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→ PAGE 3

In this issue

IN BRIEF

DRUGS & TARGETS

FUNDING OPPORTUNITIES

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NCI'S LOWY AND SCHILLER WIN LASKER PRIZE FOR DEVELOPING HPV VACCINE

By Paul Goldberg

Douglas Lowy and John Schiller have won the 2017 Lasker-DeBakey Clinical Medical Research Award for research that led to development of the human papillomavirus vaccine.

Lowy, who is completing his stint as the NCI acting director, becomes the first head of the institute—permanent or acting—to win the award, which is described as America's Nobel Prize.

The Lasker awards were announced Sept. 6.

Lowy and Schiller, deputy chief of the Laboratory of Cellular Oncology and head of the Neoplastic Disease Section at the NCI Center for Cancer Research, developed the vaccine against HPV infection, which is responsible for more than a half million cases of invasive cancer throughout the world each year.

Virtually all cases of cervical cancer are caused by HPV, and just two HPV types, 16 and 18, are responsible for about 70% of all cases.

Also, 95% of anal cancers, 70% of oropharyngeal cancers, 65% of vaginal cancers, 50% of vulvar cancers, and 35% of penile cancers are caused by one of the HPV strains.

In a conversation with The Cancer Letter, Lowy said the structure and functioning of the NCI intramural research program helped to make this discovery possible.

"The intramural program [makes it] quite straightforward for people to have long-term collaborations and work together, such as I have had with John Schiller," Lowy said. "And, our working together has really made it far easier for us to make progress in this area than might have been the case, certainly, if I had been working alone."

A conversation with Lowy is posted here.

In oncology and immunology, only one other sitting NIH institute and center director—Anthony Fauci of the National Institute of Allergy and Infectious Diseases—has ever won a Lasker award, the 2007 Mary Woodard Lasker Award for Public Service for his contributions to AIDS relief and biodefense.

Vincent DeVita, who became the NCI director in 1980, won the 1972 Albert Lasker Clinical Medical Research Award as part of a group of researchers involved in developing combination chemotherapy for lymphoma and acute leukemia.

Lasker awards have been given annually since 1945. One award important in the field of cervical cancer was won in 1950 by George Papanicalaou for discovering a method for defining, among the cells exfoliated from tissue surfaces, those which reveal the changes characteristic of specific biological processes.

Altogether, 87 Lasker winners received the Nobel Prize. In the past 30 years, more than 40 Lasker winners received the Nobel.

> "In a world in which vaccines are being irresponsibly attacked and cancer prevention is undervalued, their scientific work and its clinical benefits need the recognition that the Lasker Prize should provide."
>
> *– Harold Varmus*

The 2017 Lasker awards will be presented on Sept. 15.

In the case of HPV, the Nobel prize has already been awarded. In 2008, Harald zur Hausen, of the Heidelberg University, received the Nobel for discovering that HPV causes cervical cancer.

Harold Varmus, a Nobel laureate and Lasker award winner whom Lowy replaced in the top job at NCI, said his essay on the need for a prize for cancer prevention is about to appear in the journal Cell.

"I do make clear in that essay that zur Hausen's work established the probable cause of cervical cancer (infection with certain of the many strains of HPV), while work by John and Doug established a likely means to prevent cervical cancer (and as it turns out other HPV-associated cancers)," Varmus, the Lewis Thomas University Professor at Weill Cornell Medical College, said in an email.

"They took advantage of long experience with bovine papilloma virus, a model for human papilloma viruses that notoriously do not replicate in cultured cells, and showed that they could make virus-like particles with a single BPV coat protein (L1) and the VLPs induced neutralizing antibody that blocked infection," Varmus said.

"They then recapitulated that work with the single analogous protein from the most oncogenic strain of HPV (HPV-16), persuaded pharmaceutical companies to take up the challenge of making the vaccine, and conducted the first human trials. Along the way, they recognized and fixed a mutation in the commonly used L1 gene from HPV-16, a subtle but critical issue.

"And now they are active advocates for increasing the use of HPV vaccines both in the U.S. (where it is still underused) and in the developing world.

"In a world in which vaccines are being irresponsibly attacked and cancer prevention is undervalued, their scientific work and its clinical benefits need the recognition that the Lasker Prize should provide," Varmus said.

Barbara Rimer, chair of the President's Cancer Panel and the Alumni Distinguished Professor and dean at the UNC Gillings School of Global Public Health, said Lowy's and Schiller's work holds promise for prevention of the two million cancers a year that are attributable to infectious disease.

"Kudos to Doug Lowy and John Schiller for being awarded the highly-coveted Lasker Award," Rimer said to The Cancer Letter. "Their basic laboratory research on virus-like particles (VLPs) made it possible to create vaccines to protect against the most common forms of HPV.

"About two million new cancer cases every year are caused by infectious diseases; about 400,000 of these, including the majority of cervical cancers, are due to the most common forms of HPV. Because of the work of Lowy and Schiller, for the first time, we can imagine a future without cervical cancers," Rimer said.

"As chair of the President's Cancer Panel, I have appreciated Lowy's leadership in taking the vaccine from the laboratory work that enabled its creation through to acceptance and use in populations."

> The creation of an effective cancer preventive HPV vaccine was the crowning achievement of their work and represents the finest example of the power of scientific inquiry to better the health of millions.
>
> *– Richard Klausner*

Peter Howley, the Shattuck Professor of Pathological Anatomy at the Harvard Medical School Department of Microbiology and Immunobiology, said Lowy and Schiller are key players in a panoramic story.

"The HPV story is remarkable from discovery to successful translation for prevention," Howley, an HPV researcher and former chief of the NCI Laboratory of Tumor Virus Biology, said to The Cancer Letter. "The identification of specific HPV types in cervical cancers by zur Hausen in 1983, for which he received the Nobel Prize in 2008, followed years of work in the field trying to identify the causative venereally transmitted agent.

"From that discovery, within a decade, the VLP studies by Lowy and Schiller provided the path for the development of the current highly effective preventive HPV vaccine," Howley said to The Cancer Letter. "This translational success is no less important than the initial discovery and itself, and is quite deserving of the recognition afforded by this year's Lasker Award—at least."

"The scientific work of Lowy and Schiller is both beautiful and of enormous impact," said Richard Klausner, a biotechnology entrepreneur who, when he was the NCI director, encouraged the two scientists to produce a clinical grade vaccine. "The creation of an effective cancer preventive HPV vaccine was the crowning achievement of their work and represents the finest example of the power of scientific inquiry to better the health of millions."

"The pioneering work performed by Drs. Lowy and Schiller is a classic example of how fundamental basic science can lead to the translation of information that benefits the health of countless individuals throughout the world," agreed NIAID's Fauci.

"This year's Lasker Medical Research Awards illustrate the power of biomedical investigation to advance human health, whether scientists probe basic questions that reveal unforeseen truths or pursue goal-directed projects," Joseph Goldstein, chair of the Lasker Medical Research Awards jury. "Douglas Lowy and John Schiller discovered that a single protein from the capsule of papillomaviruses can self-assemble into virus-like particles, paving the way for HPV vaccines that prevent cervical and other cancers."

Goldstein, a Nobel laureate and a past winner of a Lasker award, is chair of the Department of Molecular Genetics at UT Southwestern Medical Center.

This year, Planned Parenthood received the public service award, and the Albert Lasker Award for Basic Medical Research went to Michael Hall of the University of Basel for research in TOR-dependent pathways in response to nutrients, growth factors and energy.

Q & A

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

CONVERSATION WITH THE CANCER LETTER

Lowy: NCI's intramural program made development of the HPV vaccine possible

> Rick Klausner, who was the director of the NCI, actually asked if I would develop a clinical-grade HPV vaccine for use in people, so that early-phase studies could be carried out. And, that is indeed what we did.

Douglas Lowy
NCI Acting Director

After getting the news that he and collaborator John Schiller have won the 2017 Lasker-DeBakey Clinical Medical Research Award, Douglas Lowy said that part of the credit belongs to the NCI intramural research program.

Lowy and Schiller got the award for their role in developing the human papillomavirus vaccine, likely preventing millions of deaths worldwide from cervical cancer and HPV-induced malignancies.

Lowy, the NCI acting director, said the institute's intramural program offered him and Schiller the opportunity to continue a three-decade collaboration, giving them access to expertise, and freedom from grant writing and the publish-or-perish rules of extramural academic medicine.

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

Congratulations. Wow! This is huge.

Douglas Lowy: Yes sir.

I guess we should probably first talk about the NCI intramural program. What does the story of the HPV vaccine say to critics of the program?

DL: I think that the intramural program at NIH has many special aspects to it. One of them is that it is quite straightforward for people to have long-term collaborations and work together; such as I have had with John Schiller. And, our working together has really made it far easier for us to make progress in this area than might have been the case, certainly, if I had been working alone.
As you probably are aware, the Discovery Channel had a three-part series about the [NIH] Clinical Center. And, there were many breakthrough discoveries that have been made there over the years, and are continuing to be made there. As a matter of fact, when members of Congress, or people from the administration, come to NIH, they are really impressed by seeing the cutting-edge research that is being performed, and meeting some of the patients who are benefiting from this research.

How long have you been working with Dr. Schiller?

DL: We have been working together for more than 30 years.

Which is uncommon, really, in the extramural world?

DL: Yes, intramurally, it is far easier to do that, because the issues of first authorship, last authorship, et cetera, are less important than what the content is of the research.

Plus, of course, you're trained in dermatology, and Dr. Schiller's expertise is immunology?

DL: Well, actually, when we started working on the vaccine, neither of us had any training in immunology. John's PhD was in bacterial genetics, and his work in animal viruses, as with mine, had mainly been on their molecular biology, transforming genes, etc.

Another dermatologic connection with the vaccine is that Reinhard Kirnbauer is the person who did most of the early work. Reinhard is a dermatologist who now is a professor at the University of Vienna in Austria.

The impact, of course, is gigantic. Could we do the numbers?

DL: Well, HPV infection is responsible for more than a half million cases of invasive cancer throughout the world each year. Cervical cancer is by far the most important of these, globally, because about 85 percent of the cancers attributable to HPV infection occur in the developing world, and about 90 percent of the deaths occur in the developing world. And, in the developing world, cervical cancer accounts for about 90 percent of the HPV-associated cancers.

HPV-associated cancer accounts for about 10 percent of female cancers worldwide. The vast majority of the cancers occurring in the developing world, because it is cervical cancer dominated, arises in women.

In the United States, the spectrum of cancer is quite different. There are a total of about 30,000 HPV-associated cancers each year in the United States. About half of them are cervical cancer. But, the other half are what often are referred to as non-cervical cancers, which include anal cancer, vulvar or vaginal cancer, penile cancer, and head and neck cancers.

About a third of these cancers arise in males. And, therefore, in the United States and other industrialized countries, HPV-associated cancer arises in a fair proportion of men, as well as in women.

What role did chance play in this discovery? Now, it looks like engineering, as things always do in retrospect. But, how much of this was clear in the beginning? How did you get interested?

DL: I would say that none of it was clear. We clearly were performing very high-risk research. We were fortunate that Reinhard was willing to take a chance. And, it actually was the first foray that John and I made into studying the genes that give rise to the structural proteins, or the particles, of the papillomavirus.

Prior to that time, we had been studying the genes that either are involved in cell transformation, or the genes that regulate the expression of the viral genes that are in the papillomavirus. So, we were extremely fortunate that the first set of experiments that we tried actually led to the expression of virus-like particles, which form with very high efficiencies, and were able to induce very high levels of neutralizing antibodies.

It was not at all preordained that this would be the case.

In fact, other investigators had started doing analogous research before we did, using HPV 16, which is the most important oncogenic HPV type. But, those experiments led to either the failure to produce virus-like particles, or when particles were produced, they were aberrant.

John and I actually were fortunate that we started our research in this area, with the bovine papillomavirus. Because, we had infectious virus available, and my lab had developed a neutralization assay for BPV, so that we knew that we had the reagents in hand, so that if we were able to get particles and induce high levels of neutralizing antibodies, they could be measured in a straightforward way. This was not feasible with HPV 16.

Therefore, after having done this initially with BPV, we were looking at HPV 16 and seeing that it self-assembled about 1,000 times less efficiently. And, this led us to hypothesize that the strain that we were working with, which was the reference strain that virtually everyone in the world was using at that time, might encode a mutant of the gene that gave rise to the particles. And, indeed, when we received genes of HPV 16 from lesions that were dysplastic rather than having progressed to cancer, we were able to determine that they self-assembled with an efficiency very similar to that of the bovine papillomavirus. And, I guess you could say, the rest is history.

After you got the initial hypothesis and the initial results, was it difficult to get the support that this project needed?

DL: Actually, no. One thing that happened was that Rick Klausner, who was the director of the NCI, actually asked if I would develop a clinical-grade HPV vaccine for use in people, so that early-phase studies could be carried out. And, that is indeed what we did. So, there actually was substantial support for vaccine development from the first. I will also say that my division director, Alan Rabson, as soon as he heard about the results, was equally enthusiastic, and also supported our research in this area, although, I should point out that John and I had no track record in the study of the structural papillomavirus protein, in immunology, or in vaccine development.

This is really a story about publicly funded research. But, the NCI needed the industry to make and test the vaccine. In this case study, what did NCI bring to the table and what did the industry bring to the table? What's NCI good at, in other words, and what's the industry good at?

DL: Well, we brought the intellectual property and, in addition, the technological approach for making the virus-like particles. MedImmune, which was the first company to make the virus-like particles according to the way that we did it in our lab in insect cells with recombinant baculovirus, really used our process directly. They subsequently sub-licensed the license to GlaxoSmithKline, which made a commercial version of the vaccine. Merck had experience making vaccines in yeast, and so they transferred the technology to express the particles in yeast. Both companies actually took a substantial risk, because the track record of making vaccines against local sexually transmitted infections had been quite poor.

For example, there had been disappointing results with herpes simplex virus type 2 vaccines, although they worked well in animals. And so, both of the companies brought their capabilities of doing development and scale up to make commercial versions of the vaccine, whose effectiveness actually has vastly exceeded our even optimistic expectations.

What are your thoughts about the uptake of this technology? Is this where you expected it to be?

DL: Since I didn't have any specific experience in vaccinology, it was difficult to predict. The uptake of the vaccine, in some countries, has been very high. And, in those countries there has been the development of herd immunity, and a dramatic reduction in the short-term effects that one sees from the vaccine. For example, a dramatic reduction in the incidence of cervical dysplasia, and for the Merck vaccines, a substantial reduction in genital warts.

In the United States, although the uptake has been lower, herd immunity has also been seen here.

My expectation going forward is that, because the vaccine was approved now more than ten years ago, and there had been no showstoppers during that time, that we will continue to see a gradual increase in the uptake of the HPV vaccine in the United States.

The big question is whether the vaccine will be taken up on a worldwide basis. Although there is tiered pricing, it is relatively expensive, and a real investment on the part of developing world countries, because the benefits, in terms of the reduction of the incidence of cervical cancer and mortality from cervical cancer won't be seen until more than 20 years after initiating vaccination.

So, the very large number of people who haven't died, haven't died. How do you make the uptake better?

DL: What we are trying to do at the NCI is to make a rigorous test of the hypothesis that a single dose of one of the FDA-approved HPV vaccines, or all of them, will be able to induce long-term protection. If this is the case, it will become much less expensive for administering the vaccine, but in addition, especially in low-resource settings, the logistics of administering one dose is far easier than that of administering more than one dose.

We are doing a clinical trial in Costa Rica, with partial support from the Bill and Melinda Gates Foundation. And, we look forward to the data, which will become available probably in five or six years, to determine whether one dose is able to do this.

The clinical trial is based on post hoc analyses that we have carried out with an initial clinical trial that was conducted in Costa Rica of the GlaxoSmithKline vaccine, that's the vaccine made by GlaxoSmithKline, which strongly suggests that a single dose of the vaccine might be sufficient to confer long-term protection.

The post hoc analysis, however, is not sufficient to change standard of care, whereas the rigorous trial that is about to start should be able to do that, if indeed our hypothesis turns out to be correct.

What does this technology mean for future cancer prevention strategies? What do you know now that you didn't know before?

DL: I would say that the first part, for future vaccines against other infectious agents that the high immunogenicity of the repetitive structure of the virus-like particle, I think is something that people have really paid attention to. As a matter of fact, there have now been several international conferences on virus-like particles, largely because of the success of the HPV vaccine.

The second part, which is trying to develop immunological approaches to reduce the risk of developing cancer that's not attributable to infectious agents, that is more speculative, but certainly worthy of research support.

Ned Sharpless, your successor at the NCI, is about to be sworn in. Based on your experience now, as acting NCI director, what would be your advice to Ned?

DL: I would say to him, first, that being the NCI director is an extraordinary opportunity to have an impact on cancer research. And, second, to try to take maximum advantage of that opportunity.

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

DL: I would say that the freedom of the research in the intramural program made the research that John and I did quite straightforward.

Another doubling in progress for NIH?
Senate appropriators slate $2 billion for NIH in FY18

By Matthew Bin Han Ong

The Senate Appropriations Committee Sept. 7 marked up its version of the fiscal 2018 Labor-HHS spending bill, giving NIH an increase of $2 billion over the current year.

The bill was approved with overwhelming bipartisan support, with a 29-2 vote, and will advance to the White House as soon as the House passes similar legislation. If signed into law, the measure would bring NIH's budget to $36.1 billion, marking the third year in a row that NIH has received a $2 billion increase.

Advocates for biomedical research say the momentum is reminiscent of the push that doubled the NIH budget in the early 2000s—and showcases Congress's commitment to funding the nation's biomedical research enterprise in vehement repudiation of President Donald Trump's FY18 proposal to slash NIH funding by 21 percent.

"If NIH receives another $2 billion increase in FY 2018 it would mean that in the three years that Sen. Roy Blunt (R-MO) and Rep. Tom Cole (R-OK) have chaired their respective subcommittees, NIH's budget will have increased by a total of 20 percent," said Jon Retzlaff, chief policy officer and vice president of science policy and government affairs at the American Association for Cancer Research. "In the decade prior, stagnant funding levels had resulted in NIH losing more than 20 percent of its ability (in terms of its purchasing power) to support the lifesaving grants that the agency supports."

The Senate measure contains $164.1 billion in base discretionary funding. Including discretionary funding offset by savings from mandatory programs changes, the bill represents approximately $800 million less in total discretionary funding than FY17. The bill is $3 billion above FY17 levels and $27.5 billion above the White House's budget request.

This means that the raise for NIH accounts for two-thirds of the entire increase in the Labor-HHS spending bill.

The legislation contains the first discretionary increase in the maximum Pell grant in over a decade and continued implementation of Year-Round Pell. Also, it slates $816 million to battle the nation's opioid epidemic—an increase of $655 million, or 440 percent, over the past two years.

"I'm proud that we were able to secure another $2 billion increase for the NIH, providing doctors and researchers more resources to help them treat and cure our most deadly and costliest diseases," Blunt said in a statement Sept. 7. "The bill also continues building on our efforts to combat the opioid epidemic and make college more affordable. These critical investments have been made possible, in part, by eliminating or consolidating dozens of programs over the past three years. I urge all of my Senate colleagues to support this measure when it reaches the floor."

The committee's vote on the Labor-HHS bill comes one day after Trump bypassed Republicans and struck a deal with Democrats to increase the debt limit—a ceiling the U.S. is slated to hit at the end of September—and prevent a shutdown by funding the federal government through mid-December.

The short-term continuing resolution, which apparently also includes an agreement to permanently remove the requirement that Congress repeatedly raise the debt ceiling, is anticipated to set up a funding fight and potential gridlock later in the calendar year as legislators debate lifting the FY18 sequestration cap enacted under the Budget Control Act of 2011.

"We are thrilled that Congress and the President have now agreed to a comprehensive plan that will avoid a government shutdown by extending funding levels for almost three months, suspend the debt ceiling un-

til mid-December, and provide help to those affected by Hurricane Harvey," Retzlaff said to The Cancer Letter. "This overall agreement will provide policymakers with additional time to finalize the FY 2018 appropriations bills, and allow them to continue working toward securing another year of a robust, sustained, and predictable funding increase for the NIH."

The $2 billion increase for NIH includes:

- $1.8 billion for Alzheimer's disease research, a $414 million increase;
- $400 million for the BRAIN Initiative to map the human brain, a $140 million increase;
- $344.3 million for the Institutional Development Award, a $11 million increase;
- $290 million for the All of US precision medicine study, a $60 million increase;
- $80 million for the National Cancer Institute's precision medicine program, a $10 million increase;
- $513 million to Combat Antibiotic Resistant Bacteria, a $50 million increase;
- $533.1 million for the Clinical and Translational Science Award, a $17 million increase;
- $12.6 million for the Gabriella Miller Kids First Research Act;
- Increases to every institute and center to continue investments in innovative research that will advance fundamental knowledge and speed the development of new therapies, diagnostics and preventive measures to improve the health of all Americans, and
- A prohibition on capping facilities & administrative costs at 10 percent, which would prevent HHS and the Trump administration from implementing any changes to "indirect" costs associated with NIH research grants (The Cancer Letter, May 26).

The Senate version of the bill breaks on Republican priorities with earlier House legislation, which was designed to defund the Affordable Care Act and the Family Planning (Title X) Program (The Cancer Letter, July 14).

While the Senate measure continues to pay for Obamacare, it does not provide any additional funding for the healthcare program and includes several oversight provisions that would eliminate the Independent Payment Advisory Board, and require the Centers for Medicare and Medicaid Services to "notify appropriate Congressional Committees two business days before any ACA-related data or grant opportunities are released to the public." On Aug. 31, the Trump administration slashed the ACA advertising budget by 90 percent—from $100 million to $10 million—in FY18.

Congress needs to approve a bipartisan budget agreement that would lift spending caps impeding medical progress, said Mary Woolley, president and CEO of Research!America.

"The $2 billion increase for the National Institutes of Health in the Senate Labor-HHS-Education subcommittee FY18 spending bill recognizes the scientific opportunities before us to prevent and eradicate diseases that continue to take a toll on families and our society as a whole," Woolley said. "As Alzheimer's disease, cancer and the opioid epidemic impact the health and economic security of communities across the country, additional funding is desperately needed to advance innovative research that will deepen our understanding of the root causes of disease and addiction.

"The $70 million increase for precision medicine research is a positive development as scientists actively gather data from volunteers to develop the right treatment for the right patient. And the $816 million increase in opioid funding will help to save lives and provide some relief to states hardest-hit by this health threat but more is needed to adequately address the scope of this epidemic."

> "I'm proud that we were able to secure another $2 billion increase for the NIH, providing doctors and researchers more resources to help them treat and cure our most deadly and costliest diseases."
>
> *– Roy Blunt*

The $2 billion increase for NIH is critical, said Lizbet Boroughs, president of United for Medical Research.

"Research funded by the NIH is an engine for medical innovation, a pathway to hope for patients and an economic catalyst, supporting nearly 380,000 jobs and $65 billion in economic activity across the United States," Boroughs said. "It is through strong and sustained funding for medical research that we will address the nation's most devastating and costly illnesses, including Alzheimer's disease, heart disease, and cancer."

GUEST EDITORIAL

How the RACE for Children Act will get drugs to kids with cancer

By Nancy Goodman
Founder and executive director of Kids v Cancer

This month, I should be taking my son, Jacob, to college. Instead, I'm participating in Curefest for Childhood Cancer on the Mall here in D.C.

When Jacob was 8, he was diagnosed with medulloblastoma. The drugs used to treat Jacob were almost 40 years old. They did not work.

At the time of Jacob's treatment, there were several exciting, molecularly-targeted therapies in development or recently approved. However, there were few pediatric trials of these novel therapies, and there was no information as to whether any might benefit Jacob.

Brain cancer is hard to treat, and effective treatments are elusive. But Jacob never even got a shot at novel drugs. Jacob's challenges and the challenges of his physicians are still the challenges facing children and physicians today.

Although there have been exciting leaps forward in the science of drug development for adult cancers, few of those insights have improved pediatric cancer protocols. Novartis's CAR-T cell therapy, which was recently approved first for children with leukemia, is the exciting exception that proves this rule.

However, many of the novel adult therapies I unsuccessfully tried to get for Jacob on a compassionate use basis are only now, after 10 years, entering pediatric trials.

Pediatric cancer is the number one disease killer of children and, while 80 percent of children diagnosed with cancer live at least five additional years, those survivors face shortened lives, chronic health issues, and significantly increased risk of secondary cancers due to the treatments they receive.

There are many reasons why pediatric cancer drug development lags behind adult cancer drug development. Biotech and pharmaceutical companies have not had the financial incentive to develop drugs specifically for pediatric populations. Meanwhile, trials of

promising adult drugs have not been open to children.

The results are grim. Of the almost 900 drugs in the adult cancer pipeline, only a handful have been approved for children with cancer. Moreover, in 20 years, only four drugs have been developed expressly for and approved specifically for a pediatric cancer.

Jacob, at the age of 10, died early on a Friday morning in January 2009. The next day, I opened my laptop on the dining room table and founded Kids v Cancer with the goal of changing the landscape of pediatric cancer research.

Our first effort was to address the problem of companies not having a financial rationale to develop cancer drugs expressly for children. In other words, there has never been a drug developed expressly for Jacob's medulloblastoma.

We drafted and advocated for the Creating Hope Act pediatric priority review voucher program (Pediatric PRV program), which Congress passed into law in 2012. It was a grassroots effort by Jacob's friends, who got members of Congress committed like no one else could.

The Pediatric PRV program provides an incentive for companies to develop drugs for children with rare and life-threatening diseases, including pediatric cancer, by creating a voucher system.

Vouchers can be earned upon FDA approval of pediatric rare disease drugs. Voucher holders have rights to faster FDA review on any other drugs; these are usually not pediatric rare disease drugs, but drugs targeting blockbuster markets. And, vouchers are fully transferable.

The Pediatric PRV program has been a resounding success and has created a rationale for companies to develop pediatric rare disease and pediatric cancer drugs. Since 2012, sales of pediatric priority review vouchers have generated $800 million in incentives, making it financially attractive for biotech and pharmaceutical companies to invest in pediatric drug development.

The Pediatric PRV program created an incentive for companies to develop drugs expressly for children with cancer, but did it not address the 900 drugs in the adult cancer pipeline that might benefit children with cancer as well. In 2013, we turned to that question.

I am very proud to report that this past summer, on Aug. 3, the President signed into law the FDA Reauthorization Act, which includes Title V, the RACE for Children Act.

The RACE for Children Act authorizes FDA to require companies developing cancer drugs for adults to also study their cancer drugs in children if the molecular targets of the drugs under development are relevant to the pediatric cancer populations. Companies will be required to submit their pediatric study plans that detail protocols with specific timetables to the FDA after phase II of their adult trials.

The RACE for Children Act is not an entirely new law, but an update of the 2003 Pediatric Research Equity Act, which requires companies developing drugs for adults to also develop them for pediatric populations. PREA has never been applied to cancer because adult and pediatric cancers originate in different organs.

Moreover, PREA requirements for cancer drugs are almost always waived because pediatric cancers are orphan diseases. The RACE for Children Act addresses both loopholes and now extends PREA requirements to the development of cancer drugs for children.

Implementation of the RACE for Children Act will occur in a stepwise fashion over the next three years. During this time, the FDA is required by statute to:

- Hold a public hearing to consider a guidance,
- Draft and issue the guidance,
- Issue a list of molecular targets that could be expected to trigger PREA requirements, and
- Issue a list of molecular targets for which a PREA waiver would be expected.

Taken together, the RACE for Children Act and the Pediatric PRV program change the landscape of pediatric cancer research. New drugs will be developed expressly for pediatric cancers. Adult cancer drugs that can benefit children with cancer will be studied in children.

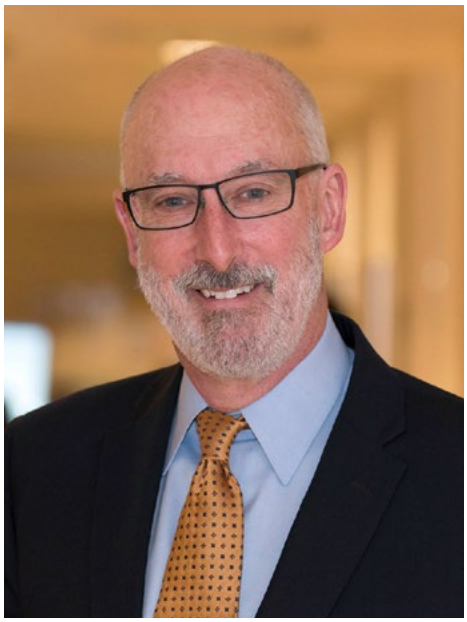
Companies will consider pediatric populations in their oncology drug development plans as a matter of course. Pediatric researchers will have dramatically increased access to novel and exciting drugs and will generate more attention to their bench science ideas by biotech companies. And children with cancer will have a shot at the newest and most promising drugs.

Jacob died when he was 10. He aspired to be a lead vocalist in a rock band or a baseball player.

If we all—FDA, academic researchers, and biotech/pharmaceutical drug developers—fully implement and take full advantage of the opportunities presented by the pediatric PRV program and the RACE for Children Act, perhaps one day there will indeed be more lead vocalists of rock bands and more baseball players.

IN BRIEF

H. Richard Alexander named chief surgical officer at Rutgers



Rutgers Cancer Institute of New Jersey appointed H. Richard Alexander as its new chief surgical officer. He is also appointed as a professor of surgery in the Division of Surgical Oncology at Rutgers Robert Wood Johnson Medical School.

Alexander was most recently a member of the faculty at the University of Maryland School of Medicine and Greenebaum Cancer Center, where he served as the head of surgical oncology in the Department of Surgery and as professor and associate chairman for clinical research.

Prior to arriving at the University of Maryland, Alexander spent 16 years at NCI, where he served as chief of the Surgical Metabolism Section, chairman of the Gastrointestinal Malignancies Section and deputy director of the Center for Cancer Research.

Alexander will be part of Rutgers Cancer Institute's Gastrointestinal Oncology Program when he arrives this fall. He is known as a leader in developing advanced treatments for peritoneal mesothelioma and peritoneal metastases from cancers of the gastrointestinal or other abdominal cavity.

His clinical expertise also includes gastrointestinal malignancies such as pancreatic, colorectal and liver cancers, as well as his role in helping to develop a unique chemotherapy technique to treat those with inoperable liver metastases from melanoma. Alexander's research also includes the assessment of molecular profiles and microenvironments of these tumors in order to personalize treatment for each patient.

Weill Cornell awarded $11.3 million SPORE grant for prostate cancer

Weill Cornell Medicine was awarded a five-year, $11.3 million Specialized Programs of Research Excellence grant from NCI to improve the detection, diagnosis and treatment of prostate cancer.

This SPORE grant is the first ever awarded to Weill Cornell Medicine, and will expand the prostate cancer program, both basic and translational, at the institution's Sandra and Edward Meyer Cancer Center and Caryl and Israel Englander Institute for Precision Medicine.

The grant is co-lead by Himisha Beltran, assistant professor of medicine at Weill Cornell Medicine. She will support four research projects focused on highly translational areas relevant to the detection and treatment of aggressive prostate cancer, each led by a basic scientist and translational clinical investigator.

Projects will be aimed at improving the detection and treatment of a rare, treatment-resistant form of prostate cancer called neuroendocrine prostate cancer; exploring a molecular subtype of prostate cancer characterized by mutations in a gene called SPOP, which occur in 10 to 15 percent of prostate cancers; and improving the understanding molecular variations in prostate cancer tumors.

The SPORE will have significant infrastructural support for big data management, featuring a team of computational biologists and biostatisticians. It will also provide dedicated resources for tissue collection, organoid creation and molecular studies on patient samples.

In addition, the grant includes earmarked yearly funding to jumpstart new high-risk and high-reward studies led by Weill Cornell Medicine researchers, as well as a career enhancement program to support junior investigators who seek to enter into the field of prostate cancer research.

The work and findings will enable Weill Cornell Medicine researchers to develop an approach to treating prostate cancer that aligns their work in both translational and genomic research with the treatment of patients with the disease.

Additional investigators on the SPORE grant include: Karla Ballman, Chris Barbieri, Julie Boyer, Robert Bristow, Olivier Elemento, Paraskevi Gianna-

kakaou, Lorraine Gudas, Juan Miguel Mosquera, David Nanus, David Rickman, Brian Robinson, Douglas Scherr, Michael Shen, Ronglai Shen and Scott Tomlins at Weill Cornell Medicine, and Francesca Demichelis at the University of Trento.

Established in 1992, SPORE grants serve as the cornerstone of the efforts to promote collaborative, interdisciplinary translational cancer research. NCI offers SPORE grants that focus on cancers that are associated with 19 specific organ sites, groups of highly related cancers, or diseases that share a common pathway.

Fox Chase receives NIH grant to establish a research center in Jamaica

Camille Ragin, associate professor in the Cancer Prevention and Control Program at Fox Chase Cancer Center, received a grant from NIH to create a center of research excellence at the University of the West Indies, a regional university with its main campus in Jamaica.

The new center's research will focus on cancer, diabetes, heart disease and stroke. It is the planned first step toward developing a broader network of Caribbean centers of excellence, which will increase research collaboration to address these diseases throughout the region.

The grant will fund multiple primary investigators collaborating from both institutions. The leadership team includes Ragin; J. Robert Beck, senior vice president and deputy director of Fox Chase; Marshall Tulloch-Reid, professor of epidemiology and endocrinology and director of the Epidemiology Research Unit; and Kenneth James, senior lecturer and coordinator of the MPH program in community health and psychiatry. Tulloch-Reid and James are both from the University of the West Indies.

The center plans to strengthen infrastructure, resources, and expertise needed to reduce the burden of these diseases.

Ragin founded and leads the African-Caribbean Cancer Consortium, which furthers the study of genetic, lifestyle, and environmental cancer risk.

NCCN Chemotherapy order templates to be integrated into MEDITECH's Web EHR

The National Comprehensive Cancer Network is working with MEDITECH to integrate the NCCN Chemotherapy Order Templates into MEDITECH's Web Electronic Health Record as standard cancer treatment protocols for use at point of care.

As part of the integration, MEDITECH's Web EHR will provide clinicians direct access to the NCCN Templates and will link to NCCN.org and the corresponding NCCN Clinical Practice Guidelines in Oncology.

The regimens will "enhance patient safety and help guide clinicians' cancer treatment efforts by providing up-to-date, evidence-based standard protocols and best practices within MEDITECH's Oncology Management solution," said Hoda Sayed-Friel, executive vice president of strategy at MEDITECH.

The information contained in the NCCN Templates enhances patient safety by empowering health care providers to standardize patient care, reduce medical errors, and anticipate and manage adverse events.

ASTRO honors 43 researchers with Abstract Awards at 2017 Annual Meeting

The American Society for Radiation Oncology has selected 43 recipients to be presented with one of its 2017 Annual Meeting Abstract Awards. These individuals will be recognized for their top-rated research abstracts at ASTRO's 59th Annual Meeting, taking place Sept. 24-27 in San Diego.

The Resident Clinical/Basic Science Research Abstract Award recognizes the top research from medical residents, with one award for the highest-scored abstracts in each of three categories: clinical practice, radiation and cancer biology, and radiation physics. Award winners receive a $1,500 honorarium.

The 2017 Resident Clinical/Basic Science Research Award recipients are:

- James Bates, University of Florida College of Medicine, Gainesville, Florida (clinical practice)
- Aadel Chaudhuri, Stanford Cancer Institute, Palo Alto, California (radiation and cancer biology)
- Sanjay Aneja, Yale School of Medicine, New Haven, Connecticut (radiation physics)

The Basic/Translational Science Abstract Award recognizes the lead authors of 12 top-rated basic and translational abstracts in clinical practice, radiation and cancer biology, and radiation physics. Award winners, who are a mix of junior and senior investigators, receive a $1,000 honorarium.

The recipients of the 2017 Basic/Translational Science Abstract Award are:

- Erica Bell, The Ohio State University, Columbus, Ohio (clinical practice senior investigator)
- Christopher Corso, Yale School of Medicine, New Haven, Connecticut (clinical practice junior investigator)
- Narek Shaverdian, University of California, Los Angeles (clinical practice junior investigator)
- Anurag Singh, Roswell Park Cancer Institute, Buffalo, New York (clinical practice senior investigator)
- Sophia Kamran, Harvard University, Boston (radiation and cancer biology junior investigator)
- Fei-Fei Liu, Princess Margaret Cancer Centre, Toronto (radiation and cancer biology senior investigator)
- Stephanie Markovina, Alvin J. Siteman Cancer Center, Washington University in St. Louis (radiation and cancer biology junior investigator)
- Catherine Park, University of California, San Francisco (radiation and cancer biology senior investigator)
- Hao Han, Stanford University, Palo Alto, California (radiation physics senior investigator)
- Sang Ho Lee, Memorial Sloan Kettering Cancer Center, New York (radiation physics junior investigator)
- Gang Yin, Sichuan Cancer Hospital and Institute, Chengdu, China (radiation physics junior investigator)
- Hao Zhang, University of Maryland School of Medicine, Baltimore (radiation physics senior investigator)

The Annual Meeting Travel Award recognizes outstanding research by early-career scientists, biologists and physicists. Lead authors of 15 high-scoring abstracts selected for the meeting will receive awards of $1,000 to support travel to the meeting.

The 2017 Annual Meeting Travel Award winners are:

- Rohann Correa, London Regional Cancer Program, Western University, London, Canada (clinical practice)
- Shrinivas Rathod, CancerCare Manitoba, Winnipeg, Canada (clinical practice)
- Antoine Schernberg, Hôpital Tenon, Paris (clinical practice)
- Monica Serban, Aarhus University Hospital, Aarhus, Denmark (clinical practice)
- Shankar Siva, Peter MacCallum Cancer Centre, Melbourne, Australia (clinical practice)
- George Grass, Moffitt Cancer Center, Tampa, Florida (radiation and cancer biology)
- Kathy Han, Princess Margaret Cancer Centre, Toronto (radiation and cancer biology)
- Wen Jiang, the University of Texas MD Anderson Cancer Center, Houston (radiation and cancer biology)
- Jonathan Leeman, Memorial Sloan Kettering Cancer Center, New York (radiation and cancer biology)
- Harish Vasudevan, University of California, San Francisco (radiation and cancer biology)
- Mireia Crispin-Ortuzar, Memorial Sloan Kettering Cancer Center, New York (radiation physics)
- Penny Fang, the University of Texas MD Anderson Cancer Center, Houston (radiation physics)
- Olga Green, Washington University in St. Louis (radiation physics)
- Giuseppe Palma, Italian National Research Council, Institute of Biostructure and Bioimaging (radiation physics)
- Leith Rankine, University of North Carolina School of Medicine, Chapel Hill, North Carolina (radiation physics)

The International Annual Meeting Scientific Abstract Award provides a $4,000 grant to a radiation oncologist from a developing country, based on the World Bank's definition, to attend ASTRO's Annual Meeting and to spend additional time at a comprehensive cancer center in the United States.

The award fosters continuing medical education, assists in career development and aids in establishing relationships with ASTRO members who may serve as scientific mentors to the award winner.

The recipient is the lead author of an abstract selected for presentation at the 2017 ASTRO Annual Meeting and has a letter of support from the chair/mentor of the U.S. institution that will host the awardee at his or her cancer center. The awardee must submit a written summary of their Annual Meeting participation and the experience garnered at the host cancer center.

The recipient of the 2017 International Annual Meeting Scientific Abstract Award is:

- Indranil Mallick, Tata Medical Center, Kolkata, India

The Resident Poster Viewing Recognition Award recognizes the highest-rated abstracts submitted by residents that were selected for paper poster presentations, with awards for the top three

resident authors in each of three categories: clinical practice, radiation and cancer biology, and radiation physics.

The 2017 Resident Poster Viewing Recognition Award recipients are:

- Corbin Helis, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina (clinical practice)
- Chan Woo Wee, Seoul National University Hospital, Seoul, South Korea (clinical practice)
- George Q. Yang, University of South Florida, Tampa, Florida (clinical practice)
- Linda Chen, Johns Hopkins University School of Medicine, Baltimore (radiation and cancer biology)
- Michael Farris, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina (radiation and cancer biology)
- Jenna Kahn, Virgnia Commonwealth University Medical Center, Richmond, Virginia (radiation and cancer biology)
- Sanne Blinde, Erasmus MC Center Institute, Rotterdam, Netherlands (radiation physics)
- Seung Hyuck Jeon, Seoul National University Hospital, Seoul, South Korea (radiation physics)

The Resident ePoster Recognition Award recognizes the highest-rated abstracts selected for digital poster discussions that have residents as the lead author, with one award each for the top abstracts in clinical practice, radiation and cancer biology, and radiation physics.

The 2017 Resident ePoster Recognition Award recipients are:

- Richard Cassidy, Winship Cancer Institute of Emory University, Atlanta (clinical practice)
- Ariel Marciscano, Johns Hopkins University School of Medicine, Baltimore (radiation and cancer biology)
- Noah Kalman, Virginia Commonwealth University, Richmond, Virginia (radiation physics)

The Annual Meeting Nurses Abstract Award honors the highest-rated abstract with a nursing designation. Award candidates must be nurses who are the lead author or co-author of an abstract selected for presentation at the 2017 ASTRO Annual Meeting. The award winner receives a $1,000 honorarium.

The 2017 Annual Meeting Nurses' Abstract Award recipient is:

- Antonia Pryor, Texas Oncology, Dallas

DRUGS & TARGETS

EC approves Merck's Keytruda for locally advanced, metastatic urothelial carcinoma

The European Commission approved Merck's Keytruda (pembrolizumab) for the treatment of certain patients with locally advanced or metastatic urothelial carcinoma.

Keytruda is approved for use as monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy, as well as adults who are not eligible for cisplatin-containing chemotherapy.

The approval in patients previously treated with platinum-containing chemotherapy was based on superior overall survival for Keytruda versus investigator-choice chemotherapy (paclitaxel, docetaxel, vinflunine) (HR, 0.73 [95% CI: 0.59, 0.91], p=0.002), as demonstrated in the randomized, phase 3 KEYNOTE-045 trial.

The approval in patients ineligible for cisplatin-containing chemotherapy was based on phase II data from the KEYNOTE-052 trial, which demonstrated an overall response rate of 29 percent (95% CI, 25-34). The approval allows for the marketing of Keytruda in these two new indications in all 28 EU member states plus Iceland, Lichtenstein and Norway at a dose of 200 mg every three weeks until disease progression or unacceptable toxicity.

"Despite advances, there remain limited treatment options available to patients with locally advanced or metastatic urothelial carcinoma who are either not eligible to receive cisplatin-containing chemotherapy – which is platinum-based and currently the standard of care – or for those patients whose cancer returns after receiving prior platinum-containing chemotherapy," said Ronald de Wit, group leader

for experimental systemic therapy of urogenital cancers, Erasmus MC Cancer Institute. "It is exciting that with this approval of Keytruda, we now also have a new treatment option for patients previously treated with platinum-containing chemotherapy that has shown a clinically meaningful and improved overall survival benefit versus chemotherapy in this difficult-to-treat population."

The approval in patients previously treated with platinum-containing chemotherapy is based on data from a multicenter, randomized, controlled trial, KEYNOTE-045, investigating Keytruda (pembrolizumab) in patients with locally advanced or metastatic urothelial carcinoma with disease progression on or after platinum-containing chemotherapy.

Patients must have received a first-line platinum-containing regimen for locally advanced/metastatic disease or as neoadjuvant/adjuvant treatment, with recurrence/progression ≤12 months following completion of therapy. Patients were randomized (1:1) to receive either Keytruda 200 mg every three weeks (n=270) or investigator's choice of any of the following chemotherapy regimens, all given intravenously every three weeks (n=272): paclitaxel 175 mg/m2, docetaxel 75 mg/m2, or vinflunine 320 mg/m2.

Patients were treated with Keytruda until unacceptable toxicity or disease progression, or for up to 24 months in patients without disease progression. The study excluded patients with autoimmune disease, a medical condition that required immunosuppression and patients with more than two prior lines of systemic chemotherapy for metastatic urothelial cancer. The primary efficacy outcomes were OS and progression-free survival (as assessed by BICR using RECIST v1.1); secondary outcome measures were ORR (as assessed by BICR using RECIST v1.1) and duration of response.

In the study, Keytruda demonstrated a statistically significant improvement in OS compared to chemotherapy. Findings demonstrated that KEYTRUDA resulted in a 27 percent reduction in the risk of death compared to chemotherapy – with 155 events (57%) observed in the Keytruda arm, compared to 179 events (66%) in the chemotherapy arm (HR, 0.73 [95% CI: 0.59, 0.91], p=0.002); the median OS was 10.3 months (95% CI: 8.0, 11.8) in the Keytruda (pembrolizumab) arm, compared to 7.4 months (95% CI: 6.1, 8.3) in the chemotherapy arm.

There was no statistically significant difference between Keytruda and chemotherapy with respect to PFS. There were 218 events (81%) observed in the Keytruda arm, compared to 219 events (81%) in the chemotherapy arm (HR, 0.98 [95% CI: 0.81, 1.19], p=0.416). The median PFS was 2.1 months (95% CI: 2.0, 2.2) in the Keytruda arm, compared to 3.3 months (95% CI: 2.3, 3.5) in the chemotherapy arm.

The ORR was 21 percent (95% CI: 16, 27) for patients receiving Keytruda, with a complete response rate of 7 percent and a partial response rate of 14 percent. In the chemotherapy arm, the ORR was 11 percent (95% CI: 8, 16), with a complete response rate of 3 percent and a partial response rate of 8 percent (p=0.001). The median duration of response for patients treated with Keytruda had not yet been reached (range: 1.6+ to 15.6+ months), compared to 4.3 months (range: 1.4+ to 15.4+ months) in the chemotherapy arm.

The approval in patients ineligible for cisplatin-containing chemotherapy is based on data from a multicenter, open-label study, KEYNOTE-052, investigating Keytruda in 370 patients with locally advanced or metastatic urothelial carcinoma who were not eligible for cisplatin-containing chemotherapy. Patients received Keytruda at a dose of 200 mg every three weeks until unacceptable toxicity or disease progression, or for up to 24 months in patients without disease progression.

The study excluded patients with autoimmune disease or a medical condition that required immunosuppression. The primary efficacy outcome measure was ORR as assessed by BICR using RECIST 1.1; secondary efficacy outcome measures were duration of response, PFS, and OS.

The efficacy analysis, with a median follow-up time of 9.5 months, showed an ORR of 29 percent (95% CI: 25, 34), a complete response rate of 7 percent, and a partial response rate of 22 percent. The median duration of response had not been reached (range: 1.4+ to 19.6+ months).

The safety analysis supporting the European approval of Keytruda was based on 3,830 patients with advanced melanoma, non-small cell lung cancer, classical Hodgkin lymphoma, or urothelial carcinoma across four doses (2 mg/kg every three weeks, 200 mg every three weeks, or 10 mg/kg every two or three weeks) in clinical studies.

In this patient population, the most common adverse reactions (>10%) with Keytruda (pembrolizumab) were fatigue (21%), pruritus (16%), rash (13%), diarrhea (12%) and nausea (10%). The majority of adverse reactions reported were of grade I or II severity. The most serious adverse reactions were immune-related adverse reactions and severe infusion-related reactions.

Keytruda is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells. Keytruda is a humanized monoclonal antibody that blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2, thereby activating T lymphocytes which may affect both tumor cells and healthy cells.

Studies of Keytruda – from the largest immuno-oncology program in the industry with more than 550 trials – include a wide variety of cancers and treatment settings. The Keytruda clinical program seeks to understand factors that predict a patient's likelihood of benefitting from treatment with Keytruda, including the exploration of several different biomarkers across a broad range of tumors.

Keytruda is administered as an intravenous infusion over 30 minutes every three weeks for the approved indications. Keytruda for injection is supplied in a 100 mg single-dose vial in the U.S.

FDA grants orphan drug status to Cellect's ApoGraft for acute and chronic GvHD

Cellect Biotechnology Ltd. said the FDA has granted orphan drug designation for Cellect's ApoGraft for the prevention of acute and chronic graft versus host disease in transplant patients.

GvHD is a transplant associated disease representing an outcome of two immune systems crashing into each other. In many transplantations from donors, and especially in Bone Marrow Transplantations, the transplanted immune mature cells, as opposed to stem cells, attack the host, patient receiving the transplant, and create severe morbidity and in many cases even death.

This disease happens as a result of current practices being unable to separate the GvHD causing cells from the much needed stem cells. Cellect's ApoGraft was designed to eliminate immune responses in any transplantation of foreign cells and tissues.

FUNDING OPPORTUNITIES

DOD Kidney Cancer Research Program publishes funding opportunities for FY17

The FY17 Defense Appropriations Act provides $10 million to the Department of Defense Kidney Cancer Research Program to support United States Army Medical Research Acquisition Activity.

As directed by the Office of the Assistant Secretary of Defense for Health Affairs, the Defense Health Agency J9, Research and Development Directorate manages the Defense Health Program Research, Development, Test, and Evaluation appropriation. The managing agent for the anticipated Program Announcements/Funding Opportunities is the Congressionally Directed Medical Research Programs.

The KCRP is providing the information in this pre-announcement to allow investigators time to plan and develop applications. FY17 KCRP Program Announcements and General Application Instructions for the following award mechanisms are anticipated to be posted on the Grants.gov website in October 2017. Pre-application (Letter of Intent) and application deadlines will be available when the program announcements are released. This pre-announcement should not be construed as an obligation by the government.

Consortium Development Award

- Investigators at or above Assistant Professor (or equivalent)
- Supports infrastructure development to establish the necessary collaborations among a Coordinating Center and Clinical Sites
- Multi-institution collaboration required
- Supports clinical trials of novel interventions with the potential to have a significant impact on patient care in kidney cancer
- Proposed trials may be Phase 0, Phase 1, or Phase 2
- Minimum of three separate institutes: one Coordinating Center and at least two Clinical Sites (other than the Coordinating Center)
- Maximum funding of **$1.6 million** total costs
- Maximum period of performance is 2 years
- Awardee will be eligible to apply for FY19 Consortium Award, if funds are available

Idea Development Award

Established Investigators: Independent investigators at or above the level of Assistant Professor (or equivalent) and 10 years or more from a terminal degree; or

Early Career Investigators: Investigators at the level of Assistant Professor, Instructor, or Assistant Research Professor (or equivalent) and less than 10 years from a terminal degree (excluding time spent in medical residency or family medical leave) at the time of application submission deadline are eligible.

- Supports new ideas that represent innovative, high-risk/high-gain approaches to kidney cancer research, and have the potential to make an important contribution to kidney cancer.
- Preliminary data is required; need not be in kidney cancer.
- Innovation and Impact are the most important review criteria.
- Clinical Trials are not allowed

Areas of Interest include:

- Microenvironment, Metabolism, Chromatin and Gene Regulation, Rare Cancers, Screening, Early Detection, Novel Imaging Technologies, Liquid Biopsy, Biomarker Development, Prognosis, Targeted Therapies, Immunotherapies, Resistance, Novel Interventions, Surgical, Ablation, Radiation, Prognosis, Managing Toxicity, Survivorship and Patient Experience, Surveillance, Genetic Risk Factors
- Maximum funding of **$400,000** in direct costs (plus indirect costs)
- Period of performance not to exceed 3 years

Concept Award

- Investigators at all academic levels
- Supports highly innovative, untested, potentially groundbreaking concepts in kidney cancer
- Emphasis on innovation
- Clinical trials not allowed
- Preliminary data not allowed
- Blinded review
- Maximum funding of **$75,000** for direct costs (plus indirect costs)
- Maximum period of performance is 1 year

Translational Research Partnership

- Investigators at or above the level of Assistant Professor (or equivalent)
- Supports partnerships between clinicians and laboratory scientists that accelerate ideas in kidney cancer into clinical applications
- Supports translational correlative studies
- Preliminary data required
- Funding for clinical trials not allowed
- Maximum funding of **$600,000** for direct costs (plus indirect costs)
- Maximum period of performance is 3 years

A pre-application (letter of intent) is required and must be submitted through the electronic Biomedical Research Application Portal (eBRAP) at prior to the pre-application (letter of intent) deadline. All applications must conform to the final Program Announcements and General Application Instructions that will be available for electronic downloading from the Grants.gov website. The application package containing the required forms for each award mechanism will also be found on Grants.gov. A listing of all CDMRP funding opportunities can be obtained on the Grants.gov website by performing a basic search using CFDA Number 12.420.

Applications must be submitted through the Federal Government's single-entry portal, Grants.gov. Submission deadlines are not available until the Program Announcements are released. For email notification when Program Announcements are released, subscribe to program-specific news and updates under "Email Subscriptions" on the eBRAP homepage. For more information about the KCRP or other CDMRP-administered programs, please visit the CDMRP website.