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NANCY DAVIDSON DESCRIBES PLANS FOR REOPENING THE SEATTLE CANCER CARE ALLIANCE AS COVID-19 WAVE RECEDES

Nancy Davidson is now in the eleventh week of managing the COVID-19 pandemic—the longest stretch experienced by any health executive in the U.S.

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Nancy Davidson describes plans for reopening the Seattle Cancer Care Alliance as COVID-19 wave recedes

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CONVERSATION WITH THE CANCER LETTER

> We're at a point where we're able now to think about how to wind up after the wind-down. And so, right now, we are, in a very thoughtful and deliberate fashion, opening about 10% new trials and 10% of our closed trials over the next week or so.

Nancy Davidson is now in the eleventh week of managing the COVID-19 pandemic—the longest stretch experienced by any health executive in the U.S.

And now, like her peers throughout the country, Davidson, president and executive director of the Seattle Cancer Care Alliance, is in the midst of ramping up plans for a comeback of cancer services.

The Cancer Letter asked Davidson to discuss these plans and share her thoughts on the way cancer care will evolve both at SCCA and nationwide.

This conversation is part of an informal series of stories, interviews, and commentaries that track cancer institutions as they seek to reopen, reorganize, and reinvent in the wake of the COVID-19 pandemic:

- Health systems and academic cancer centers are cutting expenses to make up for operational shortfalls resulting from the pandemic—laying off employees, furloughing staff, and cutting salaries and benefits (*The Cancer Letter*, May 8, 2020).
- Community oncology practices are experiencing a significant decrease in patient volume, as weekly visits dropped by nearly 40%, while cancellations and no-shows have nearly doubled (*The Cancer Letter*, May 1, 2020).

Washington was the first state to record what at the time was believed to be the first COVID-19 case—on Jan. 15, in a traveler from Wuhan, China.

Washington was also the first to register what appeared to be the first COVID-19 death, and SCCA as well as Fred Hutchinson Cancer Center, a component of the alliance, were the first major cancer institutions to take decisive action and shut down non-essential operations (*The Cancer Letter*, March 13, 2020).

At this writing, the state of Washington has 18,964 confirmed cases and 991 COVID-related deaths. The disease peaked weeks ago, and the spread has slowed. On May 15, for example, 101 new cases and 5 deaths were reported in the state. Washington ranks 18th in the number of cases.

Now, SCCA is among the first to make plans to reopen its operations.

"We are bringing our stem cell transplant and our CAR T programs back online in a very thoughtful way, and there's a lot of pent-up demand for that. We had over a hundred transplant patients who've been waiting in the queue, for example. And so, we're beginning to recall them and bring them in," Davidson said to *The Cancer Letter.*

"We looked at things like imaging, close to a thousand mammograms that didn't take place because screening mammograms were paused during this time of maximum separation. And so, we're also beginning to think about how we can thoughtfully recall those patients. Some patients who had more elective therapies also put it off for a while.

"And so, we have a pretty good idea of what the numbers are. I mean, you're right. We are actively reaching out to patients and letting them know that the system was always safe. But we're now at a position where we think that they can safely come for their in-person care.

"And I think that'll be an important thing going forward, especially in cancer. You and I know that cancer didn't take a pause during the COVID pandemic, and it isn't taking a pause in the near future. We really need to be in a position where we can try to optimize our care going forward. We do know that some of our patients are worried. They're concerned about the possibility that they would somehow increase their exposure by coming in to their visits. And so, we have very, very robust testing in place in Washington. That's also helped us."

Q & A

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

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

Paul Goldberg: You have more experience with more phases of COVID-19 than anyone else in the U.S. So, going back to the beginning, to what feels like a decade ago, you moved very, very fast and set up prioritization, and closed things down. What was it like to be on the inside of those decisions?

Nancy Davidson: Paul, you're right that we're in the 10th week of our pandemic response at the Seattle Cancer Care Alliance. As you point out, we are the first of the United States NCI-designated comprehensive cancer centers to experience this in a meaningful way. And at the time, I think that we knew that we were entering into uncharted territory, but territory that we were well equipped to deal with.

As you point out, we're in a state that has had a very robust response.

We work at an institution that has a lot of people who are already involved in research in viruses. Fred Hutch houses one of the big coordinating centers for the HIV vaccine efforts, so that we felt that we were in a good position to do this, but we were kind of learning on the job.

Oncologists, though, are very good at dynamic situations, and tackling risk; right? That's what we do for a living.

Well, you have also seen more impact on your institution and research, both clinical and basic. How would you summarize this impact?

ND: We have seen much more impact than all of us would like on our cancer research.

Obviously, our COVID research is flourishing right now, but on the cancer side, we made the decision institutionally, across Fred Hutch and Seattle Cancer Care Alliance, to really slow down our basic laboratory research in accordance with the state guidelines and with our own modeling about what we should do to try to flatten the curve.

And we also made the decision to really limit access to some of our clinical trials, particularly the phase I clinical trials, where we felt that the real goal of a phase I trial is toxicity rather than improving patient wellbeing. And we also closed some of our phase III clinical trials, because we felt that a standard treatment option was available for those patients.

But Paul, we've continued our phase II clinical trials all during this time, for patients where we thought that clinical trial participation would be important for their wellbeing, and we certainly have continued care on trial for everybody who was already on trial. The new accrual was limited more to folks who were going on to the phase II trials.

And we're now doing the reverse.

We're at a point where we're able now to think about how to wind up after the wind-down. And so, right now, we are, in a very thoughtful and deliberate fashion, opening about 10% new trials and 10% of our closed trials over the next week or so.

We'll look carefully at the impact of that, and then we hope to continue that ramp up in a stepwise fashion. And we've tried to prioritize those for trials that are in patients' best interests, trials that really reflect some of our primary research interests as an institution, and those where we think that we can try to optimize the safety of the participants and our staff.

Do you think anything has been irrevocably lost, in terms of data?

ND: I think that in some of our clinical trials, we weren't able to collect every single piece of data that might've been mandated by the clinical trial.

Certainly, we were able to collect all the data that would be vital for patient safety. And we may not be able to get all of those things, but I suspect that for the clinical trials that have remained in operation and those that will be restarting, that we'll be able to gather the information that we need to address the primary aims of the clinical trial.

I've heard it said that with randomization, problems affect both sides of the trial. So, with randomized trials, you might actually be in okay shape.

ND: I think so. Many of the randomized trials are very large trials; right? And one would hope that what we're going to see is a short period of a pause, and then, you're right, the trial will resume in its full form, and that we will not have any compromise of the primary outcome of the trial.

What about clinical care? Has that been set back?

ND: No, I don't think so. I do think that oncologists are pretty good at dealing with adversity, as are our patients. So,

we have remained operational the entire time. We've actually used this as an opportunity to accelerate some of the initiatives that we probably should have done before.

All of us have become very adept at telehealth now, and we are hoping that we'll be able to right-size how we would use that going forward. And, of course, we're hoping that the reimbursement strategies nationally will make that a viable alternative for some patients where it's appropriate.

We continued all of our infusion therapies, by and large. The one place where we made some pretty strategic decisions was to slow access to our cell-based therapy trials and treatments, our CAR T trials and our stem cell transplant trials.

As members of a healthcare ecosystem, we needed to be in line with the priorities of the state of Washington and the Puget Sound region at the time, to make sure that we freed up inpatient beds and critical care resources for what we thought would be the surge of COVID-19 patients.

And so, that meant that those transplant and CAR T patients were the patients who were the most likely to require those things, and we made the decision to slow their entry into our system. We're now restarting that, too, Paul. As of last week, we're reentering some of the most needy patients who require those particular kinds of interventions, because we feel that we have the hospital capacity to care for them should they become ill.

Have you had to do triage on COVID? On, say, ventilators?

ND: Thankfully, we have not. I think, again, the state of Washington has been very forward-thinking on this. In our state, early on there were a lot of workplaces that put people to work from home. The Fred Hutch and the SCCA did this early on; the governor has been very diligent in the state of Washington.

And so, I think we were in happy circumstances where, thankfully, our critical care capacity was higher than our needs. And so there was never a time that I'm aware of where in the University of Washington system we had to triage the use of ventilators.

What role have disparities played in this crisis?

ND: Well, gosh, I think that's an area where we're all trying to sort it through; right?

Our region has a large homeless population. That's certainly a major form of disparity. And so, I think that within the region, we're trying to work collectively with our government facilities and with our partner organizations to make sure that our homeless population has access to the kind of care that they need across the board—things that are related to prevention or treatment in COVID, as well as underlying social and health problems that they might have.

Ours is a state that has a large Native American population, and so, we're trying to make sure that we work pretty actively with our tribes, where appropriate, to make sure that they're getting the appropriate health care.

And you may know that also in our region the Yakima Valley, which is in the middle of the state, is the home of our larger Hispanic population. That region has been particularly hard hit, and I think that might have to do with the nature of the workforce and the kinds of jobs.

These are folks who often work in situations where it's hard to distance in the workplace, and they work in vital industries, and so, this is a population that's also been especially hard hit. So, we're trying very hard to make sure that we understand these individuals who are at particular risk, and we do everything we can to try to mitigate that risk within those individuals.

How soon do you think you might have some data?

ND: I don't have a good answer for you on that one right now. I think that everybody is pedaling as fast as they can, Paul, to try to get data generally. And then, also, for specific populations.

For example, populations of patients with cancer.

AACR had a session where they tried to review what we know about cancer as a risk factor for COVID, and it looks to me like we don't have a clear understanding of that as a field, either. So, there are a lot of places where we have knowledge that we really have to gain over relatively short period of time.

What about financial impact? Have you had to have furloughs or any other forms of belt-tightening?

ND: We think our workforce is incredibly important. That's obviously one of our most important resources, and so, we'd like very much to retain our workforce as best as we can going forward. We've been fortunate that many people were in a situation where they could work from home.

And so, many of our workforce members who don't have to be physically in the office or who are not directly patient-facing are working from home and they're working extremely hard.

I think it will be interesting to see how it goes over time. What the healthcare workforce looks like generally is something that we're all going to need to be thinking about as we go into the months and the years ahead—what we've learned from this, and what we can use to try to optimize the delivery of healthcare going forward generally, and also the delivery of cancer care specifically.

People talk about a rebound in demand for care—patients showing up saying, "Take care of us." You should probably be starting to see it about now, I would think. Is it happening?

ND: We are hoping that we're going to see that shortly, and, actually, we're trying to begin to promote that, if you will.

First, I told you about the fact that we are bringing our stem cell transplant and our CAR T programs back online in a very thoughtful way, and there's a lot of pent-up demand for that. We had over a hundred transplant patients who've been waiting in the queue, for example. And so, we're beginning to recall them and bring them in.

We looked at things like imaging, close to a thousand mammograms that didn't take place because screening mammograms were paused during this time of maximum separation. And so, we're also beginning to think about how we can thoughtfully recall those patients. Some patients who had more elective therapies also put it off for a while. And so, we have a pretty good idea of what the numbers are. I mean, you're right. We are actively reaching out to patients and letting them know that the system was always safe. But we're now at a position where we think that they can safely come for their in-person care.

And I think that'll be an important thing going forward, especially in cancer. You and I know that cancer didn't take a pause during the COVID pandemic, and it isn't taking a pause in the near future. We really need to be in a position where we can try to optimize our care going forward. We do know that some of our patients are worried. They're concerned about the possibility that they would somehow increase their exposure by coming in to their visits. And so, we have very, very robust testing in place in Washington. That's also helped us.

And so, we have a really good idea about the relatively few members of our staff who have tested positive, and also, the reasonably small number of patients have tested positive. Great testing capabilities, so if anybody's symptomatic, they get tested immediately through our drive-through testing facilities that we've set up.

Do you test everybody who walks in through the door, every patient?

ND: No, we don't test asymptomatic staff or patients, with rare exceptions. We are now doing testing in individuals who are being teed up for stem cell transplant, for example. Our surgeons are now doing routine testing on anybody who's slated to go to the operating room.

Our proceduralists are doing testing on anybody who's going to have a kind of procedure that might have a higher risk of infection of bystanders. We're trying to use testing in a very, very thoughtful way, to identify patients who are going to go through some sort of procedure where we want to understand it for their risk or we want to understand it for the risk of the caregivers around them.

How many patients had the disease while it was peaking? What's your cumulative for COVID?

ND: Could you say that again?

How many COVID patients have you seen through the system do you think?

ND: In the system? I don't have that number at the top of my head, but I can tell you in the Seattle Cancer Care Alliance that I think a minimal number of staff members have tested positive over the entire time.

What about patients coming through the institutions?

ND: We've been fortunate that the infection rate in our patients is quite low, and it's not out of a context with what we see in our community at large. And in the state of Washington right now, I think, about 7% of tests are positive.

How many of the state's, what percentage of the state's cases have gone through Seattle Cancer Care Alliance Institutions?

ND: Although I don't have that specific percentage, the number of infected patients at SCCA has remained minimal.

As you watch the debates about reopening the country, what are your thoughts? How should this happen?

ND: Oh , that's a pretty tough question, and one that obviously there are people who are at a higher pay grade than me who are doing this for our national interests.

I think within the state of Washington, we're trying to work very closely with our government authorities, with our governor, Jay Inslee, with our fellow healthcare providers, and, actually, we're also working with some of our big employers around town.

This state has chosen to be very thoughtful and very deliberate, in part perhaps because we were in the vanguard, and we did take steps rapidly, and we thought that we could see a very positive impact in what we were able to avoid as a consequence of these measures.

I think that across the region, there is actually an effort to think about how we're going to do this together across all of these different constituencies, and to try to come to some sort of agreement about how this is going to change, and to know that it's going to be dynamic, Paul. And also, that it may be somewhat regional.

The state of Washington is one that has some pretty rural regions that haven't been especially affected by COVID. We have some pretty urban regions, like Seattle, and the Puget Sound area obviously was a real epicenter for it.

And so, it might be that the thoughts about how you do that are going to change a little bit, depending on where you are in this state. The governor looks at this very actively. He has just opened up some of the state parks, for example. Right now, I don't know that he's going to make other major pronouncements about other changes until more towards the end of the month. And we're trying to work with him to make sure that we are all one state trying to address this in the most effective way.

Well, it helps you have better public health systems than a lot of other states.

ND: I think we're very fortunate that the public health departments here have been very active early on. They had to be, they were thrust into the center of it, with the nursing home and the Evergreen Hospital, and the fact that we had what we thought at the time was the first death within the state of Washington, the first death within in the United States.

We now know that that may not have been true, because there are these other cases that are turning up.

But you're right, I think the public health infrastructure here is quite strong. The public health interest is quite strong, and I think that we've been fortunate that people have been willing to work together on this.

From a health point of view, remember that healthcare was always essential. And so, there was never any effort to shutter healthcare across the state. It was kept running, and the only thing we did was to make some of the modifications that you and I just talked about at a time that we felt when we needed to be ramped up in case there was a very major surge of people who needed inpatient care, especially intensive care.

And we were fortunate that we avoided that. I think one of the things going forward for all of us is to recognize that we're probably going to have some COVID infection for quite some time to come, and so we have to think about how we're going to work effectively to hopefully maintain that at a low or even lower level, but also to be able to ramp up our medical care to make sure that we address some of those unmet needs that you talked about.

What will oncology look like when COVID is over?

ND: Well, I think that cancer is not going away, or cancers are not going away. So, I think those big things are not going to change; right? The needs are not going to change. I think our therapies are not going to change, so far as I can appreciate.

The interesting things that we've been thinking about are, first of all, maybe the location for some services. Oncology tends to be pretty resource-oriented. We often have a need of testing, we need a blood drawing, we have need of infusional capacity, we have need of radiation oncology. So, I can imagine that those things are not going to change, and it may not be possible to do all of those things in a remote fashion. In fact, for many of them, I think, it's going to be tough to do.

But what might change would be some of the things that are involved in longer term care, long-term follow-up. And I also personally wonder whether it's going to depend a little bit on the kind of cancer.

For example, Paul, as you know, I'm a breast cancer specialist, and I tend to like to see my patients in person for follow up, because we want to do a physical exam and cannot do that remotely.

So, I think one of the things we'll have to contend with as a field is what things do have to be done face-to-face, hands on patient, or test on patient, and what things might be able to be safely and efficiently changed over to telehealth, for example.

What do you think about this new emphasis on, maybe it wasn't the case at Seattle Cancer Care Alliance but elsewhere, on neoadjuvant treatments instead of adjuvant? Is that a good thing or not a good thing for the patient?

ND: I think that I can speak in a most informed fashion from the breast cancer perspective, because that's the area I know best. And I would tell you, Paul, that I actually was one of the first proponents for it.

I happened to be in our multidisciplinary new patient clinic for breast cancer patients, just at the time that this was all starting, and we happened that day to see several older women with very small receptor-positive breast cancers, where, first of all, we would wonder that they might be at slightly higher risk for COVID because of their age.

And second, we felt that their breast cancers were such that one could safely provide an aromatase inhibitor endocrine therapy for a few months, and then do their surgery at a later date.

I was a pretty strong proponent of that, where it was medically appropriate, in order to try to allow patients to receive effective therapy, but also to minimize their need to present to the hospital setting at a time when we didn't know exactly what it was going to look like.

And also, to minimize their own personal exposure, to allow them to stay at home. I think it's gone well. I think that the doctors and the patients were very thoughtful about doing this together, that they focused on what was best for that patient, her cancer and her as an individual.

And so, I don't believe that any patient had the delay of therapy, or a change in schedule of therapy that threatened their long-term outcomes in any way, shape or form.

In fact, I can tell you those first couple of patients that I saw—it would have been on March 1, give or take—they're going to the operating room right now, having done fine, and now in a position where everybody feels very good about their ability to go through surgery with all the resources that they need and to promote their recovery.

So, is there going to be a way to learn from this? Or to have this approach adopted, maybe, for the future?

ND: I think that's an interesting question. I think you know that there are several groups that are trying to do COVID and cancer registries of one sort or another.

A lot of efforts going on right now across a variety of organizations, and I think it would be nice to see whether or not we could harmonize that in some fashion where we could learn about what you just talked about, both with regard to what does COVID mean to the cancer patient, but also whether there's anything that we can learn about their cancer treatment and its outcomes, because of the way it was modified during this pandemic.

I don't know if that'll be possible. It may be that we won't have sufficient number of patients, thankfully, to be able to learn from. But it's an interesting question Paul.

Neoadjuvant therapy, as you know, was already a mainstay for many types of cancers anyway, and so, I think that it's something that we were already pretty comfortable with in certain circumstances and this has probably helped us to feel even more comfort.

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We didn't talk much about basic science; how has it been affected? Labs have been locked down for months.

ND: I think that's been pretty tough for our basic scientists, because you're right. Our clinical care individuals are in the workplace every day, taking care of patients; our clinical and translational researchers saw a slowdown, as you and I talked about, because of the fact that we limited a pool of new patients to clinical trials, although we continued the treatment and follow-up with those who are on existing clinical trials.

For our basic scientists, from the beginning, there was the recognition that we would need to have baseline staffing of labs to make sure that lab function was maintained.

And so, the labs never totally—quote—shut down. What's happening now is that we're slowly but surely allowing our laboratory scientists to come back into the labs in a way that again maximizes their physical distancing and still allows them to continue their work and to be able hopefully to ramp up their work.

Many of them, as you know, have tried to do what they can in terms of research from home, and so a number of people have done their writing, have done a lot of their thinking. They've done their grant writing. But I think that everybody is very much looking forward to coming back into the labs in an ever-more populated fashion, but one that is protective of their health.

There's got to be something to learn from COVID and, of course, your institution is in a great position to learn from it.

ND: Yes. I think that also the people who worked pretty much full tilt were the number of labs who were already in some sort of virology research, as well as those who turned some of their activities towards COVID research. So those labs have operated at full tilt all during this time.

Is there anything we forgot to address?

ND: No, I think that the word "unprecedented" is pretty overused right now; isn't it?

But Paul, I feel like in the medical field since I've joined it, we had the period of HIV some decades ago, where we had so much uncertainty and lack of clarity about what was going on and how to proceed. And here we are, some decades later, with a lot of wonderful progress that has been made against HIV, and still some opportunities.

It seems to me that the swine flu a decade ago presented some of the same challenges. And there's no question that this has been incredibly complex for all of us, and I think we have come out, or we will come out of it stronger. We'll know more both in terms of the cancer care world, and also in the infectious disease world, and hopefully in the public health realm.

And this probably isn't the last time we'll be confronting this. And I am hopeful that we as a society are going to be more prepared than we were this time, and we'll be able to learn from all of our progress this time and have an even more effective response in the future.

With $306M for serology research, NCI mobilizes labs, academic centers, grantees, contractors, and SBIR

By Paul Goldberg

The NCI Board of Scientific Advisors has approved concepts for an RFA and an RFP to support research in serological testing.

The plan presented to BSA May 12 is intended to distribute $306 million in new money the institute received "to develop, validate, improve, and implement serological testing and associated technologies" under the Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139).

The bill, which gives NCI new funds for the serology effort, was signed on April 24. The institute has been working rapidly to engineer the complex research plan.

The org chart—a hub-and-spoke structure reminiscent of those NCI used to manage large collaborations during the peak Moonshot years—calls for engaging NCI constituencies, but also outreach beyond oncology, to explore collaborations with immunologists and microbiologists.

"I, for one, will be very surprised and very sad if we don't get some new cancer antibody work out of this, because it's just so natural," NCI Director Ned Sharpless said in a BSA discussion of the COVID-19 serology concepts.

The concepts incorporate insights from the institute's discussions with leadership of cancer centers, reflecting the notion that the COVID-19 pandemic has demonstrated that there has been a convergence of research in oncology, immunology, and infectious diseases (*The Cancer Letter*, April 24, 2020).

The institute's serology push comes at a time when basic science labs at cancer centers remain closed amid the coronavirus pandemic. Given how quickly the program is expected to move, those vying for grants would be wise to stay vigilant.

On May 14, NCI published a Request for Information, which would remain open for 10 days. "Leaving it open for only 10 days isn't optimal, but necessary in order to stay within the time frame that we were required to work," Dinah Singer, NCI Deputy Director for Scientific Strategy and Development and one of the principal architects of the program, said at the BSA presentation.

The RFA and RFP are expected next month.

NCI role in establishing standards for SARS-CoV-2 assays

In another development related to the COVID-19 pandemic, NCI's Frederick National Laboratory for Cancer Research plays a key role in establishing criteria for evaluation of serology tests, and FDA is now starting to use this template to evaluate tests that have been allowed on the market under FDA's Emergency Use Authorizations.

"Last Monday, news hit about the FDA's revised policy on antibody tests for commercial tests of manufacturers

related to the EUAs, and providing specific clinical performance expectations for those tests," Sharpless said at the BSA meeting.

"It's a little bit hard to understand exactly what the FDA is doing there, because they couch their announcement in the careful argot of the FDA. But since I'm fluent in FDA, let me translate. The announcement says the FDA is ending enforcement discretion for these mini serological tests currently on the market.

"Manufacturers of these devices have 10 days to come in with an application to the FDA, or an EUA—or else, meaning that they will presumably be asked to pull their test from the market. The reason they can now take this much stricter approach, is because they have a pretty good idea of which tests work and which ones don't.

"And they also have confidence that a few manufacturers are now producing testing capacity in large supply. And these tests are becoming more generally available. And therefore they can be more demanding that the manufacturers meet a certain quality standard. And the reason they can be more picky about the tests and the reason they have confidence in some of these tests is in part, in large part, because of the work being done at the National Cancer Institute.

"At Frederick National Lab, we've been using our long-standing expertise in serological testing, on behalf of the federal government, in concert with the CDC and BARDA and academic partners who've been crucial in this as well.

"And we've been doing performance testing for the FDA. And have provided high-quality, dispassionate evidence that serological testing can work, that there are high quality assays—and in particular, these assays can be made widely available for the American consumer. The FDA has made our results available on their website, and we published a new post on NCI's Cancer Currents blog, that delves a bit deeper into this topic overall. And I encourage you to read that post, if you're interested in this.

"Our work continues there on behalf of the FDA and other parts of the federal government. It's been a really successful and exciting partnership across the federal government to identify an important testing modality, a benefit to the public health. And I think we'll take on a large, important role in vaccine development as well, as that gets going."

RFA and RFP concepts in COVID-19 serology research

NCI COVID-19 Pandemic Urgent RFA Concept Request

In light of the emergence of SARS-CoV-2, and the urgent need to mitigate the pathogen's spread, in the most recent COVID-19 supplemental appropriation (Paycheck Protection Program and Health Care Enhancement Act (P.L. 116-139)), the National Cancer Institute (NCI) received $306 million to develop, validate, improve, and implement serological testing and associated technologies for the purposes specified under the Act.

Working in collaboration with the National Institute of Allergy and Infectious Disease (NIAID), NCI plans to use a significant portion of the funds to establish a collaborative network focused on characterizing the immune responses elicited by this infection, understanding the mechanisms driving serological, humoral and cellular immune responses, and determining the serological correlates with disease pathogenesis and protection against future infection.

Specifically, the NCI plans to establish a Serological Sciences Network by funding 4-8 Serological Sciences Centers of Excellence, using the U54 mechanism. In addition, plans are to fund 5-10 Serological Sciences projects using the UO1 mechanism. These Centers and projects will work collaboratively with the Frederick National Laboratory's Vaccine, Immunity and Cancer Program, thereby forming the Serological Sciences Network. A coordinating center for the Network is also planned.

Funding is estimated to be approximately $2 million TC per year per U54 Center for up to 5 years and $500K TC per year for UO1 projects with funding to begin by the end of FY 2020 or early in FY 2021.

To expedite the funding of the Centers of Excellence in Serological Sciences, plans are to issue the FOA by the end of June, or earlier if possible.

Also, using the emergency FOA authorization which allows great flexibility throughout the process, the application receipt date would be July 30. Primary peer review will be expedited by the NCI Division of Extramural Activities to ensure that second level review by the National Cancer Advisory Board occurs at its September 2020 scheduled meeting.

NCI COVID-19 Urgent RFP Concept

In light of the emergence of the novel coronavirus, SARS-CoV-2, and the urgent need to mitigate the pathogen's spread, the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Disease (NIAID) plan to establish a collaborative Network of Excellence to develop serological assays of high specificity and sensitivity for rapid deployment to test for SARS-CoV2 induced immune responses.

To address these critical gaps, we plan to work with key stakeholders—FDA, ac-

ademic and commercial partners with interest and expertise in immune assay development - to standardize, harmonize and expand capacity for serological antibody testing for SARS-CoV-2. NCI plans to establish Capacity Building Centers focused on development and expansion of serological testing capacity and practice. These Centers will serve as a critical component of a Serological Sciences Network in Response to SARS-CoV-2 Infection. Funding is estimated to be approximately $3 million TC per year for each Center. In addition to the Capacity Building Centers, the Network will include the FNL serology laboratory, the Serological Sciences Centers of Excellence and the Serological Sciences projects.

The Capacity Building Centers will address unmet needs in serological: 1) standardization, 2) assay development and 3) availability of SARS-CoV-2 testing to identify those who may have been exposed to the virus. Utilizing validated EUA SARS-CoV-2 serological assays with evidence of high specificity, sensitivity and reproducibility, will increase not only the national testing capacity, but also enable comparisons of data across different studies.

Therefore, it will facilitate an understanding of natural history of the infection, vaccine development and implementation of new vaccine candidates. This work will be conducted in partnership with the other components of the Serological Sciences Network to develop and make available reagents and standards to the serology community once generated and qualified.

Sharpless on serology research program:

A transcript of Sharpless's and Singer's presentations of the serology program follows:

Sharpless: It seems as though the word "serology" has suddenly, and understandably, become a household word in the United States. Congress appreciates the high-quality work that's been provided by the NCI on this topic, and also knows how important understanding the science related to serology is and will be, for our efforts against the coronavirus pandemic.

And Congress really seems to appreciate one clear fact, which is that the NCI—with our capabilities of Frederick National Lab and our world class expertise in virology, and our extensive networks for clinical research—that given these factors, the NCI is best positioned to lead this much-needed serology research effort, and they've asked us to do that.

In this regard, Congress has passed four supplemental spending packages, providing emergency funding from the government to support the economy and small businesses, as well as to preserve critical operations in places like hospitals.

The fourth supplement was called the Paycheck Protection Program and Health Care Enhancement Act, and passed last month and was signed into law on April 24. This supplemental funding bill includes a significant new appropriation of funds to the National Cancer Institute—specifically, $306 million to develop, validate, improve, and implement serological testing and associated technologies.

Working closely with the National Institute of Allergy and Infectious Diseases, we have begun planning how to use these funds for the public benefit, and that discussion has already led to a concept that Dinah will present later today. But let me make first two very important points about these new monies.

First, know your funding is distinct from our annual appropriation. We are not being asked by Congress to work on coronavirus serology research with monies intended for cancer research. But rather, we are being provided here with extra new money for serologic research.

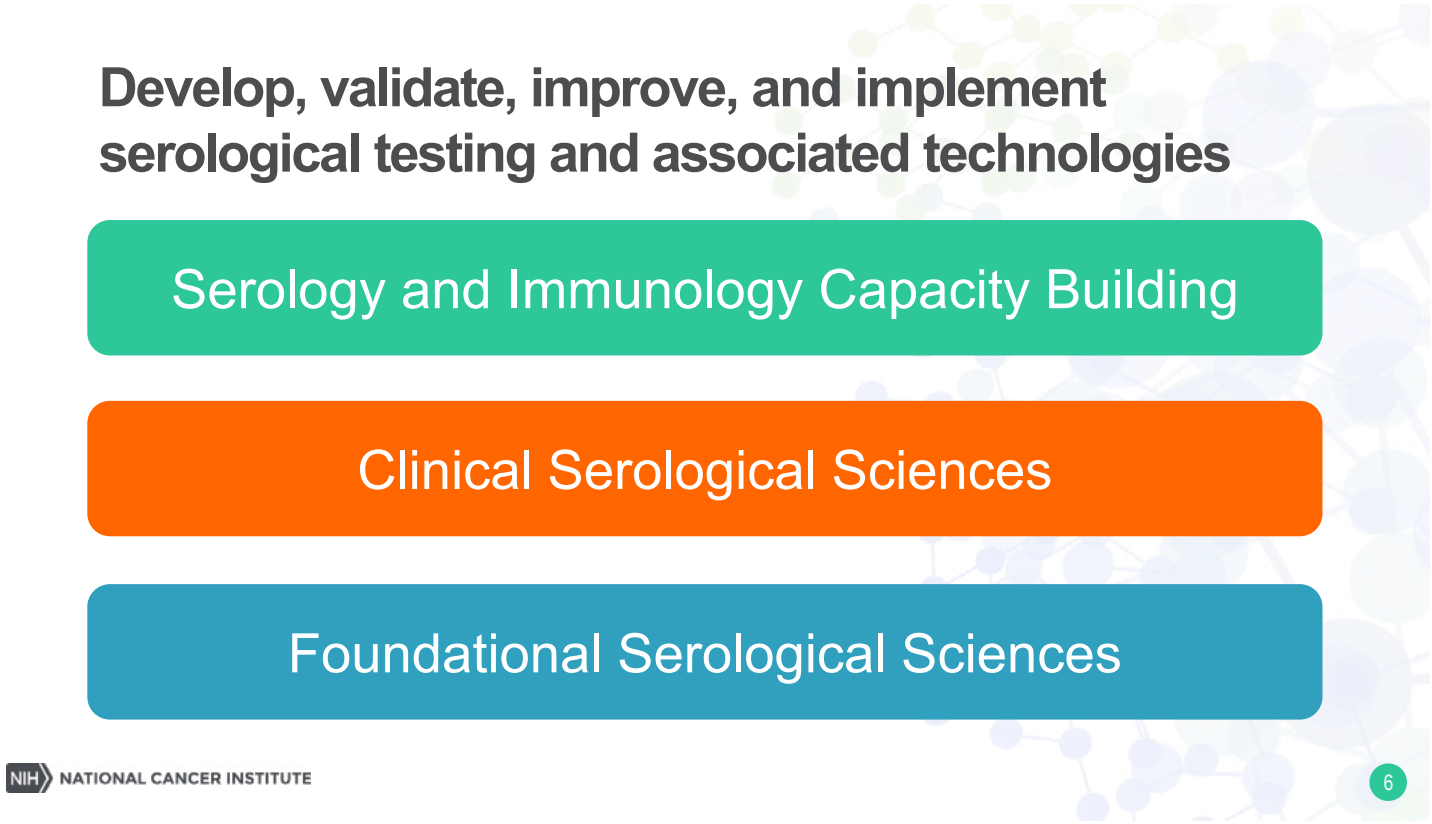
And second, the NCI does do cancer research and cancer is our clear priority. But it should be obvious to all here why progress against the pandemic will have important implications for cancer patients. So, better serology will help all patients, especially those with cancer. To be clear, this legislation is not specific to cancer.

We do not envision that this money will specifically fund serology research solely in patients with cancer. We will use it to just fund serology research. It is unusual, but it's not unheard of for the NCI to focus so strongly in an area that's not directly cancer research.

I think the last time this happened, to this extent, was probably in the 1980s, at the height of the AIDS crisis, when everyone remembers the great work the NCI did for that public health crisis. So, it is unusual for the NCI to be asked to take on something like this, but it is not unheard of. And these are very unusual times for the National Cancer Institute.

Therefore, we are eager to use these funds in the manner Congress intended with the help of NIAID to fund the best of serologic science conceivable, which will be a benefit for all Americans, including Americans with cancer.

Lastly, on the supplemental funding, we envisioned spending these monies in three buckets. The dollar amounts are still being worked out, and there's still a lot of planning to go here. But



we have been asked strongly by Congress and other parts of government to support the building of capacity, to help develop, largely, we think, academic institutions to be able to take on more serology testing, and also to be going to use those results for interesting types of clinical trials, like seroprotection studies and convalescent serum studies.

And that's the top bucket there. And then, also, we envision using some funding for clinical serological sciences, which are larger clinical trials. And things like the COVID and Cancer Consortium and the clinical trial Jim Doroshow spoke about last time, about doing COVID-19 outcomes in patients with cancer and NCORP network, and then, also, more classical serological surveys and seroprotection studies.

Then, the last bucket, the blue bucket is really funding for foundational serological sciences research. And that would create serological sciences and centers of excellence that would do more basic immunologic research related to serology and other parts of the immune system.

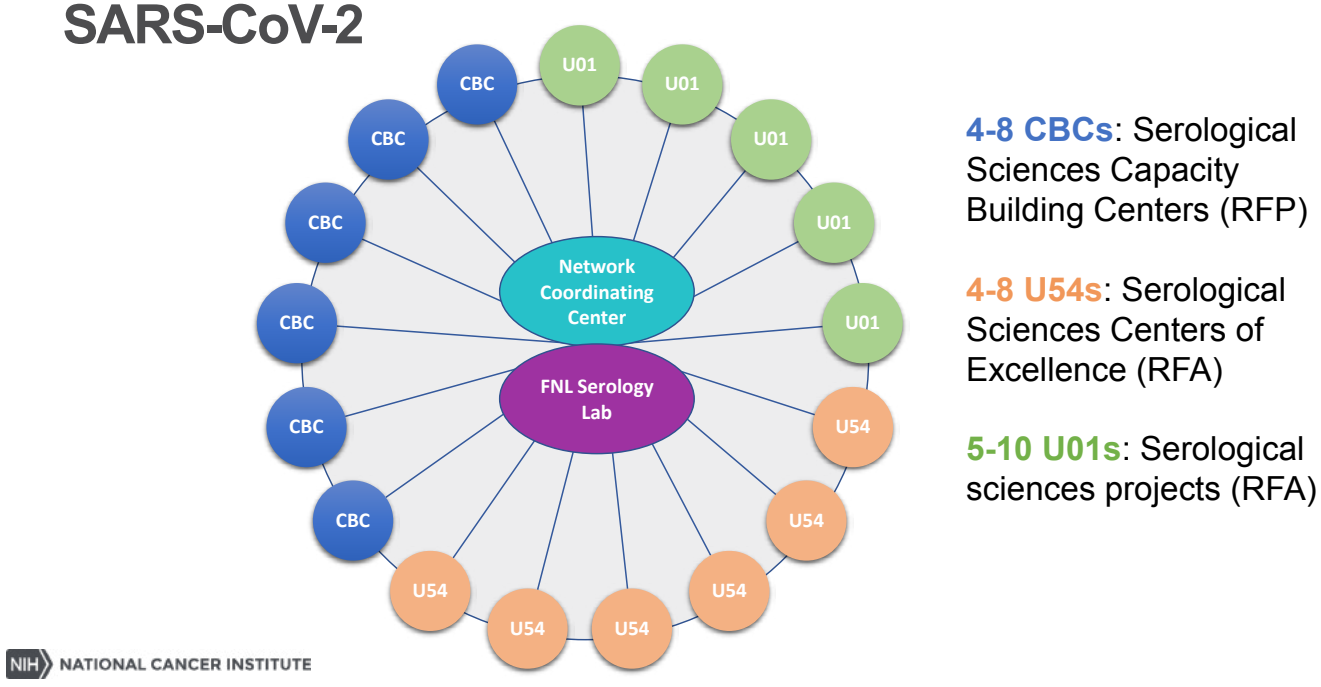
Singer on serology research program:

Singer: Ned started off the meeting by saying how almost the entire day was going to be focused on NCI's plans to advance cancer research. I'm going to end the day by transitioning to talking about COVID-19 and bring you up to date on what's happened in NCI's COVID-19 activities, since we met just last month.

In particular, I'm going to be focusing on our current plans for a Serological Sciences Network. Ned showed you this slide in his talk in which he mentioned that on April 24, Congress passed the Paycheck Protection Program and Health Care Enhancement Act.

In that bill, NCI was directed to develop, validate, improve, and implement serological testing and associated technologies. To that end, Congress appropriated an additional $306 million on top of NCI's FY 2020 budget.

I'll reemphasize the point that Ned made that these funds are separate from and do not affect the RPG pool or any of the concepts that you've heard about today. The goal of the bill is to urgently increase the serological testing capacity and our understanding of the immune response to the SARS-CoV-2 infection. As a result, we tried to move very quickly to respond, and intend to use an emergency authorization, to implement the overall plans that I'll be presenting to you today.



To rapidly support the expansion of serological testing capacity and expanded research on the effort from the effects of SARS-CoV-2 viral infection, we're proposing a Serological Sciences Network, which we've tried to illustrate in this slide, to give you an overall view of what we are proposing.

The network is intended to work collaboratively to expand national testing capacity as quickly as possible, to develop novel serological assays, and to enhance our understanding of the viral infection, and of the immune response to that viral infection.

The network, as we planned it, will consist of five components.

First, the HPV Serology Lab at the Frederick National Lab, The lab is going to focus on validating serological tests for the SARS-CoV-2.

Next will be Serological Capacity Building Centers that will either acquire or develop and validate serological tests and, importantly, implement the testing.

We're also planning Serological Centers of Excellence, as well as individual projects, which are going to pursue research programs in serological science.

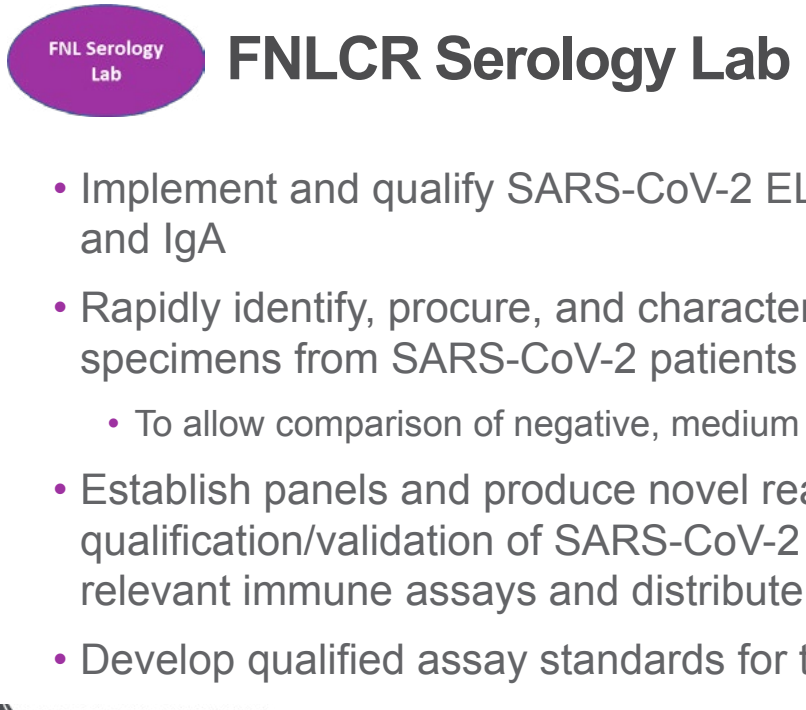
Finally, a Coordinating Center, which is the turquoise oval in the center, which will coordinate all of these activities.

The network, I should point out, is being developed in close collaboration with our colleagues and NIAID, which has participated in the development of the plan, to ensure that it complements and enhances the efforts that that institute is currently undertaking.

We plan to have them continue as collaborators in this network. In the remaining slides, I'm going to just briefly describe each of these components.

Starting with the FNL Serology Lab—that's going to be at the core of the network. At the last board meeting, Doug [Lowy] told you about the work that that lab is already doing, in partnership with FDA, to develop validation panels and validate serological testing and assays. [This] is an integral part of the network.

We expect the Serology Lab will continue to implement and qualify ELISA assays for IgM, IgG and we hope, IgA. It's going to acquire and characterize serum samples from patients and controls.
The patient samples will come from people at various stages of disease, with varying titers of the antibodies. The controls are going to include serum from individuals, which were acquired prior to last September, and from individuals known to have flu



and other coronaviruses, to be able to detect cross-reactivity, and also from HIV-positive individuals.

The samples that the lab acquires are going to be used to establish and, importantly, disseminate panels for validation by serological and other immune-relevant assays. Importantly, the lab is going to develop and disseminate assay standards for the entire community.

As effective as the Serology Lab has been, and we are certain, will continue to be, we also realize it can't meet the critical needs for testing by itself. So, the Capacity Building Centers that we're proposing are intended to extend the efforts of the Serology Lab and to collaborate with it.

The goals of these centers would be to develop and expand testing capacity across the country. To do this, the centers will be expected to either acquire already validated assays, or to develop and validate novel assays and submit them to the FDA for EUA approval. Using these set assays, the centers will be expected to deploy them to screen about 10,000 sera per week.

We're also going to require the centers to acquire convalescent serum for possible therapeutic use, and also to conduct surveillance trials in recovered patients.

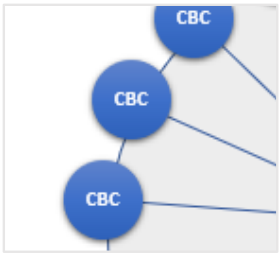
They'll also be able to pursue some limited studies in serological sciences, using the acquired serum.

We're proposing to support the centers through contracts to academic or private sector organizations. We anticipate that we'll be funding between four to eight contracts at about $3 million per year for up to four years, depending on the national needs for testing. We'd like to implement these contracts to be as flexible as possible to be able to respond to the current needs and focus their efforts appropriately.

The efforts of the Capacity Building Centers, which are contracts, and the Serology Lab at FNL, we would like to complement by a series of Serological Sciences Centers of Excellence. These centers really will be focused on basic questions of science, on understanding the mechanisms that drive the serological humoral and cellular immune responses to this virus, and to determine the serological correlates with disease, pathogenesis and protection against future infection.

So, the goals of the centers broadly writ would be to characterize the immune response to the virus and the mechanisms underlying that response, to determine the serological correlates with disease, pathogenesis, and protection, to address issues related to access and co-morbidities,

Serological Sciences Capacity Building Centers



RFP

4-8 contracts with academic and/or private sector through FNLCR

Up to $3M total costs per year, per site

Goals

- Develop and expand serological testing capacity and practice in the community
  - Implementation of serological standardization, assay development and availability of FDA-EUA authorized SARS-CoV-2 testing to identify those who may have been exposed to the virus.
  - Scale up acquired serological testing to provide increased national capacity by screening at least 10,000 patients per week with FDA-EUA authorized assays
- Acquire convalescent sera from recovered COVID-19 patients who are seropositive and conduct surveillance clinical trials in patients who have recovered from COVID-19 and are seropositive
- Pursue focused serological science

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5

as well as improved population-based models, outbreak and susceptibility.

I'll also note, relatively little is known about the immune response to SARS-CoV-2 in people with pre-cancers, those undergoing therapy, who have cancer, or cancer survivors.

We don't know whether the susceptibility to infection or disease progression is tumor type-specific. And so, for a lot of reasons, we're also planning to give preference to applications that include a component that is focused on the relationship of COVID and cancer.

We're planning to use a U54 centers mechanism for these Centers of Excellence, where each center would be expected to have two to three projects that address significant questions in the immune response to COVID-19, an administrative core, and the option of a technical core, with an anticipated budget of up to $2 million per year, for up to five years.

Included in that budget, we're going to have a set-aside of 10% to support collaborative projects across the entire network.

Again, to try to allow maximum flexibility in this very rapidly changing period, these are going to be phased awards, with an initial two years of funding, followed by the possibility of up to three years of funding, but that will give us an opportunity to pivot within these centers as necessary. We expect to make these awards by September of this year, with a very rapid turnaround.

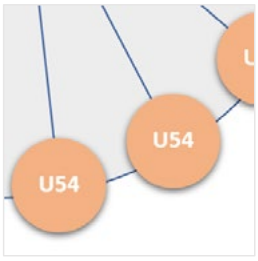
We recognize that while some groups are going to be in a position to quickly assemble a center with all of the components that we're asking for, we also know that there are going to be other groups who have meritorious proposals, but don't have the time or the resources to apply for a centers grant.

So, we'd like to also support individual projects whose goals would be parallel to those of the U54, but not require the organization of a center. These projects would be funded through the U01 mechanism, with budgets of up to about $500,000 per year for up to five years.

Like with the U54s, we put the 10% set-aside for collaborative projects, again, to work across the network. Again, these would be phased awards, to give us maximum flexibility to respond to the needs as they evolve. We would hope to fund between five and 10 of these.

What we would like to do is to publish both of the RFAs for the U54s and the U01s, using the emergency FOA authorization, and publish them in the beginning of June, with a response time

Serological Sciences Centers of Excellence (RFA)



4-8 U54 awards

Up to $2M total costs per year for up to 5 years

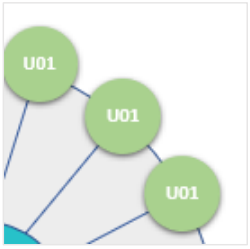
Goals

- Understand the mechanisms driving the serological, humoral and cellular immune responses to SARS-CoV-2 viral infection to inform the development of novel serological tests
- Determine the serological correlates with disease pathogenesis and protection against future infection
- Improve population-based models of outbreak and susceptibility through serology-focused studies
- Preference for cancer relevant component

Each Center will have 2-3 projects, administrative core and the possibility of technical core

Budget set-aside for collaborative projects proposed post-award

Serological sciences projects (RFA)



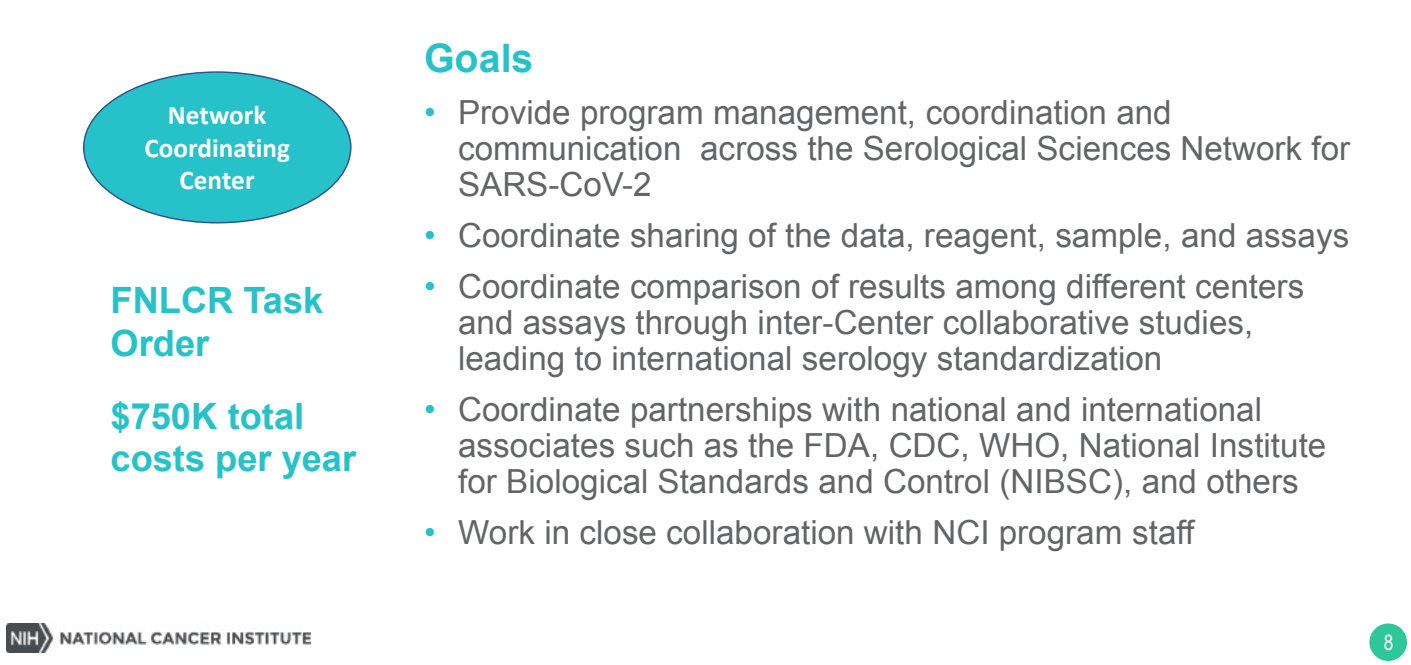
5-10 U01 awards

Up to $500K total costs per year, up to 5 years

Goals

- Understand the mechanisms driving the serological, humoral and cellular immune responses to SARS-CoV-2 viral infection to inform the development of novel serological tests
- Determine the serological correlates with disease pathogenesis and protection against future infection
- Improve population-based models of outbreak and susceptibility through serology-focused studies
- Preference for cancer relevant component

Budget set-aside for collaborative projects proposed post-award



of about one month to six weeks. To allow investigators a little bit more time to think about.preparing these applications, we're also planning to issue a notice of intent to publish as soon as possible—and as soon as the BSA concurs.

In everything I've laid out here, the fundamental assumption is that within the network structure there's going to be a close and ongoing interaction among all of the components.

We expect a rapid sharing of serum samples of resources and data and knowledge, and cross comparison of results, and a coordination of efforts.

The success of the network is going to really depend on our ability to effectively integrate across all of those components. Therefore, we'd also like to propose to establish a Coordinating Center ,at the Frederick National Lab, that would be responsible for program management, coordination and communication across the network, sharing the data, reagent, samples and assays, and, hopefully, also to facilitate partnerships with other organizations.

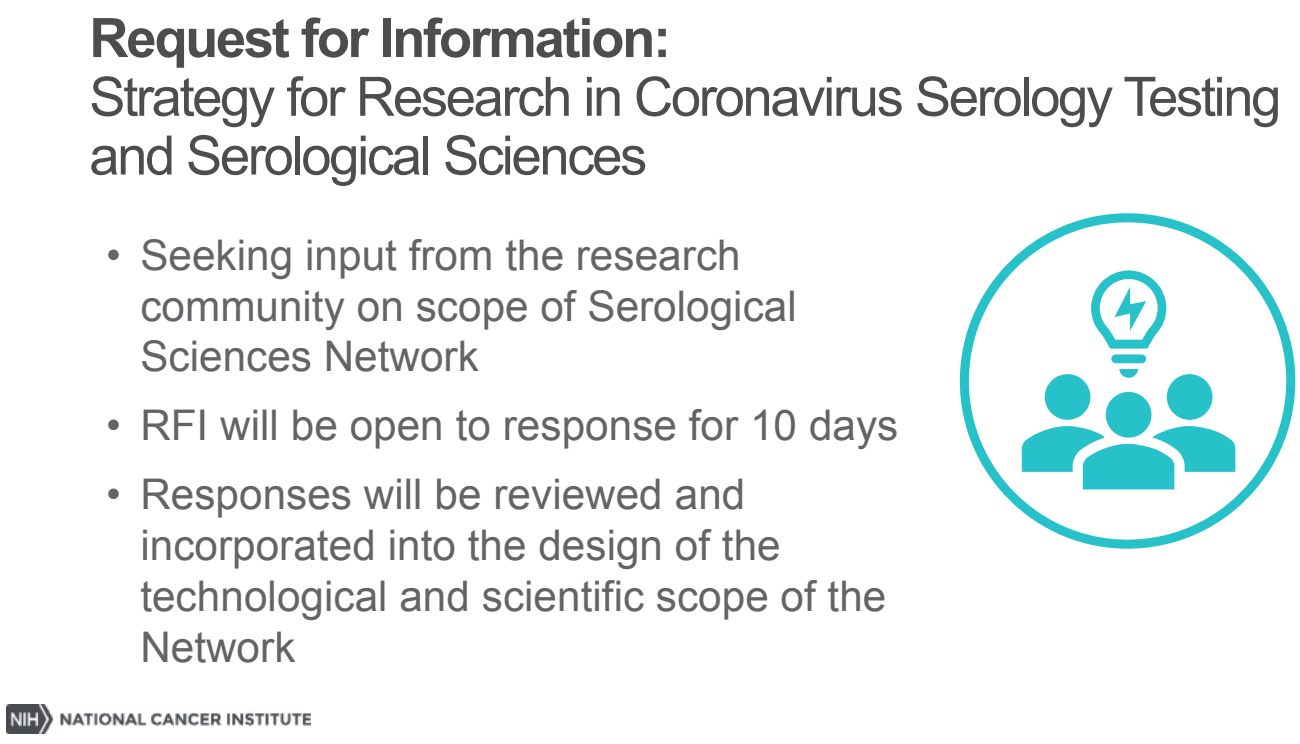
I should emphasize that in all of this, or we expect the Coordinating Center to work very closely with program staff. The Coordinating Center would be established through a task order with the Frederick National Lab. We haven't settled on an exact budget for that, we figure it will be around a 750K total costs per year. Again, with flexibility, depending on the needs at the time.

Planning for this network has moved very quickly, and we're fully aware that we need input from the broader research community on what are the critical scientific questions and the scope of science to be supported through this network.

Therefore, we're planning to publish a Request for Information. That RFI is going to be open for 10 days for responses, which would be reviewed by NCI program staff and incorporated into the design of the network. Leaving it open for only 10 days isn't optimal, but necessary in order to stay within the time frame that we were required to work.

To summarize, we're planning to establish an integrated network of cores and centers that will collaborate to advance our national capacity for serological testing as well as our understanding of the immune response to SARS-CoV-2. I'll remind you that the legislation that directed NCI to develop and implement this program was passed just two weeks ago.

We'll continue to flesh out the specifics as we hear feedback from you today and from the RFI, but given the very tight timeframe that we're



working in, we'd really like to ask for BSA concurrence to proceed with the two RFAs for the U54 centers and the U01 projects.

I'd like to close by saying how very grateful I am to the many people who've been working nonstop to make it possible for me to make this presentation today. I really sincerely thank the NCI staff listed here and our NIAID colleagues, all of whom worked tirelessly, participating in the discussions and planning that led to this network concept. With that, I'm happy to answer questions.

Dafna Bar-Sagi *[BSA chair, the Saul J. Farber Professor, Department of Biochemistry and Molecular Biology, executive vice president and vice dean for science, and chief scientific officer NYU Langone Health New York University School of Medicine]***:** Thank you so much, Dinah. We all understand how much effort is involved in putting those together with such a short turnaround time. Great, great work from you and the entire staff. Any questions that someone have here for Dina?

Maybe I will start, Dinah, by asking you... There was one thing that I didn't see there, but I'm not sure whether it was just an omission, not necessarily intentionally not there, which is, some interface with samples from clinical trials and how serological tests, or serology in general, is going to be potentially helpful for interpreting results from clinical trials. Is this something that you would be entertaining?

You talked a lot about the testing and things of this nature. I just wanted to get your thoughts about it, because I think there is potentially very important information there.

Singer: Right. This is something that we've actually been talking about, and talked about as early as this morning. I don't know, Ned, if you want to comment on that, on the extent to which the serology lab is going to be working to do that.

Sharpless: I think getting access to materials is a really important part of this. The serology lab at Frederick needs material. In fact, many of you or your cancer center directors, I contacted about sharing samples, and I really appreciate the support we've gotten from the cancer centers. It's been very, very helpful, but you know, one of the parts of the Capacity Building Centers is to do research in convalescent serum. That also has the happy byproduct of producing large volume samples that we could use for, say, creating performance panels that we could distribute to labs across the country.

Doug [Lowy, NCI principal deputy director], if he's on, may also have thoughts on this. Doug has been

largely directing the Frederick National Lab serology efforts and has thought deeply about the needs, the issues and its role in coordinating among the various mechanisms Dinah described. In any event, the faster networks would be the Capacity Building Centers, that would be a quicker mechanism through contracts, and they should be supplying samples. We also expect they will do some limited research related to serum protection and serum surveillance, but those more researchy questions will take longer, with the awarding of the RFA.

Keith T. Flaherty *[director for clinical research, Massachusetts General Hospital Cancer Center]***:** So, Dinah, this is an exceptional start, and I can only applaud the effort with which it has been put together. I wonder if it's outside of the scope of this mechanism... I'm wondering what the handoff is, to Ned's point, if I'm going to go to convalescent plasma research, but also neutralizing antibody therapeutic development. There's a very natural pass-off, as you're well aware, between those antibody responses that are truly neutralizing, and how that would inform a convalescent plasma or engineering of off-the-shelf antibody therapeutics. And so, if that's outside the domain, that's totally understandable. I'm wondering what the handshake is between this program and those efforts. And if not in year one, then when.

Singer: That question, along with the question of the antibody dependent enhancement ones that could be components of the U54. Although I think for the neutralizing antibody, the challenge will be to get either viral particles or viruses that could be used to figure out whether they're neutralizing antibodies, I think we still need to discuss it. It's sort of borderline. Clearly, it's an important issue.

Sharpless: I would say, we are well integrated with a therapeutics push related to coronavirus. That's this program called ACTIV that Francis Collins is directing. We do envision neutralization assays as being part of this proposal. So, there is a BSL-3 facility at Frederick National Lab, the neutralization assays, and we also fully expect some of the fundees that would come in on either the contract mechanism or the RFA will have neutralization assay capacity as well.

And then we're hoping people invent sort of more high throughput screening approaches that don't require a BSL-3 facility. That would be a research question we would be eager to fund. We think what we would learn from that would then be handed off to the monoclonal antibody people who make therapeutics. But the actual trial, just the passive trial of convalescent serum could happen within some of these centers, for example.

David A. Tuveson *[The Roy J. Zuckerberg Professor, director of the Cancer Center, Cold Spring Harbor Laboratory]***:** It seems like this topic is one that would be perfect also for a cancer center addendum. Probably half of all cancer centers think or work on this topic, I guess. Maybe more. And you could seed-fund it, and then just pick your winners from the 70 cancer centers to do a bigger project in years two [on], you're trying to phase it. Let everyone run, and modest amount of investment, just see who actually can deliver in a year, and then you have your natural partners to move forward.

> I, for one, will be very surprised and very sad if we don't get some new cancer antibody work out of this, because it's just so natural.
>
> *– Ned Sharpless*

> To rapidly support the expansion of serological testing capacity and expanded research on the effort from the effects of SARS-CoV-2 viral infection, we're proposing a Serological Sciences Network.
>
> *– Dinah Singer*

Singer: Yes, Dave, as you know, we did go out to the cancer centers, with a call for ideas on COVID-19. As a result of that, we are funding a collaboration on serology that will examine some of these questions. But I think for what we're looking for in terms of serological sciences, that we really want to have a broader sweep of what's out there in the community, to bring in the virologists and the immunologist who may not necessarily be in cancer centers now.

Robert D. Schreiber *[The Andrew M. and Jane M. Bursky Distinguished Professor Director, Center for Human Immunology and Immunotherapy Programs, Department of Pathology and Immunology, Washington University School of Medicine]***:** Dinah, I also want to congratulate you there. That was just spectacular. And in such a short period of time, maybe you can come over and help me write my grant.

The other thing that is just tailor-made for us, as the NCI, is the fact that we collect longitudinal samples on our patients as we monitor them. And so, there's probably goldmine sitting there, in the old ones, as well as the newer samples from patients that have gone through some of these infections, perhaps.

Especially, we don't know how many have been walking around with the infection anyway. So, I do think it's a great idea.

One thing against Dave's idea of cancer center is, this is a perfect opportunity for us as cancer immunologists, cancer biologists, to interact with our colleagues who are the microbiologists, and many of our institutions have these parallel efforts going between the different groups. This could be the thing that brings everybody together. So, I really think this is a great idea.

Sharpless: Bob, let me say, I, for one, will be very surprised and very sad if we don't get some new cancer antibody work out of this, because it's just so natural, and I agree exactly with what you said.

Cheryl L. Willman *[The Maurice and Marguerite Liberman Distinguished Endowed Chair in Cancer Research, UNM Distinguished Professor of Pathology, UNM School of Medicine Director and CEO, University of New Mexico Comprehensive Cancer Center]***:** I really agree with you, Ned. And Bob, I agree with your comments too. Just a quick question about the mechanism. First of all, Dinah, fantastic as always, and obviously you haven't been sleeping much. That's a lot of work since our call a few weeks ago. But does the funding mechanism allow for consortia between academic entities, immunologists, microbiologists, pathologists, and large reference laboratory systems, which would likely hold gazillions of samples?

Singer: What I didn't mention, and I should have, was that we would hope that some of the U54 centers will actually have private sector components, because I think that will enrich it and will increase the ability to get enough samples. We're also going to look into the possibility of having SBIR grants to bring in some small companies. So, we're exploring all those options. I just didn't have time to go through all of them in a short presentation.

Willman: In the West, we have large academic-affiliated reference labs that cover pretty vast regions. So that would be really useful, if that was allowed.

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NCI DIRECTOR'S REPORT

Sharpless: COVID-19 threatens to reverse long-running trend of decreasing cancer mortality

By Matthew Bin Han Ong

Delayed cancer diagnoses, deferred care, and postponed surgeries amid the COVID-19 pandemic will adversely impact cancer outcomes, which may show up as an increase in cancer mortality in the next few years, said NCI Director Ned Sharpless.

"I've been looking at the statistics about decreases in screening and deferred care, and I am getting very worried about this issue," Sharpless said May 12 in a virtual meeting of NCI's Board of Scientific Advisors. "The data regarding delayed diagnosis and delayed therapy are very clear from cancer research over the decades."

An uptick in overall cancer mortality trends will likely be visible in the institute's Annual Report to the Nation—jointly issued with the Centers for Disease Control and Prevention, the North American Association of Central Cancer Registries, and the American Cancer Society—in the coming years.

"I'm becoming worried that, because of the pandemic, that in 2021 or 2022 or 2023, we will have the first Annual Report to the Nation since 1993 that shows an increase in cancer mortality," Sharpless said. "And I know exactly what the statistics will mean for patients. I know that that represents more cancer suffering and more bad outcomes, and more deaths."

In related developments:

- Health systems and academic cancer centers are cutting expenses to make up for operational shortfalls resulting from the pandemic—laying off employees, furloughing staff, and cutting salaries and benefits (*The Cancer Letter*, May 8, 2020).
- Community oncology practices are experiencing a significant decrease in patient volume, as weekly visits dropped by nearly 40%, while cancellations and no-shows have nearly doubled (*The Cancer Letter*, May 1, 2020).

"I wanted to stress that we know all too well that the extramural community, as is the case in nearly every sector of the nation, things are really hurting out there," Sharpless said at the BSA meeting. "And regardless of how the back-to-business plan does roll out at various institutions, it will really take some time to bounce back.

"Delayed diagnosis and deferred care leads to worse outcomes for patients with cancer. The things we do to prevent cancer and to diagnose cancer and to treat cancer well, they work, and they can't be put off indefinitely.

"And if we do, we will lose ground, and we will give up hard-won progress."

An excerpt of Sharpless's remarks May 12 follows:

Today I would really like to keep most of the focus on regular NCI business. I'm really eager, in fact, to be talking about cancer research and concepts the NCI would like to release. And these will spur interest in cancer research and priority areas. But there is a pandemic going on and we do have some coronavirus items to address as well.

We just had a board meeting on this topic almost entirely devoted to COVID-19. We don't have to do a whole lot on that topic today. But I will just use a few slides to summarize that presentation from the joint board meeting, and remind you of how the NCI has been taking a critical role in an unprecedented response to this pandemic. Also, since things are moving so fast around here right now, there actually have been a few significant developments in the coronavirus space—since even the joint board meeting just a few weeks ago. I'll briefly summarize that news as well.

In particular, related to those developments, including a new and correct congressional appropriation. There are some COVID items that we do need, and Dinah Singer will direct that discussion at the end of today's meeting.

But let me start out our short COVID discussion by repeating a statement I made last month at the joint board meeting, which is that the primary focus of the National Cancer Institute is, and always will be cancer research and cancer care. That's a message I've been delivering in just about every presentation I've given, in every email and blog post and other materials I've written during this pandemic response.

And it's one that Dinah Singer spoke to at her virtual presentation at AACR two weeks ago on April 28. If you haven't seen this, I encourage you to check it out. Dinah also wrote a great post for our Bottom Line blog on the topic, which includes a link to the presentation.

So, this slide summarizes why the NCI is important to the pandemic response. It shows the disproportionate impact of COVID-19 on cancer patients, and patients with cancer who've survived cancer. Additionally, as I illustrated at the joint board meeting, the NCI has unique research expertise and capacity related to Frederick National Lab and our great extramural networks.

Therefore, we have to be involved in the pandemic response. And then, lastly, I think given the nature of this crisis, it has had a tremendous effect on public health. The NCI has a moral obligation to work in this area.

Impact of COVID-19 on patient outcomes

I want to call your attention though to the decrease in care delivery to cancer patients related to the coronavirus pandemic. And this is something, frankly, I've been worrying about a lot lately, and I've been hearing from a lot of you and other extramural leaders.

I've been looking at the statistics about decreases in screening and deferred care, and I am getting very worried about this issue. The data regarding delayed diagnosis and delayed therapy are very clear from cancer research over the decades.

Delayed diagnosis and deferred care leads to worse outcomes for patients with cancer. The things we do to prevent cancer and to diagnose cancer and to treat cancer well, they work, and they can't be put off indefinitely.

And if we do, we will lose ground, and we will give up hard-won progress.

And here's a very specific fear I have, in this regard. Every spring, the National Cancer Institute, with the CDC and the ACS and NAACCR, puts out our Annual Report to the Nation on our progress against cancer.

Thanks to advances in screening and prevention and treatment and survivorship, that document has become an annual feel-good story for the NCI. Every year I've been here, the report has been good news.

It's been a couple of percent drops in cancer mortality each year, and that's been going on, in fact, for decades. But with all this deferred and delayed care and postponed surgeries and later, reduced chemotherapy, and canceled appointments for mammography or a Pap smear or colonoscopy, this is going to have an impact on cancer outcomes—an impact that I think we'll see play out over years to come.

So, I'm becoming worried that, because of the pandemic, that in 2021 or 2022 or 2023, we will have the first Annual Report to the Nation since 1993 that shows an increase in cancer mortality. And I know exactly what the statistics will mean for patients. I know that that represents more cancer suffering and more bad outcomes, and more deaths. And let's all agree, we don't want that to happen, and we won't let that happen. I know COVID has caused many changes to how we care for patients.

And we have a legitimate need to be careful during the pandemic in order to protect the public health. But we need to get back to work of caring for our patients. We need our hospitals and our clinics and our infusion centers to start doing what they do best, which is care for our patients who need this. Of course, we have to do this in a manner that is smart, that

NCI COVID-19 Funding Opportunities

www.cancer.gov/coronavirus-researchers

NOT-CA-20-043	Availability of Competitive Revision SBIR/STTR Supplements on Coronavirus Disease 2019 (COVID-19)	Expires 6/26/20
NOT-CA-20-042	Availability of Urgent Competitive Revision and Administrative Supplements on Coronavirus Disease 2019 (COVID-19)	Expires 6/26/20
NOT-CA-20-048	Participation in PA-18-935 "Urgent Competitive Revision to Existing NIH Grants and Cooperative Agreements (Urgent Supplement - Clinical Trial Optional)"	Expires 1/25/22
NOT-CA-20-054	Contributing to the Global COVID-19 Crisis Response by Allowing Some NCI-supported Projects to be Redirected to COVID-19-related Research During the Crisis	

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is careful, that protects patients and staff alike from the coronavirus.

But we need to get back to work. The cost of deferred cancer care will be significant. Neglecting cancer will produce a negative impact on the public health, and one that may trouble our patients for years to come. I plan on talking a lot more about this in the coming weeks. And I haven't even spoken about the debilitating impact on cancer science, by having these labs closed and postponed—tremendous impact as well.

Just to remind you something that Dinah spoke about, and that is on the blog post as well, is the number of NCI COVID-19 funding opportunities that are somewhat new and recently posted, and still open. This is summarized here. I won't spend a lot of time on them, other than to say we're taking both administrative supplements and competitive revisions.

We also had a good discussion at the joint board meeting about allowing a change of scope of certain grants, and we have received a small number of requests to do that, and are working through that. But I think that we are still considering administrative supplements and competitive revisions, and we will be making funding decisions related to these very soon.

Regular NCI business

Now with the COVID part of the discussion behind us, at least for the next few hours, let's return to regular NCI business. Frankly, I am really excited, as I said, to be able to spend most of our time today on advancing cancer research and cancer science. Getting these concepts that the BSA will see today is really a lot of work getting these things together.

I think you will be impressed or you'll be really shocked by how much the NCI has been able to get done during a period of complete telework. I think this is a testament to the really extreme efforts of the trained professionals in the NCI to get this work done, no matter what the situation.

As always, it's good to mention where we are in the appropriations' outlook. There's really not a lot to report. At this stage right now, much of Congress's focus has been on supplemental funding related to the coronavirus pandemic, and the work on the 2021 budget has been a little a bit behind that.

But Congress has been busy and has already passed these supplemental fundings, and as is widely reported, is working on a fifth emergency appropriations bill. At the same time, appropriators are starting to take up their work on the regular FY21 appropriations bill, and I suspect we'll be

hearing more about that soon. So, stay tuned.

Some really wonderful news during the joint board meeting last month, I was able to share some news about Dan Gallahan assuming the permanent role as director of NCI's Division of Cancer Biology. And today I'm very pleased to share that Phil Castle will soon take the helm at NCI's Division of Cancer Prevention.

Those of you who know, Phil is replacing Barry Kramer in this role, but DCP has been led for over a year now by Debbie Winn, serving in an acting capacity. Debbie has done a spectacular job in this role—very hard to be an acting in this role—and I want to thank her for taking this on for the benefit of the NCI. I would like a virtual round of applause for Debbie. Yay Debbie!

Phil is joining us from Albert Einstein College of Medicine in New York, where he served as professor in the Department of Epidemiology and Population Health. He was also the executive director and co-founder of the Global Coalition Against Cervical Cancer.

Phil is no stranger to the NCI. He was a senior tenured investigator and tenure-track investigator in the Division of Cancer Epidemiology and Genetics from 2003 to 2011. While at NCI, he was the lead investigator on several epidemiologic studies, including the Mississippi Delta project, the HPV Persistence and Progression Cohort, and the guidelines cohort and cancer at Kaiser Permanente, Northern California, and the Anal Cancer Screening Study.

I'm thrilled Phil is joining the NCI in this key role, and I'm really excited to have him join and provide vision for the DCP mission regarding cancer prevention, screening and early detection. So, welcome, Phil.

CCDI; CAR T

I'd like to give a brief update on the Childhood Cancer Data Initiative. We are anxiously anticipating an upcoming working group report for the joint board meeting in June. As some of you know, Jaime Guidry Auvil kicked off the BSA working group on March 27 and provided an overview of its activities, as well as its relationship with ongoing NCI pediatric initiatives.

While we await the report, it's important to note that we are using the FY20 CCDI funding to support foundational aspects of childhood cancer research and data related to those efforts, from which to build CCDI in years FY21 to FY30. So, we are working on this at a good speed with the already appropriated funds and are eagerly awaiting more advice from the working group on the shape of this initiative.

I'll just mention that the cell-based therapy and vector production efforts at Frederick National Lab are proceeding apace. As I mentioned though at the joint board meeting, we have actually had our first trial, using a CAR T-cells prepared at Frederick, open. The virus production facility will soon come online. And we'll evaluate potential viral production projects proposed by the extramural community.

So, we envision Frederick will have capacity to make viral vectors as needed for extramural searchers. This will include both developmental and clinical trial proposals.

Needless to say, I'm thrilled with the progress and ramping up of this facility. In fact, this summer we will begin accepting applications. We've dedicated space to produce viral projects, so those of you who will need help producing virus for, say, a CAR T trial or some other related efforts, stay tuned for the announcement about the acceptance of applications.

I think many on this board are aware of the interesting pattern of prostate cancer statistics over the last few years, regarding incidence and mortality, with changing recommendations related to PSA screening. The NCI has been following this area carefully. We had a very large internal NCI meeting, spanning the gamut from basic researchers to clinical trialists, to population health science researchers, to discuss where our prostate cancer research portfolio ought to be, in light of these changing statistics, and we decided a good way to go forward would be to have a lot of advice from the extramural community.

And for that reason, we're working towards a workshop next spring to bring in extramural perspective to convene the best folks to try and understand where the NCI should be focusing its research mission related to prostate cancer now. Bill Dahut and others are leading this effort at the NCI.

Research updates

I thought I'd mentioned a few quick research updates that we found exciting. I always like to try and at least note some of the great science that NCI has done, either intramurally, or funded extramurally, and always try and bring up a few recent items.

This is work from the DeNardo lab at Washington University, published recently in Cancer Cell, related to dendritic cells in tumor immunotherapy. It proposes that the number of

dendritic cells in a tumor may explain why immunotherapy works for some cancers, but not others, and work in mice—boosting dendritic cell number triggered an immune response in pancreatic cancer, which has been traditionally difficult in terms of immunotherapy. So exciting research proposals to follow.

Work from the Richard Kitsis lab at Albert Einstein tries to better understand the relationship between daunorubicin and doxorubicin and cardiomyopathy, and developed an experimental drug to prevent this chemotherapy-induced heart toxicity. It does so without interfering with the chemotherapy's therapeutic ability to kill cancer cells in mice. So, interesting work for a long-standing problem related to the use of these agents at extended doses for patients.

In some microbiome research from Marcel van den Brink at Memorial Sloan Kettering in people with blood, hematologic malignancies, the health of their gut microbiome appears to affect the risk of dying after receiving allogeneic stem cell transplant, according to this NCI-funded study, published in the New England Journal of Medicine that got tremendous attention in the press. An exciting development to help improve outcomes for patients who need allogeneic transplantation.

Finally, in addition to our grantee blog, Bottom Line, which is now widely read, and our research enterprise blog, which is Cancer Currents, I also also want to remind everyone about an important resource on our cancer.gov site. This site is specifically designed for researchers with questions. And it is updated frequently with new information as it becomes available.

To date, we've tracked over 20,000 visits to these blogs and other researcher-focused web content. I wanted to stress that we know all too well that the extramural community, as is the case in nearly every sector of the nation, things are really hurting out there.

And regardless of how the back-to-business plan does roll out at various institutions, it will really take some time to bounce back. We know, for instance, that universities and institutions have begun furloughing staff and laying off researchers. We know clinical trials accrual is down, especially for non-treatment trials.

All of this will slow the pace of research, but beyond that and equally important, the public health crisis represents a real hardship for our families, our communities, and patients with cancer. NCI has not lost sight of this. We'll do all we can help to recover from these significant setbacks.

NCI BSA approves 11 new and reissue concepts, defers one

By Alexandria Carolan

The NCI Board of Scientific Advisors has approved 11 new and reissue concepts—Request for Applications, Cooperative Agreement, Request for Proposals, and Program Announcement with special receipt, referral and review.

The BSA voted to defer one concept, "Low-dose CT Lung Cancer Screening Image and Data Resource," to a future meeting.

The presentations are available here.

The following concepts were presented at the May 12 meeting of the BSA.

Glioblastoma Therapeutics Network (RFA): Approved

The purpose of this RFA is to improve treatment of glioblastoma in adults by developing novel effective agents and testing them in the clinic.

The project will receive funding through the U19 grant.

The anticipated budget includes up to five U19 awards, with a 5-year project period. The budget for each award is $1.1 million, with $500,000 for one network coordination center. The budget also includes $6 million, set aside for the first year of the RFA. The total cost over 5 years is $30 million.

The RFA, submitted by the Division of Cancer Treatment and Diagnosis, will establish a national infrastructure to enhance support for discovery and development of glioblastoma therapies, with five areas of research capability:

1. Preclinical qualification of new agents
2. Clinical trials driven by molecular pharmacodynamics and imaging
3. Immunotherapy
4. Improving radiation therapy efficacy
5. Improving the quality of life of patients

Key guidelines for the funding opportunity announcement include:

- Focus on late Drug Discovery through phase I clinical studies
- Possible agents include small molecules, biologics, and/or radiotherapy
- Testing in animal models that closely mimic human adult glioblastoma
  - Extensive model development is outside scope
  - Models should include assessment of passage through BBB and ideally allow for repeated testing of tumors over the course of treatment

- Aim for early-phase proof-of-mechanism clinical trials that include PK, PD and imaging; and include multiple clinical centers
    - Phase II and beyond is outside of scope

The implementation plan includes a national GBM Therapeutics Network (GTN) of crosscutting teams using the U19 mechanism. Each team would be capable of driving novel agents from the development stage through IND studies and into pilot clinical studies in humans, or; repurposing and testing approved agents and/or combinations (of new or repurposed agents, with targeted agents, immunotherapy, and/or standard-of-care—temozolomide and radiation—that appear to be efficacious in GBM). Teams would also conduct PD-driven clinical trials.

Measures of success for the program include:

- Success of GTN at the end of a 5-year grant term must include trans-U19 clinical testing of one or more novel or repurposed agents. Agents may come from within the GTN or from outside (via the steering committee).

Other successful outcomes may include:

- Promotion of one or more agents to IND stage, with plans for clinical testing after 5-year grant period
- Preclinical development of one or more novel agents for GBM based on steering committee criteria for advancement to clinic; plans for IND submission after 5-year grant period
- Preclinical development of combinations of novel agent(s) and standard-of-care therapy for GBM

Tobacco Cessation, HIV and Comorbidities in Low- and Middle-Income Countries (RFA): Approved

The goal of this RFA is to bring together transdisciplinary teams of investigators to adapt
interventions developed and tested in challenging or low-resource populations, and to test their robustness among people living with HIV/AIDS (PLWH) in low- and middle-income countries (LMICs).

This project is a global companion RFA to the domestic RFA—Improving Smoking Cessation Interventions among People Living with HIV (RFA-CA-18-027/28).

NCI's Division of Cancer Control and Population Sciences submitted the RFA. The RFA will use appropriated NIH AIDS funds, and will seek co-funding and participation from the National Institute on Drug Abuse, National Institute on Minority Health and Health Disparities, and the Fogarty International Center.

The RFA anticipates funding through four or more R01/U01 grants. The estimated total budget is $12.5 million, of which $2.5 million will be set aside for year one.

The project will also build on previous NCI/NIDA PARs (PAR-18-22/23, R01/R21) "Tobacco Use and HIV in Low and Middle Income Countries."

Research questions and goals include:

- What types of tobacco cessation interventions are most effective in PLWH in low-resource settings in LMICs to achieve improved tobacco abstinence as well as disease treatment outcomes?
- Test the robustness and translatability of interventions from challenging or low-resource settings (e.g. substance abuse or mental health comorbidities) to challenging settings of PLWH in LMICs.
- Adapt innovative but tested strategies with potential for scale-up for PLWH in LMICs, including use of community health services, mobile technology, and behavioral counseling.
- Identify and address barriers to integrating tobacco control interventions into existing health care systems and the HIV prevention and treatment context in LMICs.
- Understand the social and behavioral context of tobacco use in PLWH in LMICs influence tobacco use behavior and cessation outcomes.

Reviewers will be asked to consider:

- Prior evidence for the proposed intervention in a challenging population and/or low-resource setting (in the U.S. or LMIC),
- Relevance of the expected findings for the LMIC setting,
- Potential for the intervention to be scaled up in the LMIC setting; and
- Strength of the research environment in both U.S. and LMIC institutions, as well as evidence of prior successful collaboration.

Also, studies should be designed for dissemination (e.g., feasibility/acceptability of the intervention for PLWH and providers) and suitable for the intended context.

Aging, Cancer-Initiating Cells, and Cancer Development (RFA): Approved

The purpose of this joint NCI-National Institute on Aging concept is to expand our limited understanding of age-driven mechanistic factors and cellular interactions that contribute to cancer initiation in aged cells, establish standards for assays, and develop new or improved aging models to study cancer initiation.

The RFA was submitted by NCI's Division of Cancer Biology.

The project will be funded through the U01 grant. Applications for the U01 grant will be solicited over two receipt dates. Awardees and NCI staff will form a consortium to develop best practices, novel approaches and model systems.

The estimated budget is $10 million for the total project period, with $2 million per year that includes three to four applications. The NIA will fund an additional 5-6 U01 projects, and will set aside $3 million for year one. The estimated total cost for NIA over the project period is $15 million.

Up to five years of funding can be requested, and each application must include a model of aging and cancer. Review will be conducted by an NCI special emphasis panel to assure both aging and cancer expertise

The project will use paired funds from NCI and NIA.

The project will also support collaborative studies between cancer and aging researchers that address limited understanding of mechanistic factors and cellular interactions during aging, which contribute to cancer initiation.

Portfolio Analysis

A recent portfolio analysis (from FY2010-FY2020) using "cancer," and "aging" as keywords identified 251 awarded R01 grants (NCI -134, NIA -117). The majority of NCI grants are focused on investigating mutations, DNA damage and inflammation while NIA grants are more focused on longevity, homeostasis, senescence, and metabolism.

Only a small portion (11 NCI, 4 NIA) is relevant to this proposal and focused on mechanisms of aging and cancer development. There are no funding opportunity announcements, supporting grants or supplements for this research focus right now.

Examples of research areas:

- Identifying novel age-related genes and proteins, epigenetic modifications and/or metabolomic changes that promote cancer initiation,
- Identifying roles of senescence and novel age-related nonautonomous factors including those of the niche and inflammaging that regulate cancer initiation,
- Understanding how age-related factors are interrelated; and
- Developing new or unique age-related cancer models to study aging and their niches that lead to oncogenesis. Studies may include cell models developed from aging tissues such as organoids, induced pluripotent stem cells from aging tissues, and others.

SBIR Contract Topics (RFP): Approved

The purpose of the SBIR Contract Topics RFP is to provide 17 small business innovation research contract topics with funding in FY21. These will be awarded through SBIR grants.

There was no associated budget for this concept, which was submitted by the Office of the Director.

The SBIR and the Small Business Technology Transfer programs support commercially-directed research and small businesses, with the end goal of delivering a topic to the marketplace. In FY19, NCI allocated $175 million for SBIR and for these two programs. Most of these funds are used for investigator-initiated grants.

NCI develops these topics once per calendar year, which are approved by NCI leadership, the Cancer Moonshot program leadership, and BSA. NCI is the biggest user of SBIR contracts at NIH.

The topics presented were originally 22 ideas submitted by NCI staff, reflecting NCI technology priority areas including Cancer Moonshot topics, areas with commercial potential, and portfolio gaps. The concepts were presented to and discussed by two NCI internal technology advisory groups covering key NCI mission areas: Therapeutics, diagnostics, radiation therapy, medical devices, information technology, and behavioral products.

These two staff committees vetted the concepts for significance, innovation, and commercial potential of the proposed products. In the end, staff recommended 17 topics for publication, and these were recently approved by NCI leadership. The 17 topics are broken into five categories:

1. Therapeutics
2. Medical devices
3. Diagnostics
4. IT
5. Manufacturing

Eight of the 17 are aligned with the Cancer Moonshot initiative. These were approved by the NCI Moonshot Implementation Steering Committee. **The 17 concepts follow:**

Therapeutics

- **Next generation 3D tissue culture systems with tertiary lymphoid organs**: Submitted by the Division of Cancer Biology, Division of Cancer Treatment and Diagnosis, Center for Strategic Scientific Initiatives, SBIR Development Center, and Division of Cancer Control and Population Sciences. The goal is to fund development for IO research purposes of in vitro culture systems for these human lymph node-like structures that form in response to chronic inflammation. This concept is aligned with Cancer Moonshot recommendation J, development of new enabling cancer technologies for 3D organ-like cultures.
- **Synthetic biology gene circuits for cancer therapy:** Submitted by SBIR Development Center. The goal is to stimulate the engineering of advanced cancer therapies with gene transfer of artificial synthetic biology signaling pathways.

Medical Devices

- **Applicator-compatible electronic brachytherapy sources for cancer radiotherapy:** Submitted by the Division of Cancer Treatment and Diagnosis. The goal is to develop implantable electronic radiation sources with off switches, free of natural radiation sources.
- **Self-sampling devices for HPV testing-based cervical cancer screening:** Submitted by the Division of Cancer Prevention and SBIR Development Center. The goal is to develop user-friendly, high cellular-yield devices to allow women to self-collect cervicovaginal samples for HPV testing.

Clinical Diagnostics and Molecular Analysis

- **Quantitative imaging software tools for cancer diagnosis and treatment planning:** Submitted by the Division of Cancer Treatment and Diagnosis. The goal is to commercialize new or existing academic quantitative imaging software for use by radiologists for common cancer imaging modalities.
- **3D spatial omics for molecular and cellular tumor atlas construction:** Submitted by the Division of Cancer Biology, Center for Strategic Scientific Initiatives, and SBIR Development Center. The goal is to provide development for research purposes of scalable imaging technologies that will provide both 3D tumor architecture and single cell -omics information. This topic is aligned with Moonshot Recommendation I, on the generation of human tumor atlases.
- **Understanding cancer tumor genomic results—technology applications for providers:** Submitted by the Division of Cancer Treatment and Diagnosis, Division of Cancer Control and Population Sciences, Center for Global Health, and SBIR Development Center. The goal is to develop software to assist oncology providers in communicating genomic testing results to patients without a genetic counselor. This topic is aligned with Moonshot Recommendation A, establishing a network for direct patient engagement.
- **Single cell "unbiased discovery" proteomic technologies:** Submitted by the Division of Cancer Treatment and Diagnosis, Division of Cancer Control and Population Sciences, Center for Strategic Scientific Initiatives, and SBIR Development Center. The goal is for the development for research purposes of proteomic biomarker discovery approaches, to quantify >1,000 proteins in a typical cell. This topic is aligned with Moonshot Recommendation J, development of new enabling cancer technologies; molecular analysis technologies, and mass cytometry for individual cells.

Information Technology and Bioinformatics

- **Software to address social determinants of health in oncology practices:** Submitted by the Division of Cancer Control and Population Sciences and SBIR Development Center. The goal is to create IT tools to support systematic assessment of social determinants of health, and appropriate referral and follow up in oncology practices. This topic aligns with the Moonshot cross-cutting theme on reducing cancer health disparities.
- Digital tools to improve health outcomes in pediatric cancer survivors: Submitted by SBIR Development Center and the Division of Cancer Control and Population Sciences. The goal is to create software to support delivery of high quality cancer survivorship care for children/adolescents.

Manufacturing Technologies

- **Advanced manufacturing to speed availability of emerging autolo-**

gous cell-based therapies: Submitted by the Division of Cancer Treatment and Diagnosis and SBIR Development Center. The goal is improved cell processing methods to expedite and reduce the cost of producing cell-based therapies.

Topics from FY20 to be reissued

- **Quantitative biomimetic phantoms for cancer imaging and radiation dosimetry:** Submitted by the Division of Cancer Treatment and Diagnosis.
- **Spatial sequencing technologies with single cell resolution for cancer research and precision medicine (Moonshot):** Submitted by the Division Cancer Treatment and Diagnosis and SBIR Development Center.
- **IT tools for automated analysis of physical activity, performance, and behavior from images for improved cancer health:** Submitted by the Division of Cancer Control and Population Sciences.
- **Tools and technologies for visualizing multi-scale data (Moonshot):** Submitted by the Center for Strategic Scientific Initiatives and Division of Cancer Biology.
- **De-identification software tools for cancer imaging research:** Submitted by the Center for Biomedical Informatics and Information Technology.
- **Cloud-based multi-omic and imaging software for the cancer research data commons (Moonshot):** Submitted by the Center for Biomedical Informatics and Information Technology.

NCI SBIR Innovative Concept Award to Develop Transformational Solutions Focused on Prevention, Detection, Treatment, and Research in Pediatric Cancer and Rare Cancers (RFP): Approved

The purpose of this RFP is to support small businesses developing highly innovative and transformative technologies that have the potential to create new scientific paradigms, establish entirely new and improved clinical approaches to significantly improve cancer research, prevention, detection and care for pediatric or rare cancers.

The RFP was submitted by The Office of the Director. The concept award will be funded by the SBIR program.

The concept award, a 3-year pilot, will have one receipt date per year in the pilot round. The total estimated cost per year is $1.5 to $3 million. The RFP will fund five to 10 awards at around $300,000 each, for one year. Awardees will be in the phases 0-I of research. Clinical trials are not permitted in the program.

Standard SBIR eligibility criteria apply.

Examples of projects and activities the RFP could fund, but are not limited to:

- New mechanisms of action
- New targets
- Innovative drug delivery
- AI-driven prognostics/ diagnostics tool

Why SBIR?

- Proposal components can be modified,
- Applications require shorter proposals (15 to 20 pages with three pages for research strategy),
- One to two page letter of intent will be reviewed for responsiveness by NCI program directors,
- Review allows for more emphasis on innovation, allows modification of review criteria weightage unlike the omnibus grant mechanism,
- Assess scientific rationale given the preliminary data,
- NCI DEA Special Review Panel with mix of academic industry venture and biotech
- Quarterly reporting,
- Payment based on achieving milestones.

Cancer Intervention and Surveillance Modeling Network (CISNET) Incubator Program for New Cancer Sites (RFA/ Coop. Agr.): Approved

The purpose of the CISNET Incubator Program RFA/Coop. Agr. is to translate CISNET's model of success to cancer sites for which there has been nascent or limited population modeling efforts to date and little to no comparative modeling.

CISNET currently uses a comparative modeling approach with three to six independent modeling groups per cancer

site. The project includes one multiple PI grant per cancer site with a coordinating center. Notably, CISNET has helped the United States Preventive Services Task Force create screening guidelines in cervical cancers.

The RFA/Coop. Agr. was submitted by The Division of Cancer Control and Population Sciences. The project will be funded through the U01 grant.

The estimated budget is $4 million per year, with a total of $20 million over five years. The budget includes $180,000 direct cost per modeling group (two to three per cancer site), $90,000 for the coordinating center, $40,000 costs contribution to a junior investigators program, and four awards.

The incubator program:

- Includes multiple PI grants with 2-3 independent modeling groups that will share common data sources and compare their models as they are developed.
- One modeling group that will serve as the coordinating center for that site
  - Formulating, prioritizing, and coordinating work;
  - Negotiating common requests for outside data sources;
  - Preparing inputs and collecting and processing common outputs for model comparisons / critical evaluation of disparate results.
- Require that no more than one PI on an incubator application can also be a PI on a concurrently funded CISNET grant.

What the project is looking for:

- Up to the research community to make the case that a cancer site is amenable to this type of modeling and would have impactful public health benefits.
- Searching for cancer site specific proposals where:
  - Applicants bring together separate nascent modeling efforts focusing on important cancer control applications,
  - Data sources exist to inform the models (especially the preclinical natural history)
  - Potential interventions or strategies are sufficiently well developed to provide estimates of their operating characteristics; and
  - Priority will be given to applications that propose modeling feasible cancer control opportunities at different points across the cancer control spectrum.

The CISNET Incubator will focus on the same priority areas as the main CISNET RFA, but new incubator sites will spend considerable time on model development/refinement and consideration and study of data sources to inform the models.

Nine priority areas:

1. Precision Screening and New Screening Technologies
2. Precision Treatment
3. Overdiagnosis and Active Surveillance
4. Decision Aids (Individual and Policy)
5. Understanding Screening in Real-World Settings and Determining the Best Routes to Optimize the Processes
6. State, Local, and International Cancer Control Planning
7. Suggesting Optimal Routes to Reduce Health Disparities
8. Methods Development
9. Cancer Site-Specific Opportunities

State of population modeling in cancers beyond the six included in CISNET

- Fewer existing models, and not as well developed,
- Because of a lack of consistent funding, most are "one-off" efforts that focus on a single limited portion of cancer control spectrum,
  - Importance of including synergies across the spectrum,
- No (or very limited) comparative modeling,
  - Some post publication comparisons of models and results—difficult to do because of so many things varying simultaneously;
- Availability of new data resources to inform models; and
  - Large observational databases and specialized linkages, e.g. linkage between SEER hepatocellular carcinoma cases and state hepatitis registries.

Pediatric Preclinical Testing Public-Private Partnership (PPTP3) (Reissue RFA/Coop. Agr.): Approved

The purpose of this reissue RFA/Coop. Agr. is to establish an in vivo testing program and coordinating center for the in vivo testing program for the Preclinical Testing Public-Private Partnership. Future NCI components include a high throughput in vitro testing program and data commons.

The reissue concept was submitted by the Division of Cancer Treatment and Diagnosis.

The estimated budget for the partnership is $3.7 million in direct costs for year one, and $5.9 million in total costs for year one. The in vivo testing program is estimated to be $3.2 million in direct costs and $5.1 million in total costs. The coordinating center is estimated to be $500,000 in direct costs, and $800,000 in total costs. The cost of the in vitro testing program and data commons is to be determined.

NCI PPTP3 in vivo testing program (inVivoTP)

- Plans for eight awards for research programs for in vivo testing.
- Open competition for in vivo testing sites with plans to encourage applications from new research teams.
- Agnostic in terms of models (e.g., PDX in immunodeficient mice, murine genetic models engineered to reflect the characteristics of specific pediatric cancers, and murine syngeneic models).
- Potential disease areas of focus include: ALL, AML, neuroblastoma, osteosarcoma, rhabdomyosarcoma, Ewing sarcoma, renal and hepatic tumors, and CNS tumors.
- Each team anticipated to test eight to 10 agents per year.
- Plan for broader utilization for single-mouse trial design for agents for which tumor-regressing activity is sought.
- Selection criteria to include:
  - Number and breadth of models proposed and the extent to which the proposed tumor panels faithfully recapitulate key biological characteristics of molecularly defined subtypes of specific pediatric cancers
  - Scientific leadership that the research team is anticipated to bring to the PPTP3 and its Scientific Advisory Committee
  - Ability to conduct testing with required throughput

PPTP3 Coordinating Center components

- Administrative management, logistics, and coordination of in vivo testing sites,
- Establishment of a confidential and private project information site,
- Development of quality assurance/quality control procedures,
- Management of laboratory specimens and a biospecimen tracking system,
- Coordination of shipments of compounds supplied by companies to testing sites,
- Collection, analysis and storage of testing data from the testing sites,
- Preparation of technical study reports for agents tested through the PPTP3; and
- Collaboration with research programs in developing, presenting, and publishing manuscripts.

PPTP3 Data Commons goals (future RFA)

- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for cell lines and PDX models from both PPTP3 research teams and from external research teams,
- To aggregate/federate and analyze genomic, proteomic, and epigenomic characterization data for clinical specimens to establish as comprehensive a dataset as possible to facilitate robust comparisons to preclinical data,
- To aggregate, store, and compare existing and new testing data both from PPTP3 research teams and from external research teams,
- Provide analyses of genomic, proteomic and epigenomic data to support decision making for preclinical evaluations and for clinical development plans; and
- Make data available in ways that are easily accessible by the research community.

International Agency for Research on Cancer (IARC) Monographs Program (Reissue RFA/Limited Competition): Approved

The goal of the International Agency for Research on Cancer Monographs Program is to evaluate cancer agents

including chemicals, biological agents, occupational exposures and lifestyle factors.

NCI has supported the IARC Monographs program since 1982, through a U01 grant. The reissue RFA, which will be funded through the R01 grant, was submitted by the Division of Cancer Biology.

The estimated total cost per year is $900,878 over five years—$4.5 million total.

An advisory group consisting of senior health policy and environmental researchers meets every five years to prioritize agents for consideration for the monographs program for the next five-year cycle. The group prioritizes agents on the extent of human exposure, suspicion of carcinogenicity, public health concern and new, relevant studies.

The IARC Monographs program is a unique NIH award. There are two carcinogen identification programs in the United States: A report on Carcinogens (National Toxicology Program, National Institute of Environmental Health Sciences), Integration Risk Information System (Environmental Protection Agency).

The IARC Monographs program considers a broader number and type of agents to evaluate. The program evaluates agents of global concern, especially in low and middle income countries.

Monograph process

- Working Groups review literature comprehensively
  - Subject matter experts: interdisciplinary, international
  - Evaluate epidemiology, animal studies and mechanism data
  - Summarize exposure data
- Determination of agent as a cancer hazard
  - Known, probable, or possible carcinogen, not classifiable
- Three Working Groups per year (NCI funds two)
  - Volumes freely available as PDFs
  - Over 1,000 agents evaluated by 125 Working Groups

Agents

- Recently evaluated
  - High concern: engine exhaust, red meat and outdoor air pollution
  - Low and middle income countries (LMIC): malaria, hepatitis B and C viruses, indoor combustion/cooking
- New and high priority for 2020-2024
  - Bisphenol A, cytomegalovirus, e-cigarettes and nicotine, disinfection byproducts and cannabis smoking

Low-dose CT Lung Cancer Screening Image and Data Resource (RFP): Deferred

The purpose of this RFA is to create a new LDCT lung cancer screening image library to make screening more efficient and reduce screening-related harms, the false-positive rate must be substantially reduced, while leaving test sensitivity essentially unchanged.

One approach to reduce the false-positive rate is through development of artificial intelligence and machine learning tools to assist radiologists in interpreting LDCT screening and diagnostic images.

The RFA was submitted by the Division of Cancer Prevention. The RFP is a five year contract. The estimated cost is $4.5 million for the collection of data and images, and set-up for image storage for up to three years. Image storage and dissemination is expected to cost $500,000 per year for up to three years. Image validation set activities, including qualification as a MDDT for two years is $500,000 to $1 million.

The majority of the BSA voted to defer the concept, citing concerns that it's unclear how the composition of the library is designed to address false positive rates, and that there should be more prescriptive description of the diversity of the population with respect to smoking status, comorbidities, race and ethnicity.

NCI program staff will work on this concept in the meantime, which will be considered by the BSA at a future meeting so long as Scientific Program leadership agrees.

The RFP would:

- Have a new LDCT lung cancer screening image library obtained with current LDCT technology and in standard clinical (non-research) settings,
- Include diagnostic f/u CT images include demographic, screening outcome and clinical outcome (lung cancer incidence) data,
- Not require enrolling/consenting of patients: only retrospective collection of de-identified images and data,

- Be made available to the research community through a controlled process; and
- Hold back a subset of images for algorithm validation.

Project scale:

- 15,000 unique subjects
- 22,500 screening LDCT images
- 6,000-8,000 diagnostic CT images
- 1,500 subjects with lung cancer-associated image (diagnosed within 18 months of a screen)
- 9,000 subjects with Lung-RADS positive screen (no cancer)
- 4,500 subjects with (only) Lung-RADS negative screens (no cancer)

Social and Behavioral Intervention Research to Address Modifiable Risk Factors for Cancer in Rural Populations (PAR): Approved as RFA

The BSA voted to approve this concept as an RFA, rather than a PAR, as was originally submitted to the board. NCI's Division of Extramural Activities will review the RFA as approved.

The purpose of the social and behavioral intervention concept is to solicit applications to develop, adapt, and test individual, community, or multilevel interventions to address modifiable risk factors for cancer in rural populations (defined as USDA RUCC or RUCA non-metropolitan areas or FAR rural areas).

The concept was submitted by The Division of Cancer Control and Population Sciences. There was no associated grant or budget.

Proposals should:

- Focus on primary prevention, targeting one or more of the modifiable risk factors that contribute to cancer disparities in rural populations, and
- Assess and address myriad social determinants of health, cultural factors, policies, and health care and technology access barriers that may contribute to rural cancer disparities.

This FOA encourages implementation science research, to incorporate efficacious cancer control interventions into broader, sustainable health programs that are designed to reach rural populations and allow local customization and adaption.

Applicants are strongly encouraged to collaborate with organizations and programs with experience or infrastructure (e.g., telemedicine, behavioral health services) designed to address other health or social problems in rural populations that could afford substantial opportunities to cancer prevention and control investigators.

Examples include, but are not limited to, Federally Qualified Health Centers, community health centers, rural health centers, and community organizations.

Example applications may target:

- Behavioral risk factors for cancer in rural populations (primary outcomes)
  - Tobacco use
  - Diet, Physical Activity, and Weight
  - Alcohol consumption
  - UV exposure and sun-protective behavior
  - HPV vaccination
- Social determinants and structural/system characteristics that contribute to rural disparities in behavioral risk factors for cancer (secondary outcome measures or mediators of effect)
  - Economic and spatial barriers to healthy food access and/or physical activity in low density rural environments,
  - Technology, communication, and health information inequalities that may contribute to cancer disparities in rural populations.

Study designs

The RFA is labeled "Clinical Trial Required" to solicit intervention applications that meet the NIH definition of a clinical trial:

1. Human subjects
2. Prospectively assigned to one or more interventions
3. Health-related biomedical or behavioral outcome

These are not drug or device trials. Applications may propose either pragmatic or explanatory trials to test effects in real-world/usual conditions or under ideal/controlled conditions (e.g., experimental or quasi-experimental study designs).

Applications may propose individual, clinic, and/or community-level units of analysis (individuals or cluster randomization).

Cancer Moonshot Concepts:

3D Technologies to Accelerate HTAN Atlas Building Efforts (HTAN #1) (RFA/Coop. Agr.): Approved

The purpose of this project is to facilitate rapid implementation of promising new technologies for time-efficient, three dimensional molecular characterization of intact human tumor tissue for dynamic 3D tumor atlas construction.

The RFA/Coop. Agr. was submitted by the Office of the Director.

The RFA/Coop. Agr will be funded through the UH2 grant, and will integrate with existing Human Tumor Atlas Network U2C and U24 grants. The project will include three to four UH2 grants.

The total cost for all years of the project is around $3.3 million for four grants. The estimated budget for the project is $250,000 per year, with a duration of two years.

Applications

- PIs with relevant expertise are encouraged to apply. Non-HTAN grantees are expected to be part of HTAN and encouraged to use HTAN-procured biospecimens.
- Applications require preliminary data demonstrating the "shovel-readiness" of the technology in an HTAN-relevant tumor will be required.

This is an HTAN-focused program that leverages and complements other NIH and NCI imaging efforts.

Integration with existing HTAN network

- Leverage shared HTAN tumor sources via trans-network efforts (currently colon, breast),
- Encourage identification of collaborators within HTAN-funded research centers,
- Agree to data use and sharing policies,
- Deposit data, protocols and SOPs with the HTAN Data Coordinating Center; and
- Participate in relevant HTAN working groups and biannual face-to-face meetings.

Cancer Moonshot Data Visualization Methods and Tools Development (R33) (NET #1) (RFA): Approved

The purpose of this RFA is to stimulate the development of new cancer data visualization tools that have the potential to make data from Cancer Moonshot areas more explorable and interpretable by the broader cancer research community.

This RFA was submitted by The Office of the Director.

The R33 funding opportunity is for the development of new visualization tools and approaches addressing Cancer Moonshot-aligned use cases and priorities. Award lengths are up to four years. The direct cost is expected to be $250,000 per year. The total cost for all years is $5 million.

The R33 RFA:

- Is open to applications from all investigators,
- Is investigator-identified use cases, user communities, and insights to be gained,
- Includes proposed tools that will enable visualization of Cancer Moonshot data addressing the specified use case and user community; and
- Has an expectation of tool validation studies.

Applicants should:

- Identify a data visualization use case aligned to Cancer Moonshot and specify a targeted user community that is currently underserved by existing data visualization tools,
- Propose the development of a data visualization software tool that addresses the use case, the insights to be gained for the user community, and
- Describe plans for validation of the proposed tool(s), and plans for community engagement.

GUEST EDITORIAL

SARS-CoV-2 and oncology drugs

What do we mean when we talk about *value*?

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Drug development in COVID-19

The global pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to expectations of global deaths numbering in the hundreds of thousands. Promising therapeutic strategies have emerged slower than society would prefer. COVID-related deaths in the United States exceed 86,000 as of this writing, with projections as high as 134,000.

It is a humbling moment to reflect on not only the current situation, but also on whether drug reimbursement policy changes might help to encourage nimbler global responses to public health threats in the future.

A value-based framework centered on cost-effectiveness is one approach to guide society's provisioning of precious resources. The incremental cost-effectiveness ratio (ICER), expressed in dollars per quality-adjusted life-year (QALY), demonstrates that the best "deal" for a utilitarian society is to spend its money on medical interventions providing the greatest return on investment.

Commonly cited "willingness to pay" thresholds in the United States tend to range from $50,000 to $150,000 per QALY, but are theoretical only and are not used to guide reimbursement. In the United Kingdom, on the other hand, the threshold of £20,000 to £30,000 per QALY is used to make reimbursement determinations.

Building on this concept, the Institute for Clinical and Economic Review released guidance toward an appropriate value-based price for remdesivir. Starting from a threshold ICER of $50,000 per QALY, remdesivir data available to date, as well as system-level COVID-19 outcomes data from a locality that was overrun, an estimated "fair" price of $4,500 per treatment course was arrived upon. Using a cost recovery-based model leads to a price of $10 per treatment course.

As the Institute for Clinical and Economic Review noted in their report, now is the time to discuss connecting pricing to effectiveness, despite the uncertainties surrounding the data. This discussion, however, requires context.

Putting remdesivir's development in context

Drug development does not occur in a vacuum. Pharmaceutical companies' activities increasingly target profitable disease spaces, resulting in a stampede toward investigational oncology drugs.

Importantly, these drugs are priced as a function of what the market has been willing to pay for recently approved therapies with similar indications, irrespective of the value created. Additionally, because of higher willingness to pay as a result of legislation, the pharmaceutical industry has pivoted toward drug development for orphan diseases. Altogether this leads to relatively little attention being paid to vaccine and antibiotic development.

Despite cost-effectiveness guidance, the ICERs of therapies in oncology routinely exceed $150,000 and, in some cases, reach $900,000 per QALY. Because expensive oncology therapies are reimbursed by government payers in the United States, often without any controversy at all, these are definitionally *socially acceptable* prices and cost-effectiveness.

Development in the infectious disease space requires incentives. So, what would happen if we were to apply the cost-effectiveness metrics deemed acceptable in cancer to drugs being developed for SARS-CoV-2? What would a fair, socially acceptable price for an efficacious SARS-CoV-2 drug be if it were priced like a cancer therapy, so as to promote infectious disease drug development? A back-of-the-envelope approach can be informative.

Applying oncology pricing to a successful SARS-CoV-2 drug

To develop estimates of value-based prices for a candidate SARS-CoV-2 drug administered to inpatients, we estimate the survival benefit (in number of lives saved per 100 treated patients) as a function of the baseline inpatient case-fatality ratio (CFR) and drug efficacy (Figure 1).

Depending on these factors and their interactions with health care systems, the number of lives saved per 100 treated patients could range from 22.5, if baseline inpatient CFR is 25% and relative mortality reduction is 90%, to a more conservative estimate of 7.5, if baseline inpatient CFR is 15% and relative mortality reduction is 50%, to zero if the drug is not at all efficacious (Figure 1, from top right to left).

Observational data on COVID-19 are only recently coming to the fore, with mortality data varying by population demographics, level of preparedness, and the degree to which a health care system is overrun.

At one end of the spectrum, the reported median age of inpatients who died from COVID-19 was 69 years, while at the other end, in Italy, the reported mean age of inpatients who died was 79 years. In the absence of other data, we estimate the mean age of a patient who otherwise would have died in the hospital from COVID-19 in the United States as 74 years.

Against a life expectancy of 11.8 years for a 74-year-old male, 10 QALYs can reasonably be expected to be gained if

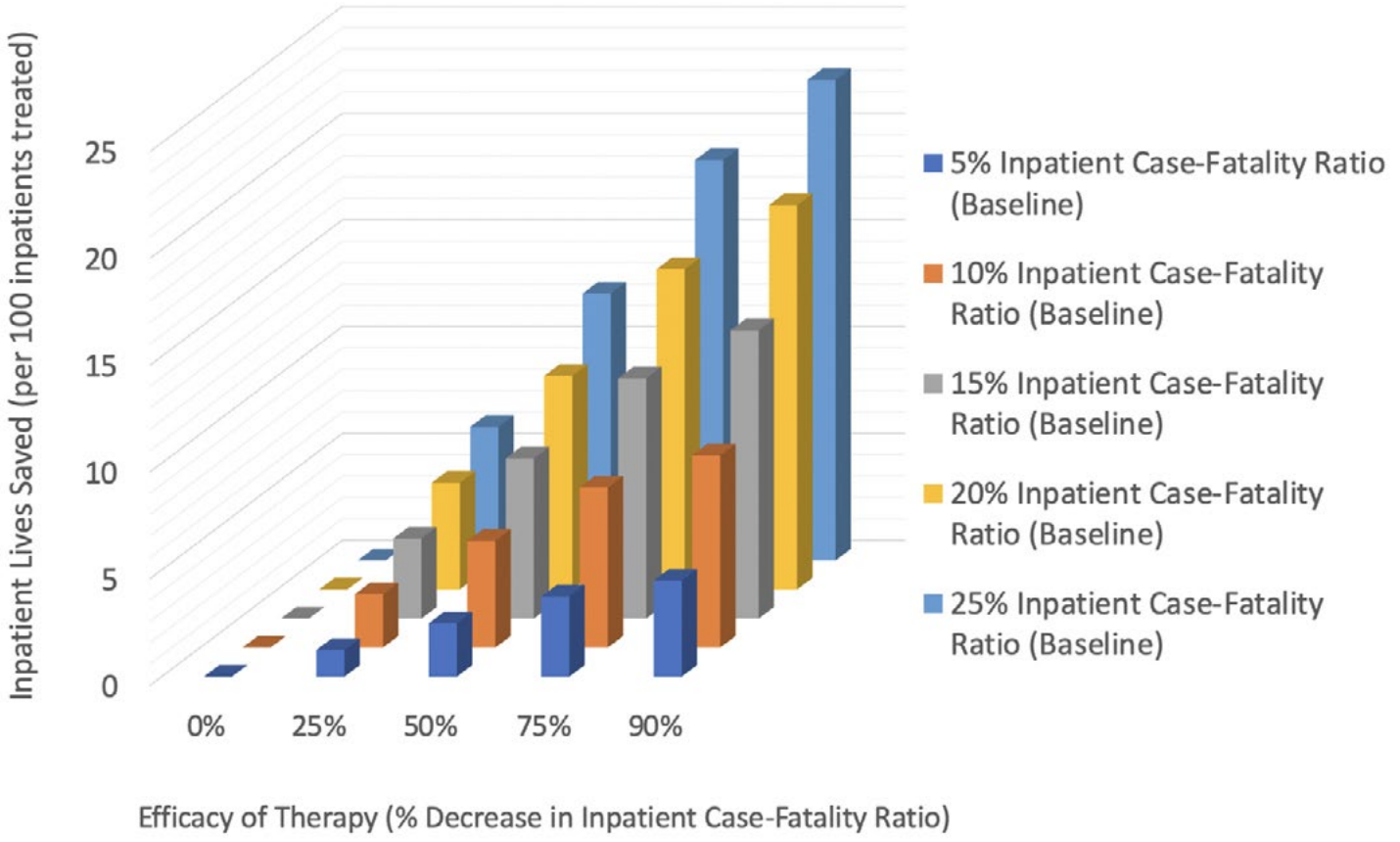

Figure 1. Inpatient lives saved from COVID-19-related fatality by an anti-SARS-CoV-2 drug under different clinical scenarios. Inpatient lives saved by a hypothetical drug per 100 patients treated (Y-axis) is a function of the drug's relative efficacy (X-axis) and the baseline case-fatality ratio (CFR) of the treated patient population (stratified by series along the Z-axis). Treating 100 patients with baseline CFR of 25% (light blue series, back row of Z-axis) with a 90% efficacious drug (right-most values of X-axis) yields 22.5 lives saved (back right column).

the patient survives and returns to his or her pre-COVID-19 health. Utilizing the earliest available data of remdesivir efficacy from the National Institute of Allergy and Infectious Diseases-sponsored placebo-controlled, double-blind randomized controlled trial in COVID allows for estimation of remdesivir's socially acceptable price.

Starting from 11.6% inpatient CFR, 30% mortality reduction, and a WTP threshold of $100,000 per QALY, the socially acceptable price nears *$34,800* per treatment course to gain those 10 QALYs. Applying the high end of oncology's WTP thresholds ($900,000 per QALY in the case of regorafenib) to remdesivir yields a socially acceptable price of $313,200 per treatment course.

Aligning development goals with value goals in the post-COVID world

And yet, this is not the conversation being had. Instead discussion centers about Gilead's pricing decisions in attempts to recover the $1 billion it believes it will have spent on the drug's development, even after donating 1.5 million vials. Early projections from one Wall Street analyst suggested a one-time $2.5 billion windfall to Gilead for remdesivir.

In the context of an estimated two trillion-dollar domestic economic output gap, the $4,500 treatment course proposed in the Institute for Clinical and Economic Review's analysis could well be a historic bargain—and that is before one considers the second-order effects resulting from the drug's ability to shorten duration of hospitalization.

Intelligently applying "payment for value" logic limits expenditures on low-value drugs in disease states that are uniformly fatal, even with additional therapy. Payment for value also can be used to incentivize development of high-value products like vaccines and antivirals.

Extending the value-based framework to include not only a novel drug's perpetuity value but also its option value and intangible value can be the beginning of an incentive structure that rewards both innovation and preparation.

> It is a humbling moment to reflect on not only the current situation, but also on whether drug reimbursement policy changes might help to encourage nimbler global responses to public health threats in the future.

Two policy proposals flow naturally. First, as previously proposed, large, global prizes to incentivize generation of option value and intangible value could be created. Second, the pharmaceutical industry's repurposing prowess as well as its ability to generate accelerated discovery, development, and domestic manufacturing processes capable of withstanding supply shocks could be gleaned from the application of "war games" or "stress tests".

Designing and building a system capable of withstanding and mitigating the next pandemic is sorely needed. Society's takeaways from the COVID-19 pandemic will shape the narrative that emerges in the coming weeks and months. A cataclysmic event like a global pandemic carries the potential to reshape society's priorities, and a time of great stress should provide the perspective necessary for it to clarify what it means when it talks about *value*.

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OBITUARY

Isaiah Fidler, founder of MD Anderson Department of Cancer Biology, dies at 83

Isaiah "Josh" Fidler, DVM, PhD, died on May 8, at his home in Houston following a long illness.

Fidler was born in Jerusalem on Dec. 4, 1936 to Shoshana Stern and Pinchas Fidler. His father, a world renown soccer player, died in Israel's war of independence in 1948. After attending school and serving in the Israeli army, Fidler came to America to study veterinary medicine.

In 1963, Fidler earned his veterinary medicine degree from Oklahoma State University. He worked as a surgical oncologist at the University of Pennsylvania's School of Veterinary Medicine, and in 1970 he earned a doctoral degree in human pathology at the university's School of Medicine.

His experience as a veterinary surgeon taught him that the lethality of cancer is mainly due to the ability of cancer cells to spread, or metastasize, to other organs, so he devoted his career to the study of metastasis at a time when no one else was focusing on this topic. In 1975, Fidler joined the National Cancer Institute, where he led the metastasis program at the Frederick Cancer Research Facility. His eight years there produced some of his early innovative work in unraveling the riddles of how cancer spreads.

In 1983, Fidler joined MD Anderson Cancer Center as professor and founding chair of Cancer Biology, a department he led until 2008. Fidler held the R.E. "Bob' Smith Distinguished Chair in Cell Biology. For many more years, he continued his academic pursuits and leadership responsibilities, which included his role as director of MD Anderson's Cancer Metastasis Research Center and Metastasis Research Laboratory. In 2019, Fidler fully retired and was appointed the title of professor emeritus.

"As a researcher at NIH, Josh was already a giant in his field of tumor biology, but his stated reason for leaving to join us at MD Anderson was: "In my life I want to cure people and not just mice," said Andrew C. von Eschenbach, a longtime friend and colleague. "That dream to save lives by eliminating cancer metastases will come to fulfillment because this brilliant unrelenting pioneer showed us the way."

Fidler was a pioneer in understanding how cancer spreads to other organs and then grows. His work exposed the origins of metastases, the processes by which these cells spread and thrive in other organs, the molecular diversity that makes them so hard to treat and the crucial supporting role of their surrounding microenvironment. These discoveries proved the need for specific targets for metastatic cancer cells and showed why some treatments are less successful against metastatic disease.

His later work focused on brain cancer. Fidler's team showed that tumors that spread to the brain trick brain cells, called astrocytes, into protecting the cancer, making the tumors resistant to chemotherapy. Another study explored combining the oral chemotherapy drug temozolomide with macitentan, a drug originally approved for treating pulmonary hypertension, as a potential treatment for glioblastoma.

"Josh is an MD Anderson icon who spent 36 years building the foundation of metastasis research and making seminal contributions that play a critical role in oncology today," said Peter WT Pisters, president, MD Anderson. "He was committed to advancing science for the benefit of humanity, and he was passionate about developing the careers of the next generation of researchers. His brilliance, kindness and booming personality will be remembered and cherished by all who knew him."

Fidler's career of more than 50 years includes more than 820 publications in peer-reviewed journals. He oversaw numerous former trainees and mentees who now hold faculty leadership positions of their own in research institutions around the world. In 2007, an international blue-ribbon group of cancer researchers gathered at MD Anderson to present lectures for the symposium "Forty Years of Metastasis Research: A Symposium in Honor of Dr. Isaiah J. Fidler."

Fidler was internationally respected and extended his service to many professional activities. He was founding editor of Cancer and Metastasis Reviews and served as president of the American Association for Cancer Research (AACR) and the International Society of Differentiation.

"It is impossible to capture the full impact that Josh Fidler has had on cancer research and on his admiring colleagues and friends. He was lauded during his remarkable career with many awards for his innovative cancer science," said Margaret Foti, Ph.D., M.D., chief executive officer, AACR. "Josh was the second president I had the privilege of serving, and I learned so much from him. I will always remember him not only for his amazing intellect and dedication to the cause, but also for his personal strength, kindness, and engaging personality."

Among the many recognitions of Fidler's scientific contributions are his 2007 selection as a prestigious fellow of the American Association for the Advancement of Science and his appointment as an inaugural member of the Academy of the AACR in 2013. His numerous awards from MD Anderson include the 1983 Ernst W. Bertner Memorial Award; the 2004 Charles A. LeMaistre, MD, Outstanding Achievement Award; and the President's Award in 2007, which he received along with his wife, Margaret Kripke.

Organizations worldwide honored him as well. Among them: two NCI Outstanding Investigator Awards (1987 and 1995), AACR's G.H.A. Clowes Memorial Award for Accomplishment in Basic Cancer Research (1988), the World Health Organization's Gold Medalist for Biological Sciences (1997), the Bristol-Meyers Squibb Award for Distinguished Achievement in Cancer Research (1999), the American Cancer Society's Distinguished Service Award (2004), ACS's Distinguished Service Award and Medal of Honor in Basic Research (2013), the Gold-Headed Cane Award from the American Society for Investigative Pathology (2016) and AACR's Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research (2018).

Fidler with John Mendelsohn, then MD Anderson president, and Waun Ki Hong, then head of the Division of Cancer Medicine.

> "As a researcher at NIH, Josh was already a giant in his field of tumor biology, but his stated reason for leaving to join us at MD Anderson was: 'In my life I want to cure people and not just mice.'"
>
> *– Andrew C. von Eschenbach*

When presenting him with the President's Award, former MD Anderson President John Mendelsohn, said, "I consider Fidler as the chief gadfly at MD Anderson. He always challenges and always has insightful comments. He makes us think because he is a truly original thinker."

Fidler is survived by his wife, Margaret Kripke, who was founding chair of Immunology at MD Anderson and served as executive vice president and chief academic officer before her retirement in 2007. Fidler also is survived by his daughters Morli Josza of Palm Beach Gardens, FL, and Katharine Kripke Tsela of Washington D.C., his brother and sister-in-law Yaron and Talia Fidler, and his grandchildren Eden, Evan, and Jake Josza.

Memorial gifts may be sent to MD Anderson Cancer Center (gifts.mdanderson.org).

Source: *MD Anderson Cancer Center*

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AN APPRECIATION

The Class of 1983; Remembering Josh Fidler

By Irwin Krakoff and Rosemary Mackey

We moved to Houston together with Rosemary's daughters, Catharine and Claire, in August of 1983 when Irv accepted the position of head of the Division of Medicine at MD Anderson Cancer Center.

Fidler with wife Margaret Kripke, founding chair of Immunology at MD Anderson

We soon began to wonder what we were doing in Texas and how we might survive it. During our first few weeks there we met another recently arrived couple, Josh Fidler and Margaret Kripke, who soon became our best friends… The Class of '83 was born!

To seal our friendship, when we married five months after our arrival, our wedding cake, a favorite of Josh's, was an Italian rum cake and bore their names rather than ours. The story behind that is far too long to tell, but was pure Josh!

We spent many weekends together, vacationed together, shared one another's triumphs and misfortunes and laughed and cried together. We had regular Sunday suppers with our families and on one such occasion used our assembled collective degrees and brilliance to help our daughter Claire with a science homework, for which she received her only "D" while in high school.

Josh was a major factor in helping the girls adapt to their translocation to Houston from a small town in New Jersey where they had grown up. When Irv found it possible to be out of town for two of Catharine's Father/Daughter dinner-dances, it was Josh who stood in *in loco parentis*—even allowing her to drive his beloved Nissan 280Z to one of the events.

The four of us were at a wedding in Austin when we received multiple calls from Philadelphia, where Josh's son Daniel had invited Catharine to his senior prom. Josh told us that she was in the hospital with appendicitis, but that we shouldn't worry, because he had called the hospital, told them he was a surgeon (true—although technically just for animals) and that he had authorized them to go ahead with surgery. He was furious when Rosemary laughed, because Catharine had her appendix removed when she was 5. Turned out she had food poisoning and sadly, missed the prom.

Fidler with Kripke, and friends Rosemary Mackey, former MD Anderson director of planning, and Irwin Krakoff, former head of the Division of Medicine.

We all decided to embrace Texas with a vengeance, and this resulted in trips to the Hill country and eventually Big Bend National Park where we enjoyed the superb scenery and rafting.

It was on one of those trips that we had to coax Josh out of the raft on the Mexican side since he was convinced that only setting foot in Mexico would produce serious GI problems. Other pioneering adventures took us from Chihuahua on a train to the Copper Canyon in Mexico (with lots of booze and snacks to ward off any maladies) and to Alaska where we explored the Inside Passage with naturalists in a small ship.

Sometimes Josh and Margaret went further afield without us, which on one occasion had a disastrous result. Josh, on horseback was trying to outrun a zebra while on a safari in Kenya. It was Rosemary who received a call from Pan Am asking that she arrange an ambulance to meet him at Bush Intercontinental Airport in Houston, and she then got him into St. Luke's Hospital where she was on the staff (now a CHI institution), where he underwent major orthopedic reconstruction of his severely broken leg bones.

Since 1993, when Irv retired from the Anderson and we began our subsequent healthcare-related consulting in Scotland, Mexico and New York, our families have remained intertwined. We always knew there would be a warm welcome when we visited them in Houston with spirited conversation about science, politics, and life in general. Birthdays, anniversaries, weddings, vacations—we have done them all.

Irv is soon to be 97, and he finds travel—particularly by air—rather tiring, but in December of last year, we decided to do a day trip on a Saturday from our home in Savannah to Houston to visit Josh and Margaret.

How glad we are that we got to spend several hours together with Josh and Irv talking about past scientific successes and musing about the future of cancer research and treatment, the fields they have both loved and enhanced so much.

It is just one more detail for the memory bank of a man we were privileged to call a dear and very close friend for more than 37 years.

Josh… life won't be the same without you.

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***Krakoff** is a former head of the Division of Medicine and **Mackey** is a former Director of Planning at MD Anderson Cancer Center.*

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OBITUARY

Oncology pioneer John W. Yarbro dies at 88

By Eric T. Rosenthal and Donald L. "Skip" Trump, MD, FACP, FASCO

Oncology pioneer John W. Yarbro, MD, PhD, died April 13 in Miramar Beach, Florida. He was 88.

Yarbro was one of the cancer experts called to testify before Congress to speak in favor of the draft legislation that became the National Cancer Act of 1971. At that time, he was founding director of the department of medical oncology at Philadelphia's American Oncologic Hospital (now Fox Chase Cancer Center), and he noted that the accomplishments of many of the leading cancer research centers—including Roswell Park, MD Anderson, and Memorial Sloan Kettering—were due more to the support of state legislators and private philanthropists than the medical establishment.

He further made the point that cancer studies were underrepresented in medical research presentations and publications. He pointed out that between 1966 and 1971, only 5% of the papers presented at the annual meetings of the American Society for Clinical Investigation dealt with cancer while 17% of U.S. population died of cancer, and during the same period, 45% of the papers presented at the meetings dealt with heart disease and related cardiovascular diseases when 40% of deaths at the time were due to heart disease.

We were fortunate to have spoken with Yarbro and his wife, Connie, a founder of the Oncology Nursing Society, shortly before his death when researching our book, *Centers of the Cancer Universe*, due to be released next year during the 50th anniversary of the National Cancer Act.

During that conversation, Yarbro shared his experiences as first director of the National Cancer Institute's cancer centers program, which was created to enact a prime provision of the National Cancer Act--to establish "15 comprehensive cancer centers."

Richard L. Schilsky, executive vice president and chief medical officer of the American Society of Clinical Oncology, recalled first meeting Yarbro when he joined the faculty of the University of Missouri-Columbia in 1981, after completing his NCI fellowship.

"John was clearly the intellectual force in the division and he took me under his wing. He had a keen interest in science, specifically biochemistry and DNA synthesis. He was a wonderful mentor in that he took a deep interest in my work, offered critiques, challenged conclusions and helped me become a better researcher. He was also a shrewd administrator with a keen understanding of local and national 'onco-politics' and his insights and advice helped me navigate some of the challenges we faced at our institution during those years," Schilsky said.

Yarbro was "a fabulous editor with a clear vision for where the science of oncology was heading and how new biological insights could be applied to improve cancer care," Schilsky said. "His selection of topics and authors for *Seminars in Oncology* over many years reflected his scientific 'taste' and appreciation of innovation. I learned a great deal from John early in my career and, although we only worked together for a few years before I moved to the University of Chicago, we remained close friends."

Yarbro was born in Chattanooga, TN, raised in Louisville, KY, and received

both his undergraduate and medical degrees from the University of Louisville. After joining the U.S. Army Medical Corps, he interned at Tripler Army Hospital, and then trained in internal medicine at the University of Minnesota, where he served as chief medical resident and also received a PhD for research in nucleic acids.

> John was clearly the intellectual force in the division and he took me under his wing. He had a keen interest in science, specifically biochemistry and DNA synthesis. He was a wonderful mentor in that he took a deep interest in my work, offered critiques, challenged conclusions and helped me become a better researcher.
>
> *– Richard L. Schilsky*

In addition to his time at NCI and Fox Chase, Yarbro also served as: director of the division of hematology at the University of Kentucky; director of the Missouri Cancer Program; director of the Regional Cancer Center, Memorial Medical Center in Springfield, Illinois; president of the Association of Community Cancer Centers; and secretary-treasurer of the American Society of Clinical Oncology.

He chaired numerous national committees including the Panel of Hematologic and Neoplastic Diseases of the United States Pharmacopeia; served as editor of *Seminars in Oncology* for 34 years; and was instrumental in launching *The Journal of Clinical Oncology*.

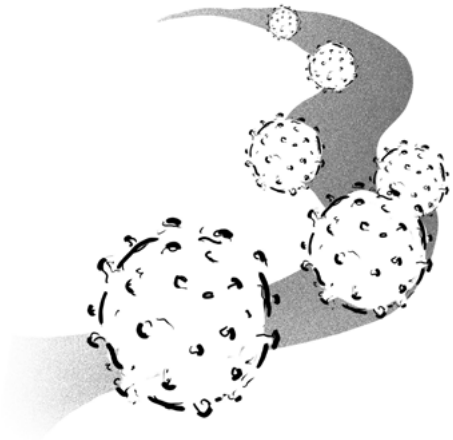
Yarbro authored more than 200 scientific papers, abstracts and book chapters. His interests included cancer research, patient care, problem-based medical education, cancer center administration, and the relationships among clinical research, quality of care, and health care funding.

He is survived by his wife of 40 years, Connie Yarbro; a grandson, Paul and his wife Pamela; great-grandchildren, Francys and Leonardo; and his dog Tzu Hsi. He was preceded in death by his daughter, Francys Elena, and his second wife, Geraldine Yarbro, MD.

Trump *retired from his position as Founding CEO and Executive Director of The Inova Schar Cancer Institute in the Inova Health System, Fairfax, VA. While at Inova he was also a professor of medicine in the cancer center at the University of Virginia. During his career, Trump worked as a GU medical oncologist and held leadership positions at several NCI-designated cancer centers, most recently CEO and President of the Roswell Park Cancer Institute (2007-2014).*

Rosenthal *is an independent medical journalist who has covered issues, controversies and trends in oncology for more than three decades. He founded the National Cancer Institute-Designated Cancer Centers Public Affairs Network in 1990.*

COVID-19 UPDATES



Heartland NCORP sites implement drive-through laboratory service

Two component institutions of Heartland Cancer Research NCORP have created drive-through laboratory services for outpatients during the COVID-19 crisis.

The service does not test patients for coronavirus infection, but provides a mechanism for patients with cancer and blood diseases to have laboratory studies for treatment or clinical trial requirements in the safest possible manner. The drive-up laboratory sites meet the requirements of the state and local governments' shelter-in-place orders.

At both Springfield Clinic (Springfield, IL; Preet P. Singh, Sub-PI for Disparities and Cancer Care Delivery Research) and Missouri Baptist Medical Center (St. Louis, MO; **Bryan A Faller**, principal investigator), upon arrival, the patient drives into a designated parking area, calls the registration area and registers for the visit by telephone.

A phlebotomist is sent to the patient's vehicle and performs the blood draw with the patient's arm extended through the window. After the drive-through visit, the patient obtains results and further instructions by telephone or via the patient portal.

Springfield Clinic has developed an educational video for patients, describing the service. The service has been popular at both NCORP sites and may be a model for patient-centered service after the pandemic subsides.

Roswell Park to assess immunotherapy combination in cancer patients with COVID-19

An immunotherapy combination, rintatolimod and interferon alfa, first evaluated at Roswell Park Comprehensive Cancer Center as an approach for treating some solid tumor cancers will soon be available to cancer patients with COVID-19 through a clinical trial at Roswell Park.

FDA has authorized clinical researchers at the center to conduct a study assessing the safety and effectiveness of giving both rintatolimod and interferon alfa to cancer patients with COVID-19. The study is one of very few worldwide to repurpose an experimental cancer therapy as treatment for COVID-19.

"It's a rare example of a concept for COVID-19 therapy that emerged from academic researchers rather than a pharmaceutical company, and it was a Roswell Park team that looked at the way these two drugs work and saw a possibility for them to enhance each other's effects—first against cancer and now as a possible treatment for COVID-19," Roswell Park President and CEO Candace S. Johnson said in a statement.

Pawel Kalinski, vice chair for translational research at Roswell Park, was the first researcher to propose giving these two immune-modulating drugs in combination as treatment for cancer, and is scientific lead on five clinical studies in progress or in development assessing the combination in patients with solid-tumor cancers including breast and colorectal cancer. He and clinical principal investigator Brahm Segal, will lead the team investigating whether the two drugs may function effectively together as antiviral agents that could benefit patients with COVID-19.

"There are similarities between cancer and COVID-19, which both manage to avoid activating the interferon pathway," scientific lead on the study Kalinski, who is also director of Cancer Vaccine and Dendritic Cell Therapies, Rustum Family Professor for Molecular Therapeutics and Translational Research and Professor of Oncology at Roswell Park, said in a statement. "This helps them to go undetected and spread in patients' bodies, and differentiates them from viruses that cause the common cold,

which cause rapid symptoms and are rapidly cleared by the immune system."

"We believe that the two agents to be tested in our trial, given together, can activate the missing interferon response in COVID-19-infected cells," he said. "This would induce protective interferons and other antiviral factors in adjacent cells, stopping the virus from spreading in patients' bodies and generating a synergistic effect that could help cancer patients with mild or moderate COVID-19 to fight the virus before it causes serious damage to the lungs or other organs."

"SARS coronaviruses such as SARS-CoV-2, the virus that causes COVID-19, take hold because they're able to evade the innate immune system," Segal, chair of Internal Medicine and chief of Infectious Diseases at Roswell Park and professor at Roswell Park and the University at Buffalo, said in a statement. "The premise for the trial is that by activating the interferon pathway with these two agents, we may be able to deprive the virus of the ability to replicate, knocking it out before it has a chance to cause severe lung damage or other serious effects. Promising results would pave the way to a larger clinical trial that would include non-cancer patients at high risk for COVID-19 complications."

Patients with cancer and COVID-19 have a risk of severe illness up to five times higher than people without cancer, underscoring the importance of work to develop new treatment options.

Interferon alfa-2b is an FDA-approved drug that has been used in the treatment of some cancers and can boost antiviral immunity. Rintatolimod (brand name Ampligen, manufactured by AIM ImmunoTech Inc.), a form of double-stranded RNA that mimics viral RNA, is an investigational agent that can be recognized by our immune system and activates antiviral defense pathways.

The study will test the safety of this combination regimen in patients with cancer and mild to moderate COVID-19, and the extent to which this therapy will promote clearance of the SARS-CoV-2 virus from the upper airway. Earlier published research from Kalinski's lab has demonstrated that the combination of rintatolimod and interferon alfa-2b shows synergistic activity in preclinical cancer treatment models.

The phase I/IIb study will enroll approximately 40 patients in two stages. Phase I will see 12-24 patients receiving both rintatolimod and interferon alfa-2b at escalating doses. Once that initial phase is complete, further study participants will be randomized to two arms, or groups: one receiving the two-drug combination and a control group who will not receive rintatolimod or interferon alfa but will receive best available care.

AIM ImmunoTech has agreed to provide rintatolimod at no charge for this study.

MSK Kids study: Children with cancer are not at a higher risk for COVID-19 infection or morbidity

Researchers from MSK Kids at Memorial Sloan Kettering Cancer Center found that children with cancer are not at a higher risk of being affected by COVID-19.

This new research led by Andrew Kung, chair of MSK Kids and his colleagues, was published May 13 in *JAMA Oncology*. Pediatric cancer patients are no more vulnerable than other children to COVID-19 infection or morbidity resulting from COVID-19. Of all children with cancer infected with COVID-19, 95% had mild symptoms and did not require hospitalization. MSK Kids clinicians also tested asymptomatic children with cancer finding only a 2.5% rate of positivity compared to nearly 15% in their adult caregivers.

Only half of the children with COVID-19 positive caregivers were themselves also COVID-19 positive. The researchers also found a very significance sex skewing with the vast majority of COVID-19 infections occurring in males. Together, these results suggest that children with cancer are not more susceptible than other children to infection or symptoms resulting from COVID-19, and that children are not an unrecognized reservoir of asymptomatic COVID-19 infection.

From March 10 through April 12, MSK Kids researchers instituted a screening and testing plan to mitigate risk associated with infection with COVID-19. MSK Kids patients were screened for exposure to contacts with known COVID-19 infection or for the presence of symptoms of COVID-19 illness at MSK.

Researchers performed COVID-19 testing on pediatric patients and their adult caregivers. Of the 178 unique pediatric cancer patients tested, the rate of positivity for COVID-19 was 29.3% in children with symptoms, but only 2.5% in asymptomatic children. Of the 20 patients who tested positive for COVID-19, only 3 were female.

Only one patient with COVID-19 illness required non-critical care hospitalization for COVID-19 associated symptoms. All other pediatric patients had mild disease symptoms and were managed at home. Of the 74 adult caregivers tested,

13 caregivers of 10 patients were found to be positive for COVID-19, including a 14.7% rate of COVID-19 infection in asymptomatic caregivers. Only half of the patients with COVID-19 positive caregivers were themselves also COVID-19 positive, suggesting low infectivity in children despite close household contacts.

While the overall numbers in the study are small, the data confirms that the overall morbidity of COVID-19 illness in pediatric cancer patients is low with only 5% requiring hospitalization for symptoms of COVID-19 infection; and that the rate of COVID-19 infection among asymptomatic pediatric patients is very low.

GRYT Health and BMS launch COVID-19 Advocacy Exchange

GRYT Health and Bristol Myers Squibb Co. developed the COVID Advocacy Exchange, a virtual platform to connect patient advocacy organizations, patients, policy makers, healthcare practitioners, and industry in the exchange of information.

The COVID Advocacy Exchange will invite close to 100 global and local advocacy organizations, spanning disease states, to virtually meet and support patients with serious diseases while navigating the current COVID-19 pandemic. The virtual platform will provide access to data and information, as well as the opportunity to participate in weekly live, interactive sessions to foster discussion and collaboration.

The virtual platform will provide advocacy organizations and patients with access to materials and information offering support across the following disease areas: oncology, cardiovascular, immunology & fibrosis, hematology and multiple sclerosis. Participants will have access to materials from Bristol Myers Squibb, other advocacy organizations and third-party experts, including curated best practices, white papers, peer-reviewed articles and multimedia content addressing the unique advocacy challenges associated with the COVID-19 pandemic for advocates and patients. Resources to address digital fundraising and other issues exacerbated by the pandemic will also be available.

Exhibitor information and the first weekly live, interactive session will be available here, launching the week of May 18. To register for free access to the platform and the series, visit www.covidadvocacyexchange.com.

IN BRIEF

ASCO highlights: 2020 annual meeting scientific program lineup

Five studies from the virtual scientific program of the 2020 American Society of Clinical Oncology Annual Meeting were highlighted in a press briefing and released May 13:

- **Greater Decline in Cancer-Related Deaths Seen in Medicaid Expansion States in First Nationwide Study**: States that adopted Medicaid expansion following passage of the Affordable Care Act of 2010 saw greater decreases in cancer mortality rates than states that did not, according to the first nationwide study of its kind.
- **Maintenance Therapy With PARP Inhibitor Olaparib Extends Survival By Over 1 Year in Patients With Relapsed Ovarian Cancer and BRCA Mutation:** Maintenance therapy with olaparib (Lynparza) extended overall survival by nearly 13 months (12.9) compared with placebo in women with platinum-sensitive relapsed ovarian cancer with BRCA 1 or 2 mutations, in a randomized phase III trial.
- **Videoconference Intervention Significantly Reduces Anxiety and Distress Among Remote Caregivers of People With Cancer:** A videoconferencing intervention significantly reduced levels of anxiety and distress among "distance caregivers" who live more than an hour away from the patients with cancer they support, according to the results of a federally funded study.
- **Quitting Smoking at Any Point, Even Close to a Lung Cancer Diagnosis, Improves Chances of Survival:** People who quit smoking at any time—even less than 2 years before a lung cancer diagnosis—improve their chances of survival after being diagnosed with the disease, according to the results of a large international study.
- **Integrating Geriatric Assessment and Management Into Cancer Care Improves Quality of Life, Reduces Hospital Admissions for Older Patients**: Older people with cancer set to receive anti-cancer therapy had significant improve-

ments in quality of life when comprehensive geriatric assessment and geriatrician-led management was integrated into their care plan.

The theme of this year's Annual Meeting is Unite and Conquer: Accelerating Progress Together. The meeting's scientific program will be held virtually May 29-31 and provide an engaging lineup of scheduled and on-demand scientific content across a variety of approaches, disciplines, and specialties.

Approximately 2,215 abstracts were accepted for virtual presentation, and more than 3,400 additional abstracts were accepted for online publication. The vast majority of these abstracts have been publicly released and are now available on ASCO's Meeting Library. Late-Breaking Abstracts, including Plenary abstracts, will be released online on Thursday, May 28, at 5:00 p.m.

Long, Smith, Quinn named to new positions at Roswell Park

Three leaders were appointed to Roswell Park Comprehensive Cancer Center:

- **Mary Ann Long was named senior vice president of nursing**. Long will focus on evaluating service in inpatient, outpatient and community practices, and will provide leadership to all nursing teams across the center.

  Long was previously director of Magnet at Roswell Park until her retirement in 2012, and also served as assistant director of nursing and director of patient care services, in addition to more than 30 years of service as an intensive care unit nurse.

- **Laurie J. Smith was named vice president of clinical research services**. As vice president, Smith will support more than 400 active clinical trials a year and supervise staff engaged in study submission, study implementation, data collection and management.

  Smith previously served as an independent consultant and, prior to that, as vice president of clinical research for AMITA Health in Chicago.

- **Timothy Quinn was named chief of critical care**. Quinn, previously co-director of the Intensive Care Unit, has been named to the newly created role of chief of critical care. He will work with members of Roswell Park's Intensive Care Unit and Intermediate Care Unit to provide cutting-edge and evidence-based oncologic care to patients. A critical care anesthesiologist at the Center, Quinn's research interests include preoperative evaluation of high-risk patients, intraoperative care and postoperative quality-improvement initiatives.

DFCI and Silverberry Genomix form population health initiative for research and education

Science Health Education Center at Dana-Farber Cancer Institute launched the SHE Biobank initiative, a large, long-term study that will investigate the impact of genetic predisposition and environmental exposure to the development of disease

The SHE Center's goal is to bring best practices, better health outcomes, and increased stability to developing countries including the Middle East and North Africa, a region urgently in need of all three.

Navid Madani, director of the SHE Center and a senior scientist at Dana-Farber Cancer Institute, has led educational workshops and training programs in the region, which reinforced the understanding of the current lack of health data infrastructure and solidified the need for such platforms in the region.

"Biobanking is crucial to this research and helps researchers, healthcare providers and governments to health policies and assign resources properly. In recent years, due to advancements in healthcare technologies, data availability and decreasing DNA sequencing costs, various biobanks have been created around the world," Madani said in a statement.

"However, the majority of such projects have been launched in developed countries, contributing to an increasing gap between developed and developing countries. This initiative aims to decrease that gap," Madani said.

The SHE Biobank offers researchers to conduct studies and the infrastructure it provides so the data can be put into action for public good. It also helps increase readiness of the healthcare community to prevent or combat future disease outbreaks.

"The recent COVID-19 pandemic has shown the importance of availability of digital health platforms to provide access to data and enable research and collaboration at scale for a large size of population," Shayan Mashatian, founder of Silverberry Genomix, said in a statement. "By making the Silverberry platform available to this critical endeavor, we are facilitating a rapid launch of the project, connecting the researchers, healthcare institutions and other interested parties so more people can take advantage of scientific advancement, preventing disease or empower the emerging field of precision medicine."

Researchers, universities, government agencies, companies, and foundations as well as individual participants, are invited to participate in the initiative.

Paczesny, Mehrotra named co-leaders of cancer immunology at Hollings Cancer Center

Sophie Paczesny and Shikhar Mehrotra were named co-leaders of the cancer immunology program at Hollings Cancer Center at the Medical University of South Carolina.

Paczesny begins her appointment on July 1 as a professor and chair of the Department of Microbiology and Immunology at MUSC in the College of Medicine. Mehrotra, whose appointment began March 2, is an associate professor in MUSC's Department of Surgery in the College of Medicine, and is also the co-director of the MUSC Clean Cellular Therapy unit.

Mehrotra has been with Hollings Cancer Center since 2006. His research focuses on understanding T-cell signaling and metabolic pathways to improve the functionality of T cells in adoptive cell therapy.

Paczesny is a member and counselor for the American Society for Clinical Investigation, co-chairperson for both the Center for International Blood and Marrow Transplant immunobiology working group and the American Society of Hematology task force on immunotherapies.

Other areas of her research include developing and translating biomarkers for the outcomes following allogeneic hematopoietic stem cell transplantation (HCT); discovering inhibitors of drug targetable biomarkers for HCT patients; finding novel therapies to treat graft-versus-host disease and improve graft-versus-leukemia reactions, including cellular therapies; and exploring the Alarmin Interleukin-33/ST2 signaling pathway as a novel immune checkpoint in myeloid malignancies and other cancers.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

Atezolizumab combination improves survival in HCC

Researchers at the University of California, Los Angeles found that a first-line combination of atezolizumab, an immunotherapy drug that boosts the body's natural defenses, and bevacizumab, an anti-angiogenesis drug that inhibits the growth of tumors' blood vessels, significantly improves survival for people with hepatocellular carcinoma, the most common type of liver cancer.

The combination improved overall survival and reduced the risk of death by 42%. It also decreased the risk of the disease worsening by 41%, and the percentage of patients whose cancer shrank or disappeared more than doubled.

Tecentriq (atezolizumab) and Avastin (bevacizumab) are sponsored by Genentech, a member of the Roche Group.

Results from the clinical trial were published in the *New England Journal of Medicine*, and the combination is being reviewed for approval under FDA's Real-Time Oncology Review pilot program.

Until now, no new first-line therapy has been shown to improve survival in advanced HCC since sorafenib was approved in 2007.

Atezolizumab and bevacizumab are monoclonal antibodies that have been used alone and in combination with other therapies to treat other cancers.

Atezolizumab targets a protein produced by cancer cells that shuts down the immune system's infection-fighting T cells. Bevacizumab interferes with a tumor's blood supply, preventing the cancer from growing and spreading through the body.

"By using these two drugs with different mechanisms of action together, we have increased the number of patients who respond to this treatment and have increased the duration of these responses as compared to the standard treatment, sorafenib," Finn said.

The trial included 501 people, age 18 up, from multiple centers worldwide, who had advanced metastatic or unresectable hepatocellular carcinoma. Two-thirds of participants were randomly assigned to receive the atezolizumab and bevacizumab combination, while one-third received sorafenib.

Twelve months after the start of treatment, the rate of survival with the combination was 67.2%, compared with 54.6% for the group on sorafenib.

DRUGS & TARGETS

FDA approves Retevmo, first therapy for lung and thyroid cancers with RET gene alterations

FDA has approved Retevmo (selpercatinib) capsules to treat non-small cell lung cancer, medullary thyroid cancer and other types of thyroid cancers in patients whose tumors have an alteration in a specific gene (RET).

Eli Lilly & Co. sponsors Retevmo.

Retevmo, a kinase inhibitor, is the first therapy approved specifically for cancer patients with the RET gene alterations. Specifically, the cancers that Retevmo is approved to treat include:

- Non-small cell lung cancer that has spread in adults,
- Advanced medullary thyroid cancer or MTC that has spread, in patients 12 and older who require systemic

therapy (a treatment option that spreads across the entire body, is not targeted), and

- Advanced RET fusion-positive thyroid cancer in those age 12 and older that requires systemic therapy that has stopped responding to radioactive iodine therapy or is not appropriate for radioactive iodine therapy.

Retevmo was approved by FDA based on the results of a clinical trial involving patients with each of the three types of tumors.

Patients received 160 mg Retevmo orally twice daily until disease progression or unacceptable toxicity. Major efficacy outcome measures were overall response rate and duration of response.

Efficacy for NSCLC was evaluated in 105 adult patients with RET fusion-positive NSCLC who were previously treated with platinum chemotherapy. The ORR for the 105 patients was 64%. For 81% of patients who had a response, their response lasted at least six months. Efficacy was also evaluated in 39 patients with RET fusion-positive NSCLC who had never undergone treatment. The ORR for these patients was 84%. For 58% of patients who had a response, their response lasted at least six months.

Efficacy for MTC in adults and pediatric patients was evaluated in those 12 and older with RET-mutant MTC. The study enrolled 143 patients with advanced or metastatic RET-mutant MTC who had been previously treated with cabozantinib, vandetanib or both, and patients with advanced or metastatic RET-mutant MTC who had not received prior treatment with cabozantinib or vandetanib. The ORR for the 55 previously treated patients was 69%.

For 76% of patients who had a response, their response lasted at least six months. Efficacy was also evaluated in 88 patients who had not been previously treated with an approved therapy for MTC. The ORR for these patients was 73%. For 61% of patients who had a response, their response lasted at least six months.

Efficacy for RET fusion-positive thyroid cancer was evaluated in adults and pediatric patients 12 years and older. The study enrolled 19 patients with RET fusion-positive thyroid cancer who were radioactive iodine-refractory and had received another prior systemic treatment, and eight patients with RET fusion-positive thyroid cancer who were RAI-refractory and had not received any additional therapy.

The ORR for the 19 previously treated patients was 79%. For 87% of patients who had a response, their response lasted at least six months. Efficacy was also evaluated in eight patients who had not received therapy other than RAI. The ORR for these patients was 100%. For 75% of patients who had a response to the treatment, their response lasted at least six months.

FDA approves Lynparza + bevacizumab as maintenance treatment for ovarian, fallopian tube, or primary peritoneal cancers

FDA has expanded the indication of Lynparza (olaparib) to include its combination with bevacizumab for first-line maintenance treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.

The combination is indicated for adult patients with complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency positive status defined by either a deleterious or suspected deleterious BRCA mutation, and/or genomic instability.

Lynparza is sponsored by AstraZeneca. Myriad myChoice CDx (Myriad Genetic Laboratories Inc.) was approved as a companion diagnostic for olaparib.

Efficacy of this new indication was investigated in PAOLA-1, a randomized, double-blind, placebo-controlled, multi-center trial comparing olaparib with bevacizumab versus placebo plus bevacizumab in patients with advanced high-grade epithelial ovarian cancer, fallopian tube, or primary peritoneal cancer following first-line platinum-based chemotherapy and bevacizumab. Randomization was stratified by first-line treatment outcome and tumor BRCA mutation status, determined by prospective local testing. All available clinical samples were retrospectively tested with Myriad myChoice CDX test.

Patients were randomized (2:1) to receive olaparib tablets 300 mg orally twice daily in combination with bevacizumab (n=537) 15 mg/kg every three weeks or placebo plus bevacizumab (n=269). Patients continued bevacizumab in the maintenance setting and started olaparib after a minimum of 3 weeks and up to a maximum of 9 weeks following their last chemotherapy dose. Olaparib was continued for up to 2 years or until disease progression or unacceptable toxicity.

The major efficacy outcome measure was investigator-assessed progression-free survival evaluated according to RECIST 1.1. An additional efficacy endpoint was overall survival. Estimated median PFS in the subgroup of 387 patients with HRD-positive tumors was 37.2 months in the olaparib with bevacizumab arm and 17.7 months in the placebo plus bevacizumab arm (HR 0.33; 95% CI: 0.25-0.45). Results from a blinded independent review of PFS were consistent with the investigator-assessed PFS analysis. OS data were not mature.