcomes of the supported technologies progress toward improving and saving lives of my fellow Texans and others worldwide in years to come.

"I leave with a strong sense of pride in our financial successes too. From the approximate 15 percent, or $98 million, of CPRIT's budget, that was allocated to efforts to develop potentially quality-of-life and life-saving therapies for Texans, we attracted an additional $252 million investment from other sources to further

leverage our efforts. We truly helped establish Texas as a source of 'smart money' as much of the additional investments into CPRIT-funded companies came from top tier venture funds with no prior history of investment in Texas. Importantly, the aggregate potential return to Texans based on our present commitments is $370 million.

"With 288 Texans dying of cancer every day, CPRIT is an enormous asset to the state and unique enterprise in the nation, and I wish everyone the best in continuing the mission and optimizing this endeavor."

State officials appear to have known that the latest CPRIT scandal was brewing.

Two days before the Peloton revelation, Kenneth Shine, the UT System executive vice chancellor for health affairs, wrote a letter to MD Anderson faculty and staff, urging them to delineate the turmoil at CPRIT from controversies at their cancer center.

Shine said he objected to a routine story in the Houston Chronicle, which place the Cobbs departure in the context of this year's tumultuous events at CPRIT and MD Anderson.

"I must take serious issue with last week's Houston Chronicle article on the resignation of Mr. Jerry Cobbs from CPRIT with references to Dr. Lynda Chin and the MD Anderson incubator grant in the same piece," wrote Shine, who recently announced that he would retire.

The letter, dated Nov. 27, is remarkable, because it demonstrates eagerness on the part of Texas officials to draw fine distinctions within what has become a long continuum of events, which, at least for now, conclude with Shine's decision to issue a waiver that allows DePinho to continue his relationships with several companies he co-founded (The Cancer Letter, Oct, 26, Nov. 8).

In essence, Shine's letter urges MD Anderson staff to abandon the view that events at MD Anderson and events at CPRIT are a part of the state's forsaking peer review and instead emphasizing commercialization.

While drawing these fine lines, Shine also expressed support for DePinho's "Moon Shots Program," aimed at eventual eradication of several cancers.

The text of Shine's email follows:

As Executive Vice Chancellor for Health Affairs at The University of Texas System, I was responsible for directly negotiating the recruitment and terms of employment of Dr. Lynda Chin to the MD Anderson faculty.

In view of her superb credentials and outstanding contributions to cancer research, she was an important addition to the clinical and research efforts at the institution. I also nominated Dr. Chin for the CPRIT Established Investigator Program Award, which was strongly supported by the CPRIT out-of-state scientific review process.

I must take serious issue with last week's Houston Chronicle article on the resignation of Mr. Jerry Cobbs from CPRIT with references to Dr. Lynda Chin and the MD Anderson incubator grant in the same piece. When allegations first arose with regard to the incubator grant, I asked the UT System compliance office to review the events. This independent review (http://www.mdanderson.org/newsroom/news-releases/2012/utmdacc-cprit-compliance-review-report-2012-06-14.pdf) showed that CPRIT policies were not followed as the direct result of a request from CPRIT to a newly recruited MD Anderson administrator to provide a business plan for the incubator without a scientific review by CPRIT and without involving MD Anderson's provost office in the process.

The compliance report findings stated, "This procedure resulted in a departure from the customary CPRIT grant submission process and accordingly, notice of the grant's submission failed to reach the Provost's office."

The report also added that, "CPRIT did not reject the email application from… and it did not make a follow up request to submit the same through the CPRIT web portal."

The report further noted, "UTMDACC did not receive any notice from CPRIT that anything was amiss or inappropriate about this commercialization proposal, and it was reasonable for UTMDACC personnel to assume that it was an appropriate submittal process for a commercialization grant proposal as opposed to a research grant."

Moreover, Dr. Chin's name was attached to the proposal, rather than the names of others involved in the proposal, at the direct request of CPRIT. There was no evidence of any inappropriate institutional conduct.

CPRIT is a critically important program for Texans and one which I strongly support.

I do not know if CPRIT conducted its own review of these events. If so, that report could be made public in the same manner as the UT System has made its independent compliance review public.

I am very proud of MD Anderson and its extraordinary accomplishments. Further, Dr. Chin is an outstanding recruitment to Texas and MD Anderson,

and I am particularly proud of her recent election to the prestigious Institute of Medicine, one of only four MD Anderson faculty members to have that distinction.

I also look forward to the continued productivity of MD Anderson in preventing cancer and helping patients through its many programs, including the newly announced Moon Shots Program.

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Drug Approvals

Zaltrap Receives Positive Opinion For European Market from CHMP

The Committee for Medicinal Products for Human Use of the European Medicines Agency adopted a positive opinion and recommended the granting of marketing authorization for Zaltrap (ziv-aflibercept) Injection.

The opinion covers intravenous infusion in combination with FOLFIRI chemotherapy in adults with metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.

The action was announced on Nov. 16.

Zaltrap is co-developed by Sanofi and Regeneron Pharmaceuticals Inc.

A final decision is expected from the European Commission in the first quarter of 2013. The CHMP opinion was based on data from the VELOUR trial.

The drug is approved for use in the U.S. After a recent controversy over pricing, the company said it would offer rebates of 50 percent (The Cancer Letter, Nov. 2, Nov. 8, Nov. 16).

The VELOUR trial was a phase III multinational, randomized, double-blind trial comparing FOLFIRI in combination with either Zaltrap or placebo in the treatment of patients with metastatic colorectal cancer.

The study randomized 1,226 patients who previously had been treated with an oxaliplatin-containing regimen. Twenty-eight percent of patients in the study received prior bevacizumab therapy.

The VELOUR trial showed that in patients previously treated with an oxaliplatin-containing regimen, adding Zaltrap to FOLFIRI significantly improved median survival from 12.06 months to 13.50 months (HR=0.817 [95% CI 0.714 to 0.935]; p=0.0032), an 18 percent relative risk reduction.

A significant improvement in progression-free survival from 4.67 months to 6.90 months (HR=0.758 [95% CI 0.661 to 0.869]; p=0.00007), a 24 percent relative risk reduction, was also observed.

The overall response rate in the Zaltrap plus FOLFIRI arm was 19.8 percent vs. 11.1 percent for FOLFIRI (p=0.0001).

The most common adverse reactions reported at a higher incidence in the Zaltrap-FOLFIRI arm, in order of decreasing frequency, were leucopenia, diarrhea, neutropenia, proteinuria, AST increased, stomatitis, fatigue, thrombocytopenia, ALT increased, hypertension, weight decreased, decreased appetite, epistaxis, abdominal pain, dysphonia, serum creatinine increased, and headache. The most common Grade 3-4 adverse reactions reported were neutropenia, diarrhea, hypertension, leucopenia, stomatitis, fatigue, proteinuria, and asthenia.

In a related development, the European Commission approved Eylea (aflibercept) for the treatment of patients with neovascular (wet) age-related macular degeneration (wet AMD) on Nov. 27.

Eylea was approved for the treatment of neovascular (wet) AMD in the U.S. in November 2011.

Bayer HealthCare plans to launch Eylea in these countries later in 2012 and into 2013. In the United States, Eylea was also approved for the treatment of Macular Edema following Central Retinal Vein Occlusion in September 2012.

Bayer and Regeneron Pharmaceuticals are collaborating on the global development of Eylea and Regeneron maintains exclusive rights to Eylea in the U.S.

Obituary

Surgeon Carolyn Elaine Reed Held Key Positions at MUSC

By Fred Crawford

Carolyn Elaine Reed, a thoracic surgeon at the Hollings Cancer Center at the Medical University of South Carolina, died of pancreatic cancer Nov. 16. She was 62.

Reed played numerous roles in the development of the Hollings Cancer Center, serving as associate director for clinical affairs (1998-2000), director of the Hollings Cancer Center (2000-2004), and associate director of medical affairs (2004-2012).

She achieved a national and international reputation as a thoracic surgeon and oncologist with

specific expertise in lung and esophageal cancer.

Beginning in 1996, Reed was recognized each year on one or more "Top Doctors" lists. She became the "go-to" thoracic surgeon in the state of South Carolina not only for patients but also for her peer physicians around the state.

Reed was the editor of the text, General Thoracic Surgery (7th Edition), which is widely recognized as the "bible" for general thoracic surgery.

She made over 120 scientific presentations at national and international thoracic surgical meetings. Reed was an investigator in numerous cancer related clinical trials. During her career she was the author of over 100 peer-reviewed publications as well as 20 book chapters.

She was elected to membership in the American College of Surgeons, American College of Chest Physicians, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Surgical Association, and the Halsted Society. Most notably, she served in leadership roles in many of these organizations.

In the Southern Thoracic Surgical Association, she served as council member, secretary-treasurer, and in 2006 served as the president, the first woman to serve as president of a major thoracic surgical organization.

Reed played numerous leadership roles in the Society of Thoracic Surgeons including service on the executive council, the program committee, and a five-year term as treasurer of this largest organization of thoracic surgeons in the U.S. She served on the Council of the American Association for Thoracic Surgery, the most prestigious thoracic surgical organization in the world.

She served on the boards of the Thoracic Surgery Foundation for Research and Education and the Joint Council for Thoracic Surgery Education. Reed was the first woman elected to the American Board of Thoracic Surgery, the accrediting body for thoracic surgeons in the U.S. She subsequently was elected as chairman of the American Board of Thoracic Surgery (2005-2006), again the first woman to serve as leader of this organization.

She served as a governor in the American College of Surgeons and vice chair of the Thoracic Surgery Residency Review Committee. She served on numerous editorial boards including, The Journal of the American Cancer Society, The Annals of Thoracic Surgery, and Surgical Laparoscopy and Endoscopy. Of the numerous honors that she received, perhaps the one that meant the most to her was being selected as the commencement speaker in 2005 at her alma mater, the University of Maine, at which time she was awarded an honorary degree. She was an outspoken proponent for the role of women in surgery and specifically in thoracic surgery.

Reed was born March 4, 1950, in Farmington, Maine, the daughter of Margaret E. Reed and Clayton E. Reed. She grew up in Farmington and graduated with honors from the University of Maine in 1972 as a member of Phi Beta Kappa. She received her M.D. degree from the University of Rochester where she was a member of Alpha Omega Alpha Honor Medical Society.

She then moved to New York, where she received general and cardiothoracic surgery training at the New York Hospital-Cornell Medical Center.

During this time, she spent one year as a fellow in surgical oncology at the Memorial Sloan-Kettering Cancer Center.

Upon completion of training, she was recruited to the Medical University of South Carolina in 1985 as an assistant professor in the Division of Cardiothoracic Surgery to succeed Edward F. Parker, the father of thoracic surgery in the state of South Carolina.

At MUSC, her academic progress was rapid, and she was promoted to Associate Professor in 1989 and to full professor with tenure in 1997. At the time of her death she was the Alice Ruth Reeves Folk Endowed Chair of Clinical Oncology at MUSC.

She is survived by her mother, Margaret E. Reed, twin sister Joyce Greenacre and brother in-law Allen Greenacre, Lisa Drummond and husband Richard Drummond, adored twin great-nieces Anna and Emily Drummond, and several cousins.

In lieu of flowers, donations may be sent to The Carolyn E. Reed, M.D., Distinguished Endowed Chair in Thoracic Surgical Oncology. Mail to the MUSC Foundation, 18 Bee Street MSC 450, Charleston, SC, 29425-8610. Funeral arrangements will be announced at a later date. Visit our guestbook at www.legacy.com/obituaries/charleston.

The author is a distinguished university professor at the Medical University of South Carolina.