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CANCER RESEARCH UK AWARDING £20 MILLION GRAND CHALLENGE GRANTS TO CANCER RESEARCHERS WORLDWIDE

Cancer Research UK calls its Grand Challenge “the most ambitious cancer research grant in the world.” And it may be just that.

→ PAGE 3

MEDICAL RESEARCH FUNDING:
WHY WE MUST KEEP OUR
FOOT ON THE ACCELERATOR

→ PAGE 11

ANTI-MORCELLATION
ADVOCATE FILES “WRONGFUL
DEATH” SUIT AGAINST KARL
STORZ AND BRIGHAM &
WOMEN’S HOSPITAL

→ PAGE 14

IN BRIEF

10 PHYSICIANS WIN NCI CANCER
CLINICAL INVESTIGATOR TEAM
LEADERSHIP AWARDS

→ PAGE 17

DRUGS AND TARGETS

FDA APPROVES TREATMENT TO
REDUCE RISK OF BREAST CANCER
RETURNING

→ PAGE 21

In this issue

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-
- 3** Cancer Research UK awarding £20 million Grand Challenge grants to cancer researchers worldwide
 - 6** Klausner: CRUK Grand Challenge—more than just another grant
 - 11** Medical research funding: Why we must keep our foot on the accelerator
 - 14** Anti-morcellation advocate files “wrongful death” suit against Karl Storz and Brigham & Women’s Hospital
 - 19** Hayley Walker becomes hospitalist at Fox Chase
 - 19** ACCC developing care coordination model for Medicaid patients with lung cancer
 - 20** UC Davis-led group receives \$17 million NCI grant

DRUGS & TARGETS

- 21** FDA approves treatment to reduce risk of breast cancer returning
- 21** FDA accepts for priority review BMS application for dasatinib in children with CP Ph+ CML

IN BRIEF

- 17** 10 physicians win NCI Cancer Clinical Investigator Team Leadership Awards
- 18** House Appropriations Committee approves fiscal 2018 Labor-HHS spending bill
- 18** ASCO issues position statement on drug prices
- 19** Martine Extermann appointed program leader of Senior Adult Oncology at Moffitt

CANCER RESEARCH UK AWARDING £20 MILLION GRAND CHALLENGE GRANTS TO CANCER RESEARCHERS WORLDWIDE

By Paul Goldberg

Cancer Research UK calls its Grand Challenge “the most ambitious cancer research grant in the world.” And it may be just that.

The challenge, now in its second phase, plans to give out several £20 million awards over five years to researchers who would be willing to address one of eight challenge areas.

The strategy—borrowed from mathematics—is to identify the most significant barriers to making progress and challenge scientists all over the world to join forces to answer them. The Grand Challenge provides the largest single response-mode grants available in cancer research, CRUK said.

The approach of focusing the attention of an entire discipline on a specific set of questions originated with David Hilbert, a German mathematician. In 1900, Hilbert identified 23 problems and presented 10 of them at the Paris conference of the International Congress of Mathematicians. His list of challenges had in effect set the course for research in mathematics through much of the 20th century.

In 2003, Hilbert’s approach was adapted to global health research by the Bill and Melinda Gates Foundation.

Answers to the foundation’s challenges were reviewed by the Gates Foundation in partnership with the Foundations for NIH. Later, NCI Director Harold Varmus channeled the approach into his signature Provocative Questions program, which despite being scaled down over the years, continues to make [grants](#).

“The grant systems around the world have become atomized,” said Richard Klausner, a biotechnology entrepreneur, former NCI director, and chair of the Grand Challenge advisory panel. “The best model is the [NIH] Ro1, which is into funding *projects*—and that’s fine. I’m not criticizing them, but what we’re trying to do with the [CRUK] Grand Challenge is to fund the *solutions* of problems.”

Klausner, former executive director of the Global Health Program at the Bill

& Melinda Gates Foundation, said the idea for grand challenges arose from his conversation with Bill Gates.

“There are several reasons why it’s so exciting, but I think, most importantly, it gets at actually why people want to go into science,” Klausner said to The Cancer Letter. “No one goes into science because they want to do a series of projects. They want to take on big problems; right? They want to take big problems that seem important, that seem on the edge of doable, pushing the envelope of being doable and really a stretch, but not unrealistic.”

A conversation with Klausner appears on [page 6](#).

In the new round of the CRUK Grand Challenge, collaborations will be asked to:

- Devise approaches to prevent or treat cancer based on mechanisms that determine tissue specificity of some cancer genes.

- Create novel tumor vaccinology approaches that establish or enhance successful immune responses beyond what is revealed by current checkpoint therapy.
- Define mechanistic rules for combinatorial treatments to overcome resistance and avoid toxicity.
- Distinguish between lethal cancers which need treating, and non-lethal cancers that don't.
- Identify and target tumor cells that remain dormant for many years after seemingly effective treatment.
- Detect cancer earlier by interrogating medical and non-medical data sets using machine and deep-learning.
- Improve treatment responses by manipulating the composition and status of the microbiota.
- Determine the mechanisms that cause cancer without known mutagenesis, such as obesity, in order to devise novel interventions.

Now, with eight challenges articulated, researchers will have six months to assemble teams and submit outline proposals before the shortlisted teams are announced in the autumn. Cancer Research UK will then seed-fund shortlisted teams, thus allowing them to develop full applications which the advisory panel will review before determining those that display the ambition and high quality to receive funding.

Additional information on the Grand Challenges is posted [here](#). The recipients will be announced in the fall of 2018.

The CRUK Independent Scientific Advisory Panel includes:

- **Klausner**;

- **Adrian Bird**, the Buchanan Professor of Genetics at the University of Edinburgh;



No one goes into science because they want to do a series of projects. They want to take on big problems; right? They want to take big problems that seem important, that seem on the edge of doable, pushing the envelope of being doable and really a stretch, but not unrealistic.

– Richard Klausner



- **Suzanne Cory**, of the Walter and Eliza Hall Institute of Medical Research;
- **Ed Harlow**, professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School;
- **David Lane**, chief scientist of the Agency for Science, Technology and Research (A*STAR) in Singapore, scientific director of Ludwig Cancer Research, and chairman of Chugai Pharmabody;
- **Christopher Wild**, director of the International Agency for Research on Cancer;
- **René Bernards**, is professor of molecular carcinogenesis at Utrecht University and head of the section of molecular carcinogenesis at the Netherlands Cancer Institute-Antoni van Leeuwenhoekziekenhuis;
- **Brian Druker**, director of OHSU's Knight Cancer Institute, Jeld-Wen Chair of Leukemia Research;
- **Nic Jones**, professor and director, CRUK Manchester Centre; and

- **Elizabeth Jaffee**, deputy director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, the

Dana and Albert “Cubby” Broccoli professor of oncology, and professor of pathology at the Johns Hopkins University School of Medicine.

In 2016, during the first phase, nine teams were shortlisted from 56 bids, against seven Grand Challenges.

The inaugural four teams undertaking Grand Challenge projects are working to:

- Study tumor metabolism from every angle. Lead investigator: Josephine Bunch, National Physical Laboratory, UK.
- Prevent unnecessary breast cancer treatment. Lead investigator: Jelle Wesseling, Netherlands Cancer Institute, The Netherlands
- Create virtual reality maps of tumors. Lead investigator: Greg Hannon, Cancer Research UK Cambridge Institute, UK.
- Identify unknown preventable causes of cancer. Lead investigator: Mike Stratton, Wellcome Trust Sanger Institute, UK.

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&

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

A



CONVERSATION WITH
THE CANCER LETTER

Klausner: CRUK Grand Challenge—more than just another grant

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You don't have to be British, and it's for anyone in the world that would want to come together to convince this review group, which is the same group that struggled to articulate the grand challenges, to convince us that this is a worthwhile attempt.

”



Richard Klausner

Chair of the Grand Challenge advisory panel, former executive director, Global Health Program at the Bill & Melinda Gates Foundation, and former NCI director

How is this grant different from all the other grants?

Richard Klausner: Well, all the other grants you can do sitting up, or lying down, but this grant you have to do while reclining ... No ...

Okay.

RK: I have to say, nothing has given me more pleasure in the grant world, than this whole approach of grand challenges. You may know, we started the first of this, interest in grand challenges when I was with Bill Gates. We set up the [Grand Challenge in Global Health](#).

It was not only productive, it was inspiring. The reason is, and you know this, that largely, the grant systems around the world have become atomized.

The best model is the Ro1, which is into funding *projects*—and that's fine. I'm not criticizing them, but what we're trying to do with the [CRUK] Grand Challenge is to fund the *solutions* of problems.

There are several reasons why it's so exciting, but I think, most importantly, it gets at actually why people want to go into science. No one goes into science because they want to do a series of projects. They want to take on big problems; right? They want to take big problems that seem important, that seem on the edge of doable, pushing the envelope of being doable, and really a stretch, but not unrealistic.

It's not just a wish like, "Let's cure cancer." It has a specificity to it, but it's about attempting to solve a problem. The responses you get to these Grand Challenge articulations are fabulous.

This is the second round for the CRUK Grand Challenges.

And everyone involved—I feel I can speak for them—felt that all the work was justified by the quality of the proposals we got. Not all of them, but certainly the ones that were awarded last year, I will say, Paul, were among the most inspiring and beautiful grants I have ever read.

And you read them and you say, "Ah-ha, if they achieve what they're trying to achieve in this aspect of cancer, we will be able to look at before this grant and after this grant, and think that their field has changed."

And that's the goal here.

And this is another 100 million dollars over five years; right?

RK: Or more. So, let me just say, it could be more, and the reason I say that is that as we did last time, once we got all these proposals and we ranked them, we then—and we're doing this now—went out to a variety of funders and invited them.

And so, there is philanthropic money to add to the CRUK money, and we're going to try to do that again.

CRUK has set aside a certain amount of money that it's able to do for this. And it's really wonderful. I have to say I can't give them enough credit for their vision, their openness—and remember this is the first time that this UK cancer research entity is opening this up to the world.

You don't have to be British, and it's for anyone in the world that would want to come together to convince this review group, which is the same group that struggled to articulate the grand challenges, to convince us that this is a worthwhile attempt.

I think that's really important that here is a major grant that is totally internationalized. And so that's what's exciting about it. The panel—and you can see who is on the panel—has spent a lot of time together, but articulating grand challenges is really hard.

I can imagine.

RK: It's really hard to do, which is one of the reasons it's so interesting. And do we know that we get it right?

No.

In the end, getting it right is probably only determined by the quality and the nature of the proposals we end up getting. And everyone that gets funded may be against one grand challenge or multiple grand challenges. It really depends upon whether the group really feels that what comes together is a really interesting, exciting and novel shot.

When we get applications that look like the same old people doing the same old things, just looking for a £20 million grant, they don't make it very far.

Fascinating.

RK: It's really about challenging the community to solve problems. This gets at an issue that I think gets lost, and that is the relationship between what we as a research community do and the public. And that is, it's really hard to articulate, and communicate that as, "Ah-ha, this is what you people do."

But when you make an attempt to articulate the solving of a problem, and in that you can articulate if you solved this, what will change about our approach to cancer, I think it's so much more understandable to the public

and, again, I really think that in our times of skepticism about science, it's extremely important that we as a scientific and biomedical scientific community are capable not of justifying, but communicating and explaining that the reason we do all this is to solve their problems.

You've mentioned how these grants are different from RO1s. How are they different, say, from Stand Up to Cancer as an approach, philosophically?

RK: I love Stand Up to Cancer, and I think Stand Up to Cancer is another wonderful alternative. It's much more about a very specific translation. And that's terrific, and it links together scientists and clinicians to do a very specific translation.

This is basically to solve overarching problems in cancer, like what is the difference between a lethal and nonlethal cancer? Last year, we funded something that's never been done, and that is to create a Google map of a tumor.

How do we think about actually mapping at every dimension, cellular, molecular, genetics, interaction, all the components of the organ we call a tumor?

If you think about it, there's never been a picture of that.

And the solutions that have been proposed by several groups that were funded are quite remarkable. And again, once we have that picture, we really think we'll think about tumors differently than we currently do. That's very different than the type of very directed, let's try something in the clinical approach of Stand Up to Cancer.

There's no one type of grant that should define grant-making.

How is it different from Harold Varmus's Provocative Questions?

RK: I happen to think that Provocative Questions are a close cousin to this. Remember Harold was one of the co-chairs that I invited into the Grand Challenge in Global Health, and I view the Provocative Questions as very much a close kin of that experience that Harold had.

So, there's some similarities, but the way they're formulated is different. In other words, they're formulated as, here's a set of really wonderfully provocative questions, which I love, I think it's fantastic that that was done.

What we try to do with the [CRUK] Grand Challenge is take it one step further and basically talk about a multi-pronged approach to identifying the very specific bottlenecks that exist that get us from the lack of understanding to an understanding that would create impact on cancer.

There's just more structure to the Grand Challenges. But, as I say, I think they're closely related.

This may be a provocative question, but how does it differ from, say, the industry, what the industry can do?

RK: Well, industry, honestly, isn't in any way set up to step back and attempt to answer big fundamental questions.

Even though there are some challenges that sound like applied research, such as challenging how we look at as treatment regimens vis a vis a science of both resistance and toxicity, we're looking for things that will change the

framework of how industry thinks about cancer and how it sees opportunities for interventions.

These are not really about building the interventions. These are about making the breakthroughs to demonstrate how you would create a new set of interventions. Like the tumor vaccinology challenge, which is laid out very specifically, and that is, we think we have an understanding of why checkpoint therapy works, but we have no idea why it only works in the fraction of patients that it works in.

We are not asking for a biomarker of response. Industry is doing that. We rather mean this as a deeper intellectual question.

The fact is, it's not that there's no underlying immune response in patients who fail to respond, so what really are the controlling processes? If you understood that, you would then understand what it is that determines the 10, or 20 or 30% that respond and what you would do to increase that.

What industry does is try to find biomarkers that say you won't respond, or you will respond. That's not the same as solving the mechanistic problem.

Underlying another of this year's challenges is the fact that we've known since the beginning of finding tumor genes and tumor suppressors, that there's this totally mysterious question of tissue specificity. VHL is in every cell of the body, and it's only associated renal cell carcinoma. Why?

What is that specificity telling us about the actual mechanism of tumor development and survival? To go from these actual universal pathways to a specific tumor, and does that create interesting sensitivities and points of intervention, and it's amazing, but what we want is not an example. We want to solve the problem.

That's the challenge here of what could possibly be determining tissue specificity of uniformly expressed tumor suppressor genes, for example.

Who came up with the idea of the grand challenge? Was it you, or Gates, or Harold, or somebody else?

RK: No, I invited Harold and [then NIH Director] Elias [Zerhouni] after Bill and I conceptualized the Grand Challenges in Global Health. The whole idea of the Grand Challenge [in Global Health] happened one evening in Bill Gates's office.

He and I were just spending the evening together at his Microsoft office, and we were literally in an argument about the value of funding research. I was positive, he was negative.

I hadn't been at the foundation very long, we were just developing our strategy. We were doing that together.

I kept pushing, and he was skeptical. And then, somehow, in the conversation Bill asked whether I knew or had ever read about the grand challenges in mathematics, formulated in 1900, by [German mathematician David Hilbert].

He excitedly, and very knowledgeably, started talking about those mathematical grand challenges, and how for a hundred years, that formulation defined the most critical, important questions to be answered in mathematics. Amazing how long they'd been there.

We started discussing that remarkable piece of science history, and what it meant and how, because Bill was able to see, "Ah-ha, there's an example of how one can articulate big problems."

Whereas he felt if we were just going to get into supporting research, it was

just supporting an endless amount of projects. And he was right.

And so, as that night went on, we basically agreed together, I said to him, "Why don't we do grand challenges in global health?"

And he just lit up. And we started going back and forth, what would this mean, what would this look like? And it was done. That's how it started.

So how does Harold fit in, because he came in with the idea of calling them Provocative Questions?

RK: And they were, yeah. So what happened is that because at the Gates Foundation I wanted to bring NIH further into this world of global health with the Gates Foundation, I went to Elias, and told him about this idea of grand challenges, and said, "Is there a way to do this together?"

And it turned out there was no real way. It was just too difficult. But what we did to was to give a grant to the FNIH, and then enabled the FNIH to grow their ability to manage these things, and they helped us manage the grand challenge process, and then I asked Harold, who was developing, post-NIH, an increasing interest in global health, I asked Harold and Elias to join me, so I chaired it, and they were the two co-chairs. The three of us were the triumvirate that sort of managed over the program.

In addition, we had a big scientific advisory board and we had review committees and an amazing staff both at the Foundation and the FNIH.

But the three of us really were the intellectual managers. And I think Harold loved it. In fact, it's all described in his book. And there's no question, because

when Harold told me he was going to become NCI director, I said, "Let's do grand challenges in oncology."

It's interesting, because I covered this. I had no idea. I mean, I knew about all the pieces that you're describing, but I didn't quite put them together.

RK: Anyway, that's exactly the story.

That's very helpful to know.

RK: Actually, Paul, I think this issue of grand challenges and how we think about inspiring, not just funding, but inspiring and motivating the community, the whole process of this, to me, is really fascinating. It will be great, actually, to take even more time, because I think there's a lot of interesting issues that are raised by the whole process.

Let's do that.

RK: And I can't imagine someone covering this better than you.

Let's totally get back to that. Is Cancer Research UK playing a greater role or planning to play a greater role in the U.S.?

RK: You know, this is their first foray into doing something that's not limited to the UK. And all I can say is all of us on the board, from all different parts in the world, just keep applauding them. We think that's fantastic.

So, it's really that. It's not so much that they want to fund in the U.S., but they're basically saying that if this is a process where a community or a subset of a community has said these are worthy challenges, they understand that if it's worthy, wherever the potential solutions come from ought to be funded. I really applaud them for that.

How did you get involved in Cancer Research UK?

RK: Well, actually I've had a long relationship with them. You know, I helped peripherally with the formation of CRUK. You probably remember that in the 90s, there were two cancer research charities in the UK, the Cancer Research Campaign and the Imperial Cancer Research Fund.

And I got very involved in the discussions with the heads of both as they began thinking about whether should they merge.

In fact, while I was NCI director I was also a member of the board of ICRF, the scientific board. Actually with Harold, we were both members.

So, I had this long relationship with the both the Cancer Research Campaign and the Imperial Cancer Research Fund, and with CRUK, which was the merger of these two.

And I just remain friendly and close to them, had no formal relationship, and their CEO, Haropal Kumar called me about two and a half years ago about this idea of doing grand challenges in oncology, and would I help them and chair it. And so that's the origin.

One of the challenges is in health services research. Or certainly the question of over-treatment. It's nice to see that.

RK: Yes, well, honestly, the Grand Challenge most relevant to this question of overtreatment is determining what distinguishes lethal versus nonlethal cancers, in other words, what are cancers we should ignore.

Many of us believe that there's a lot more of these nonlethal early cancers than what one would conclude based on treatment patterns of early cancer. And that is Grand Challenge No. 5. Grand Challenge No. 6 is about using artificial intelligence machine learning to look at all sorts of medical and health systems aspects of a new way to think about early detection.

That said, we did not choose to try to do grand challenges in health systems per se. We just felt that was not cancer-specific. It's an interesting question. We came up with this at the Gates Foundation, where we realized that you could say, let's do a Grand Challenge to get rid of poverty.

And that would take care of a lot. Unfortunately, that doesn't have the mechanistic specificity that's required to fit our definition of a fundable Grand Challenge.

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When we get applications that look like the same old people doing the same old things, just looking for a £20 million grant, they don't make it very far.

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GUEST EDITORIAL

Medical research funding: Why we must keep our foot on the accelerator



By Michael A. Caligiuri

President of the American Association for Cancer Research, and director, The Ohio State University Comprehensive Cancer Center and chief executive officer of the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

It's been a long time since we've seen the kind of strong national commitment that exists today to support medical research.

Of course, this enthusiasm is more than justified because of the large number of unprecedented research opportunities that are at the ready to propel us toward defeating cancer and the numerous other diseases that afflict so many Americans.

Congress underscored this commitment in April when it passed the fiscal year 2017 Omnibus Appropriations Bill, which provided the National Institutes of Health with its second consecutive \$2 billion annual funding increase.

The prior year's funding increase represented the largest annual funding boost the agency had received in a decade.

Additionally, the Beau Biden Cancer Moonshot Initiative, one of the key ini-

tiatives of the 21st Century Cures Act, was funded at \$300 million in FY 2017.

These recent Congressional actions signal an awareness of the critical role that NIH-funded research plays in preventing, detecting, diagnosing, and treating cancer and other diseases.

Four passionate and determined champions for medical research have been leading the charge to make the NIH a national priority:

- Senate Appropriations Subcommittee Chairman Roy Blunt (R-MO),
- House Appropriations Subcommittee Chairman Tom Cole (R-OK), and
- the two respective Ranking Members, Sen. Patty Murray (D-WA) and Rep. Rosa DeLauro (D-CT).

Their actions are allowing our nation's researchers and physician-scientists to significantly accelerate the pace of progress against cancer, as well as any number of the hundreds of other diseases that afflict millions of Americans.

Both Chairman Blunt and Chairman Cole have led in a bipartisan fashion and talked repeatedly about the importance of robust, sustained, and predictable annual funding increases for the NIH ever since they assumed leadership of their respective subcommittees in January 2015.

Since then, funding for the NIH has increased by a total of 13.3 percent. In the decade prior, stagnant funding levels had resulted in the NIH losing approximately 25 percent of its purchasing power, when adjusted for inflation.

In addition, Sen. Murray's leadership as the Ranking Member on the Senate Health, Education, Labor, and Pensions Committee, was instrumental in her securing an additional \$4.8 billion for targeted initiatives at the NIH, including the Beau Biden Cancer Moonshot Initiative.

This funding was authorized over a period of 10 years in the 21st Century Cures Act, a bipartisan law that is changing the way we treat disease. For example, the FDA Oncology Center of Excellence, a key component of the 21st Century Cures Act, will expedite the development of novel combination products and support an integrated approach to tackle this devastating disease that touches so many American families.

The center is the first disease area (in oncology) at the FDA to have a coordinated clinical review of drugs, biologics and devices across the agency's three medical product centers.

Given the widespread bipartisan support for the NIH, as well as the aston-



The president's irresponsible proposal would risk irreversibly harming our nation's ability to further understand the complexity of cancer and other diseases and postpone the development of lifesaving therapies for patients.

—Michael Caligiuri



ishing progress NIH-funded researchers are currently making to improve our nation's health and save lives, we were shocked when President Trump's FY 2018 budget proposed cutting the NIH budget by \$7.2 billion, a 21 percent reduction from its current funding level.

The National Cancer Institute's budget is also slated for a significant cut of \$1.2 billion, a 20 percent reduction from its current funding level.

The president's irresponsible proposal would risk irreversibly harming our nation's ability to further understand the complexity of cancer and other diseases and postpone the development of lifesaving therapies for patients.

United for Medical Research, an advocacy group based in Washington, D.C., estimated that the President's budget would mean 5,000 to 8,000 fewer grants, and the elimination of nearly 90,000 jobs.

Fortunately, the president's FY 2018 budget proposal was roundly criticized by members of both parties on Capitol

Hill, many of whom vowed to vehemently oppose his proposal for the NIH.

Chairman Cole expressed concern that the president's proposal would "stall progress and potentially discourage promising young scientists from pursuing biomedical research."

Cole also stated that the "NIH will remain a priority in my budget, and we're going to do everything we can to stay on the course we're on."

Chairman Blunt also affirmed his commitment for the NIH because "the investments we make in NIH research will not only save lives, they'll lead to new frontiers in drug and device development that are critical for reducing health care costs, growing our economy, and maintaining America's competitive edge in innovation."

Even one of President Trump's most trusted advisors, former Speaker of the House Newt Gingrich, penned an Op Ed a couple of years ago in which he stated, "We are in a time of unimaginable scientific and technological progress. By funding basic medical research, Congress can transform our fiscal health, and our personal health, too."

Although we are growing increasingly confident that Congress will reject outright the president's FY 2018 budget proposal for the NIH, the medical research community is also facing a

complicated and worrisome challenge in the form of the spending caps that are currently in place for FY 2018.

These shortsighted and restrictive spending caps were set in the 2011 Budget Control Act, also known as the sequester.

If the NIH, NCI, the FDA, and other vitally important scientific agencies are to receive the resources that are necessary to drive advances across the clinical cancer care spectrum and save an increasing number of lives from cancer, it's going to require that Congress negotiate a bipartisan budget deal to raise the discretionary budget caps for FY 2018.

There's an effort to break the caps on the defense side of the budget, while leaving the non-defense side of the budget caps in place. With regards to this proposal, we agree with Rep. Nita Lowey (D-NY), the top Democrat on the House Appropriations Committee, who said, "It is clearly time to lift the budget caps in FY 2018, but for more than just the Pentagon."

As Rep. Lowey has stated, the non-defense discretionary side of the budget ledger should grow at a comparable rate in order to support vital research and patient needs, as these and other programs "need attention just as badly as we need new jets, tanks, and ships."

As Congressional leaders approach the final two months before the beginning of FY 2018 on October 1, we encourage the entire medical research community to make your voices heard by asking your respective members of Congress to:

- Ensure that funding designated through the 21st Century Cures Act for targeted initiatives such as the Beau Biden Cancer Moonshot Initiative is fully appropriated in FY 2018;
- Increase the FDA budget in FY 2018 to \$2.8 billion, an \$80 million increase above its FY 2017 level, and fully fund the FDA Oncology Center of Excellence, to ensure support for regulatory science and to accelerate the pace of development of medical products that are safe and effective; and
- Negotiate a bipartisan budget deal to raise the discretionary budget caps for FY 2018 and beyond, which would allow our nation's policymakers to continue to invest in priority areas, such as biomedical research funded by the NIH.

By continuing to pursue an appropriations strategy that provides annual funding increases that are robust, sustained, and predictable for the NIH, NCI, and FDA, and by ensuring the funds available for the Beau Biden Cancer Moonshot Initiative and the FDA Oncology Center of Excellence are fully appropriated, Congress can continue to help us transform cancer care, spur economic growth, and maintain our position as the global leader in science and medical research.

Most importantly, we can continue to bring hope to the millions of people everywhere who are touched by cancer.

- Continue to support robust, sustained, and predictable growth for the NIH budget by providing an increase of \$2 billion for the NIH in FY 2018, for a total funding level of \$36.2 billion;

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Anti-morcellation advocate files “wrongful death” suit against Karl Storz and Brigham & Women’s Hospital

By Matthew Bin Han Ong

Hooman Noorchashm, the cardiac surgeon who, with his late wife, ran a campaign against power morcellation, is stepping up his family’s legal complaint against Karl Storz and Brigham & Women’s Hospital.

The “wrongful death” filing comes less than two months after Noorchashm’s wife, Amy Reed, died from complications of abdominal sarcomatosis (The Cancer Letter, [May 26](#)).

Reed died on May 24. She was 44.

Reed, formerly an anesthesiologist at Beth Israel Deaconess Medical Center and the Hospital of the University of Pennsylvania, underwent power morcellation at BWH in 2013. The procedure, which was performed with a Storz morcellator, contributed to the dissemination of her undetected cancer in her abdomen and pelvis (The Cancer Letter, [Nov. 21, 2014](#)).

Noorchashm’s lawsuit, filed on July 12, amends earlier medical malpractice and product liability claims against the defendants to add claims for wrongful death and punitive damages. The complaint also names Michael Muto,

associate professor at Harvard Medical School and director of the Gynecologic Oncology Fellowship Program at BWH, and Karen Wang, an assistant professor at Johns Hopkins Medicine who, at the time, was Reed’s surgeon at BWH.

Reed and Noorchashm had made an unusual precondition for any possible settlement: they said that they would not discuss settlement unless Storz, a German company, pulls its power morcellators off the market. Noorchashm said his July 11 deadline was not met and the case was therefore amended to include a wrongful death claim.

“Withdraw from the power morcellator line of products by July 11 at the close of the business day and we will provide you with the opportunity to negotiate a private settlement—do not comply with this requisite condition and we will proceed with filing ‘Wrongful Death’ charges and a private settle-

ment will be unlikely,” Noorchashm said in a statement to the press.

Noorchashm’s complaint can be downloaded [here](#).

In April 2014, FDA issued an advisory, concluding that the risk for dissemination of occult uterine sarcoma via morcellation was one in 350—almost 30 times higher than the rate touted by pro-morcellation advocates and gynecology professional societies.

Ethicon, the Johnson & Johnson subsidiary that manufactured nearly three-quarters of laparoscopic power morcellators on the market, requested a withdrawal of the controversial devices in July 2014 (The Cancer Letter, [Aug 1, 2014](#)). The Wall Street Journal reported in [March 2016](#) that J&J has settled nearly 70 of the estimated 100 legal claims that the devices harmed women by spreading undetected cancer.

About 50 suits related to harm caused by Storz morcellators have been filed in Los Angeles, according to Sean Tracey, a Texas personal injury lawyer. At least thirteen of those cases are going to trial, he said.

According to Noorchashm, the defendants filed a motion to withhold internal documents related to the power morcellation problem from the plaintiff, citing concerns that Noorchashm would violate confidentiality and leak those documents to the press.

In an email July 10 to the defendants' counsel, Noorchashm wrote:

"You, your firms and the other attorneys on your side have put yourselves in the unfortunate position of defending clients whom, I know you would not forgive if you yourselves or your loved ones were on the receiving end of their carelessness and negligence—as my family is."

It is highly unusual for plaintiffs to directly communicate with or seek

withhold internal documents from Noorchashm.

"Of course! I would share any information that would be relevant to these corporations' wrongdoing to the public," Noorchashm said to The Cancer Letter. "This was a public health hazard that damaged a lot of families around the world—including mine. Frankly, the fact that these defendants even filed this motion demonstrates that they have something sinister to hide.

I am stumped by the idea that a judge would endorse such corporate protectionism in the state of Massachusetts—I mean, really, to withhold critical information to a case from the plaintiff? Talk about the sanctity of the judicial process!

"The defendants know that vocal transparency and publicity has been at the core of the anti-morcellation campaign from the beginning, and so should the judge. There is nothing wrong with transparency when it comes to people's lives in harm's way.

uct from the global marketplace. I suggest the defendants take this promise very seriously."

Storz officials did not respond to an email from The Cancer Letter.

"If you do not fight to achieve this Storz market withdrawal, your culpability will be formally demonstrated to the public in court," Noorchashm wrote in an email July 12 to BWH leadership. "Let me assure you that with Amy's death, there is no way that my children and I will settle privately with you so long as the deadly instrument that killed Amy in your physician's hands is on the market harming others."

BWH officials declined to comment, citing pending litigation.

The text of Noorchashm's July 11 press statement follows:

Members of the Press,

This statement is to inform you that tomorrow morning, our attorneys at Greene LLP in Boston will be formally amending "Wrongful Death" charges to our legal complaint against the Brigham and Women's Hospital (BWH), Dr. Michael Muto, Dr. Karen Wang and the Storz company.

This escalation has come about for two reasons.

First, the immediate cause of my wife's death on May 24, 2017, was abdominal sarcomatosis resulting from her incorrect pre-operative work-up and subsequently the inappropriate use of an unsafe power morcellator device manufactured and negligently marketed in the United States, and worldwide, by the German company, Storz.



If you do not fight to achieve this Storz market withdrawal, your culpability will be formally demonstrated to the public in court. Let me assure you that with Amy's death, there is no way that my children and I will settle privately with you so long as the deadly instrument that killed Amy in your physician's hands is on the market harming others.

—Hooman Noorchashm



to influence defendants and their counsel. On July 20, after reviewing Noorchashm's email, a Boston judge granted Storz and BWH the right to

"With this latest shenanigans from the defendants, it's unlikely that I would submit to a private settlement—unless STORZ publicly withdraws their prod-



This was a public health hazard that damaged a lot of families around the world—including mine. The defendants know that vocal transparency and publicity has been at the core of the anti-morcellation campaign from the beginning, and so should the judge. There is nothing wrong with transparency when it comes to people's lives in harm's way.



Second, in February 2017, prior to Dr. Reed's death, the defense counsel, unsolicited, approached our lawyers in an attempt to seek a private settlement. Dr. Reed and I responded by demanding a specific precondition to any settlement discussions. Namely, that the Storz company permanently remove the morcellator line of products from its repertoire of over 1,500 medical devices—as was done by J&J's Ethicon subsidiary in 2014 following an FDA hearing, which demonstrated the severe hazard to women's health. This precondition was met with silence from the defense at that time. Following Amy's death on May 24, 2017, and per my wife's instructions, I delivered an ultimatum to Storz executives and defense counsel via our attorneys at Greene LLP:

Withdraw from the power morcellator line of products by July 11 at the close of the business day and we will provide you with the opportunity to negotiate a private settlement—do not comply with this requisite condition and we will proceed with filing “Wrongful Death” charges and a private settlement will be unlikely.

As the set deadline has now passed, our lawyers and I have proceeded with amending charges of “Wrongful Death” to our lawsuit against BWH, its physicians and the Storz company.

As we proceed with prosecuting our case against Dr. Reed's BWH physicians and the BWH and Storz corporate entities over the next year we aim to publicly demonstrate that the physicians and the BWH and Storz corporate defendants are guilty of negligence while violating federal law, state statute, the principles of medical ethics and safe surgical practice leading to the wrongful death of my wife, Dr. Amy Josephine Reed - mother of 6, wife, daughter, physician, scientist and

advocate for women's health - and others. Additionally, given the limited malpractice insurance coverage of the BWH physicians in “Wrongful Death” cases, we are prepared to seek punitive damages from all involved physicians personally.

It is simply an astonishing fact that a multinational conglomerate supposedly committed to health and safety of patients, Storz, finds itself unable to withdraw a product from the marketplace in the face of undeniable, forgivable and totally avoidable harm—and in a setting where its largest competitor did so over three years ago. Very certainly, it is an ominous sign for the corporation when this company's risk managers and lawyers are neither capable of moving quickly to protect women in harm's way, nor of effectively abrogating their corporate clients' liability exposure in the marketplace.

Moreover, it is difficult to understand how the Storz co-defendants at BWH, who are no longer offering morcellation operations at their institutions, have not publicly voiced their professional opposition and recommendation to Storz, and the wider GYN community, that the company and the specialty withdraw from the power morcellator line of products. These facts will serve to severely damage the defendants as the case is prosecuted. We specifically aim to demonstrate that these two corporate entities, their doctors, their executives and their insurers are jointly and publicly liable for negligently causing my wife's wrongful death, as the case moves forward in court now.

Sincerely,
HN.

IN BRIEF



10 physicians win NCI Cancer Clinical Investigator Team Leadership Awards

Ten investigators nationwide received the NCI's Cancer Clinical Investigator Team Leadership Awards.

The award recognizes and supports outstanding clinical investigators at NCI-designated cancer centers who participate extensively in institute-funded collaborative clinical trials and whose leadership, participation, and activities promote a culture of successful clinical research.

Established in 2009, the awards are intended to help retain investigators in academic clinical research careers. Each of these investigators is a full-time faculty member who is a board-certified physician and has practiced medicine between three and eight years post-fellowship.

Each recipient was nominated for the award by their cancer center director on the basis of qualifications, interests, accomplishments, and motivation, and based upon the nominee's intent and

ability to promote a successful clinical trials culture and to pursue an academic career in clinical research.

The recipients will devote 15 to 20 percent effort to the activities associated with this award, and the sponsoring cancer centers have agreed to protect the awardees' time for these activities. The award provides partial salary support for two years for the recipient to engage in activities and efforts related to the award.

The recipients for 2017 are:



Ajjai Alva
University of Michigan Comprehensive Cancer Center



Lisa Barroilhet
University of Wisconsin Carbone Cancer Center



Ursa Brown-Glaberman
University of New Mexico Comprehensive Cancer Center



Shira Dinner
Robert H. Lurie Comprehensive Cancer Center, Northwestern University



Jean Hoffman-Censits
Sidney Kimmel Cancer Center, Thomas Jefferson University



Kevin Kalinsky

Herbert Irving Comprehensive Cancer Center, Columbia University



Eric Roeland

Moore's Comprehensive Cancer Center, University of California, San Diego



Christopher Lieu

University of Colorado Comprehensive Cancer Center



April Salama

Duke Cancer Institute, Duke University Medical Center



Rahul Parikh

University of Pittsburgh Cancer Institute

programs and current funding levels for the Centers for Disease Control and Prevention cancer screening and early detection programs. This version of the bill eliminates funding for the Affordable Care Act and the Family Planning (Title X) Program (The Cancer Letter, [July 14](#)).

"United for Medical Research applauds the increase to the budget for NIH contained in the Labor, Health and Human Services, and Education funding bill approved by the House Appropriations Committee yesterday," UMR President Lizbet Boroughs said in a statement. "We are deeply appreciative of Subcommittee Chairman Tom Cole's unwavering support for boosting funding for medical research."

"We also want to thank Ranking Member Rosa DeLauro and full Committee Chairman Rodney Frelinghuysen and Ranking Member Nita Lowey for making funding for medical research a high priority in this bill. We look forward to working with the Senate on its Labor-HHS funding bill and with the full Congress to ensure a 2018 budget solution that enables increased funding for the NIH and the medical research initiatives called for by the 21st Century Cures Act."

ASCO issues position statement on drug prices

The American Society of Clinical Oncology issued a position statement on pricing of cancer drugs.

The statement asserts that any solutions must preserve patients' access to care and foster innovation, analyzes a wide array of options and recommends that a panel of stakeholders be established to determine which proposals will be effective and develop a uniform approach for assessing the value of drugs.

House Appropriations Committee approves fiscal 2018 Labor-HHS spending bill

The House Appropriations Committee marked up the fiscal 2018 Labor-HHS [funding bill](#) with a vote of 28-22 on July 19.

The bill includes a \$1.1 billion increase for NIH, a \$82 million funding boost for the NCI, and preserves the individual

Developed by ASCO volunteer leaders and adopted by the society's board of directors, the ASCO Position Statement On Addressing the Affordability of Cancer Drugs analyzes a range of cost-cutting proposals, from allowing Medicare to negotiate drug prices, to legalizing the importation of drugs, to adopting bundled payment programs.

Specifically, ASCO proposes that a diverse group of stakeholders from across the healthcare sector:

- Identify, prioritize, and test potential solutions to address the affordability of cancer drugs
- Help define a standard approach to assessing the value of drugs that could be applied broadly to inform drug pricing and reimbursement.

While new classes of drugs have achieved unprecedented success in a growing number of cancers, in some cases the price of a new drug bears no relation to its effectiveness. According to one study, only 19 percent of cancer drugs recently approved by the FDA produced clinically meaningful outcomes for patients, despite their high prices.

ASCO suggests that:

- The FDA consider using meaningful clinical outcomes when assessing new and supplemental drug applications, rather than small benefits that achieve statistical significance in large trials. In 2014, ASCO published a policy statement recommending a definition of clinically meaningful outcomes for cancer clinical trials, which the FDA could use when approving new cancer treatments and drug indications.
- Medicare test the feasibility of a "value-based pathway" approach designed to incentivize providers to use higher-value drugs and the

pharmaceutical industry to develop high-value treatments.

The full text of ASCO's position statement is posted [here](#).

Martine Extermann appointed program leader of Senior Adult Oncology at Moffitt



Martine Extermann was appointed program leader of Senior Adult Oncology.

Extermann served as interim chair for several months, during which an international search was conducted.

Extermann joined Moffitt nearly 20 years ago, after completing a Moffitt fellowship in medical/geriatric oncology.

She has received several honors and awards, among them the Pfizer Visiting Professorship Award at the University of Texas, The American Society of Clinical Oncology B.J. Kennedy Award for Scientific Excellence in Geriatric Oncology, the Paul Calabresi Award from the International Society of Geriatric Oncology, and the Lifetime Achievement Award in Geriatric Oncology from the German Society of Geriatrics and German Society of Hematology/Oncology.

Hayley Walker becomes hospitalist at Fox Chase



Fox Chase Cancer Center has hired Hayley Walker to the Department of Medicine as a hospitalist.

Walker completed her residency at the Hospital of the University of Pennsylvania. She received her medical degree from Harvard Medical School, and her undergraduate degree at the University of Pennsylvania, where she was recognized as a Dean's Scholar.

During her residency, Walker published research on emotions and attitudes toward endocrine therapy in young women with breast cancer.

ACCC developing care coordination model for Medicaid patients with lung cancer

The Association of Community Cancer Centers has initiated a three-year initiative focused on developing an optimal care coordination model for Medicaid patients with lung cancer through

Funding and support for this project is provided by a grant from the Bristol-Myers Squibb Foundation.

Phase one, conducted throughout 2017, focuses on research. Drawing on a literature review and environmental scan, extensive on-site information gathered at five cancer programs that served as development sites, and with the insight and guidance of the project's Advisory Committee and Technical Expert Panel, ACCC developed a beta version of the care coordination model.

The OCCM builds directly on the Multidisciplinary Care Assessment Tool created by the National Cancer Institute Community Cancer Centers Program, a 2007-2014 NCI-funded initiative. The model, which is designed to be used at cancer programs of all resource levels, focuses on 13 areas of care for patients with lung cancer.

- Patient Access to Care
- Prospective Multidisciplinary Case Planning
- Financial, Transportation, and Housing
- Management of Co-morbid Conditions
- Care Coordination
- Treatment Team Integration
- Electronic Health Records (EHR) and Patient Access to Information
- Survivorship Care
- Supportive Care
- Tobacco Cessation
- Clinical Trials
- Physician Engagement

• Quality Measurement and Improvement

During the second phase, ACCC would test the beta optimal care coordination model. To select testing sites, ACCC conducted a comprehensive, competitive application process. Seven ACCC member cancer programs have been selected to test the model by conducting quality improvement initiatives in one or more of the 13 OCCM assessment areas listed above:

- Cowell Family Cancer Center (Munson Healthcare) - Traverse City, MI
- Northwest Medical Specialties - Tacoma, WA
- Ascension Wheaton Franciscan Cancer Care - Milwaukee, WI
- Florida Hospital Memorial Medical Center - Daytona Beach, FL
- Genesis Cancer Care Center - Zanesville, OH
- Advocate Lutheran General Hospital Cancer Care Program - Park Ridge, IL
- Southern Ohio Medical Center - Portsmouth, OH

The third phase, testing the model, will be from October 2017-September 2018. Data and outcomes from this phase will be used to further refine and modify the OCCM to ensure that it is a practical guide for cancer programs interested in advancing patient-centered, multidisciplinary, coordinated care for their lung cancer patients on Medicaid.

UC Davis-led group receives \$17 million NCI grant

Breast Cancer Surveillance Consortium investigators received a \$17 mil-

lion program project grant renewal from NCI to study the effectiveness of different breast cancer screening and surveillance strategies using digital mammography, digital breast tomosynthesis, and breast MRI.

The consortium seeks to ensure that women get personalized care based on their individual risk and preferences. It is co-led by UC Davis researcher Diana Miglioretti.

Established in 1994, the BCSC is a nationwide research collaboration that includes UC San Francisco, the University of North Carolina, Geisel School of Medicine at Dartmouth, the University of Vermont, the University of Illinois, Advocate Health Care and Kaiser Permanente Washington. The consortium has a long history of evaluating the benefits and harms of different screening approaches.

The grant renewal expands on prior research by evaluating surveillance imaging of breast cancer survivors in addition to screening women without a history of breast cancer. BCSC research has helped fuel the shift from a one-size-fits-all screening approach to consideration of women's breast cancer risk and preferences.

The ultimate goal is to tailor each woman's screening regimen to her risk of screening outcomes based on family history, breast density and other risk factors, while also considering her personal preferences around balancing the potential benefits and harms of screening. Previous BCSC studies have been used to update the national breast cancer screening guidelines of the U.S. Preventive Services Task Force and the American Cancer Society.

The grant renewal will fund three projects to better match women with the most appropriate screening or surveillance regimens. For example, the consortium will investigate which women benefit most from tomosynthesis or

breast MRI, and which will be better served by digital mammography alone.

They will investigate different ways to maximize early detection while minimizing failures and false alarms among all women receiving screening and among breast cancer survivors receiving surveillance for second breast cancer occurrences.

The ultimate goal is to develop a clinical algorithm that uses a woman's information, such as personal and family history of breast cancer, race, age, breast density, history of breast biopsy and body mass index, to determine the ideal combination of imaging and other approaches to detect cancers early, when they are most treatable, while minimizing harms.

DRUGS & TARGETS



FDA approves treatment to reduce risk of breast cancer returning

FDA approved Nerlynx (neratinib) for the extended adjuvant treatment of early-stage, HER2-positive breast cancer. For patients with this type of cancer, Nerlynx is the first extended adju-

vant therapy, a form of therapy that is taken after an initial treatment to further lower the risk of the cancer coming back. Nerlynx is indicated for adult patients who have been previously treated with a regimen that includes the drug trastuzumab.

The FDA granted the approval of Nerlynx to Puma Biotechnology Inc.

Nerlynx is a kinase inhibitor that works by blocking several enzymes that promote cell growth. The safety and efficacy of Nerlynx were studied in a randomized trial of 2,840 patients with early-stage, HER2-positive breast cancer who completed treatment with trastuzumab within the previous two years.

The study measured the amount of time after the start of the trial that it took for the cancer to come back or for death to occur from any cause (invasive, disease-free survival).

After two years, 94.2 percent of patients treated with Nerlynx had not experienced cancer recurrence or death, compared with 91.9 percent of patients receiving placebo.

Common side effects of Nerlynx include diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, swollen and sore mouth (stomatitis), decreased appetite, muscle spasms, indigestion (dyspepsia), liver damage (AST or ALT enzyme increase), nail disorder, dry skin, abdominal swelling (distention), weight loss and urinary tract infection.

FDA accepts for priority review BMS application for dasatinib in children with CP Ph+ CML

Bristol-Myers Squibb Co. said the FDA accepted its supplemental New Drug Application to include an indication

for Sprycel (dasatinib) to treat children with Philadelphia chromosome-positive chronic phase chronic myeloid leukemia, as well as a powder for oral suspension formulation of Sprycel.

The application has an action date of Nov. 9.

The sNDA includes data from CA180-226 (NCT00777036), an ongoing phase II, open-label, non-randomized trial studying Sprycel in pediatric patients with CP-CML that are resistant to or intolerant of imatinib and in pediatric patients newly diagnosed with CP-CML.

The efficacy endpoints included cumulative major cytogenetic response rate among imatinib-resistant or intolerant patients and cumulative complete cytogenetic response rate in newly diagnosed patients.

Additional efficacy measures were time to and duration of response, progression-free survival, overall survival and major molecular response. Safety was also assessed.

Sprycel first received FDA approval in 2006 for the treatment of adults with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase who are resistant or intolerant to prior therapy including imatinib.

At that time, Sprycel was also approved for adults with Ph+ acute lymphoblastic leukemia who are resistant or intolerant to prior therapy. Sprycel is approved and marketed worldwide for these indications in more than 60 countries.

Sprycel is also an FDA-approved treatment for adults with newly diagnosed CP Ph+ CML (since October 2010). Sprycel received accelerated FDA approval for this indication. This indication is approved in more than 50 countries.