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KAREN KNUDSEN'S AACI PRESIDENTIAL INITIATIVE: REDUCE CANCER DISPARITIES ACROSS NORTH AMERICA

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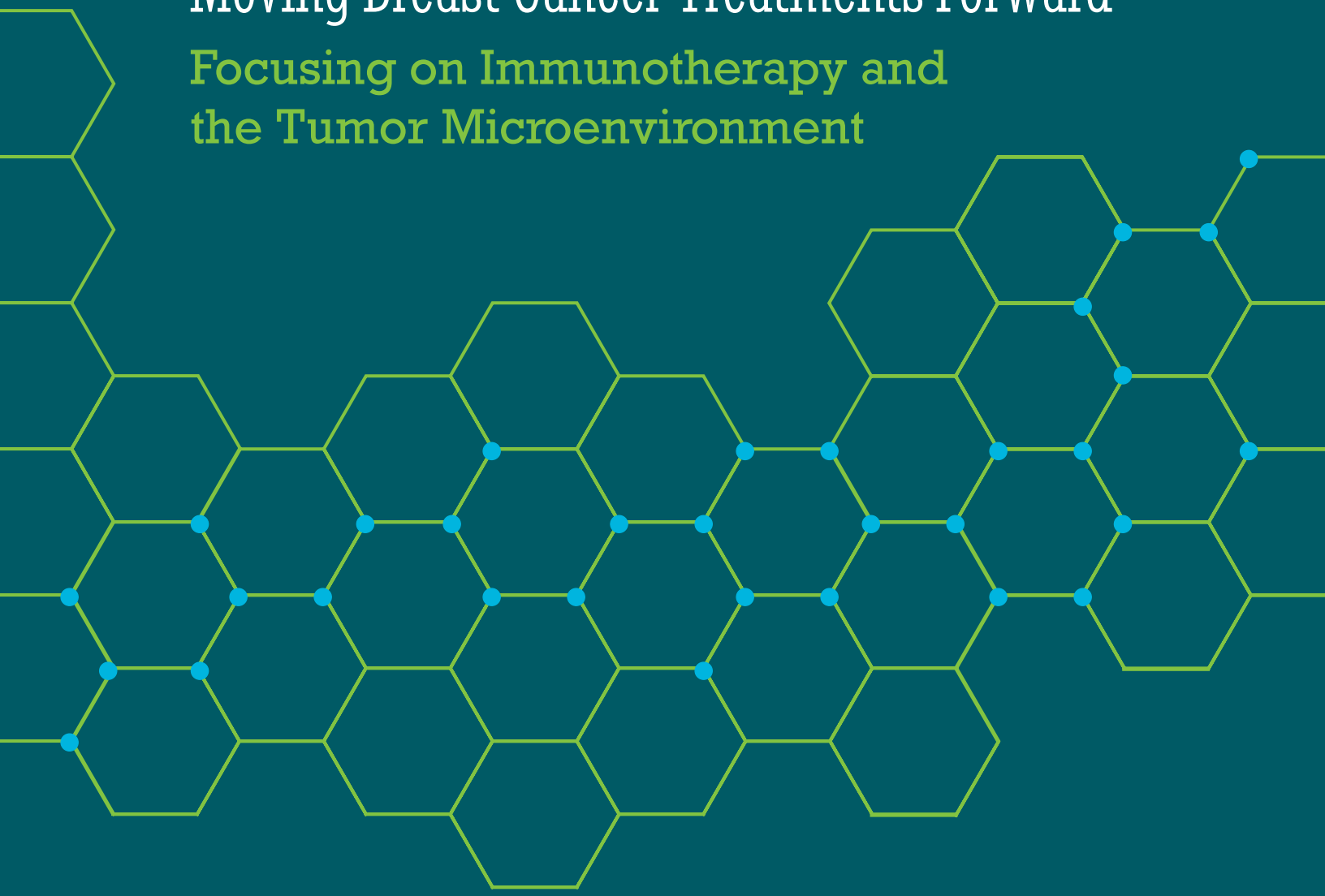

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KAREN KNUDSEN'S AACI PRESIDENTIAL INITIATIVE: REDUCE CANCER DISPARITIES ACROSS NORTH AMERICA

By Matthew Bin Han Ong

Over the next two years, as president of the Association of American Cancer Institutes, Karen Knudsen will challenge her colleagues at North America's premier cancer centers to focus on reducing cancer disparities.

"We know that AACI has a proven track record as a catalyst to affect change. And in this case, the change we're asking for is to reduce cancer disparities," Knudsen, enterprise director of the Sidney Kimmel Cancer Center at Jefferson, said at the virtual AACI annual meeting Oct. 13. "So, I would ask all of us that are watching this presentation, if not the 102 leading cancer centers in North America, then who? We are well positioned to work together, to play a major part in reducing cancer disparities across North America and beyond."

Knudsen's presidential initiative dovetails with NCI's efforts to seize a watershed moment in a global movement for racial equity.

"Cancer research really can't solve systemic racism and injustice by itself, but we can certainly look at our own work as individuals and as a community of practice and commit to taking action to make things better where possible," said NCI Director Ned Sharpless, who also spoke at the virtual annual meeting. "One of the clear goals here is to create an enduring structure to take these pernicious problems on in a systematic and enduring way, so not just write a single report and say, 'Okay, now we're done with racism,' but, rather, create a process of continuous monitoring, learning, and improvement."

Cancer centers should identify strategies to reduce disparities in their catchment areas, Knudsen said.

AACI will be contacting cancer centers to construct a plan for reducing cancer disparities.

Here are the steps Knudsen proposes:

- Surveying cancer centers to study their programs for addressing cancer disparities,

- Identifying disparities in their patient populations to understand the commonalities and differences across centers, and
- Creating a framework of best practices and mitigation strategies.

Knudsen's announcement follows *The Cancer Letter*'s publication of results from a survey of diversity in leadership at North American cancer centers.

The survey, conducted by *The Cancer Letter* in partnership with AACI, looked inward at the cancer centers in order to examine diversity in the leadership of these institutions—at the director and deputy and associate levels. The survey prompted cancer centers to assess their success in hiring and promoting diverse faculty.

An analysis of the data is available here, and a slideshow presentation can be downloaded here.

"At first blush, looking at those data [from the *TCL*-AACI survey], I think that we have a real challenge here. There just aren't enough underrepresented minorities in the pipeline," Knudsen said. "And so, clearly, we need to start at an earlier stage to try to understand how it is that we can enhance underrepresented minority individuals from desiring and sustaining a career in both research, but also oncology care."

NCI is well-positioned to make a difference in diversity, equity, and inclusion efforts in oncology, said Sharpless.

"I commend the AACI on their work in this area and the important data they've gathered recently through a survey and editorials just published in *The Cancer Letter*," Sharpless said. "Just as AACI's undertaking new efforts in this area, at the NCI, we are in early stages of a new equity and inclusion program as well."

NCI has created an equity council and three working groups focused on cancer health disparities, training the scientific workforce, and workplace culture to address these issues.

"To be clear, I think that these are areas where the NCI has some success and some good things going on. I would argue the disparities research portfolio of the NCI is among the strongest in all of biomedical research, probably in part because of the Cancer Center program, in fact—an interesting thing to discuss," Sharpless said. "But that doesn't mean it couldn't be better. I think that we need to look at the portfolio of cancer health disparities research and make sure we're funding the right things in the right amounts and the right time."

Sharpless's remarks appear on page 15.

"The mechanisms here will be surveys of strategies, as well as podcasts with cancer center leaders, as well as key stakeholders, including those from the community, the communities that we serve, elected officials and others," Knudsen said. "The deliverable will be a report out on the progress of AACI cancer centers to date.

"What's worked and where are we struggling? What are best practices and what are the common pain points and gaps? It goes without saying we'd like to engage NCI as well in both the generation of these surveys and reports as well as in their discussion.

"I'll be reaching out to all of you and I look forward to your input, your partnership, and your objective feedback along the way. So, I'm really excited about getting started the second that this meeting is over."

Knudsen's remarks at the virtual AACI annual meeting follow:

Thank you, everyone, for joining us. I'm Karen Knudsen, the executive vice president of oncology services for Jefferson Health and enterprise director of the Sidney Kimmel Cancer Center here at Jefferson. I'm very excited to join you as the incoming president of the Association of American Cancer Institutes.

It's really an honor as the president of AACI to represent all of you and to have an opportunity to work with the members, the board and the staff on a specific presidential initiative that I'd like to present to you today, associated with mitigating cancer disparities. I do have a few disclosures for both research support and consultancy and advisory groups, which have no bearing on today's presentation. And I will not discuss off-label use or investigational use in my presentation.

Before we get going with what I have planned for 2020 to 2022, I definitely would like to thank Dr. Roy Jensen, who has served so admirably as the president of AACI, leading us all and teaching me what's ahead and what can be done through this phenomenal organization. I look forward to continuing to work with Dr. Jensen as the past president. He can't get out so easily as to not continuing to work on a presidential initiative, in this case associated with mitigating cancer disparities.

I'm also thrilled to have an opportunity to work with our new vice president and president-elect Dr. [Caryn] Lerman from USC Norris Comprehensive Cancer Center, and very much excited to hear her views as we move forward together as the cancer center voice for North America.

To remind you, AACI has a very specific mission and purpose. And that mission is to accelerate progress against cancer by enhancing and

A CATALYST FOR CHANGE

The presidential initiative is an opportunity for the AACI president to advance AACI's mission and the interests of the cancer centers.

Diversity, inclusion, and equity are important issues, not only to our nation's cancer centers, but to our nation as a whole. To embody these values, we must work to close gaps in cancer research and care.

The 2020-22 Presidential Initiative will leverage the expertise of North America's 102 leading cancer institutes to understand and mitigate cancer health disparities.

Focus on disparities includes (but is not limited to) addressing needs of diverse populations, and diversity in the home institution.

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> We have every expectation of filling this mission through providing a unified voice and a platform for best practices, education, public policy advocacy, which was the focus of the last presidential initiative and collaboration.

empowering the nation's leading academic cancer centers in their mission to alleviate suffering from cancer.

We have every expectation of filling this mission through providing a unified voice and a platform for best practices, education, public policy advocacy, which was the focus of the last presidential initiative and collaboration. We'll need all of those things to encompass strategies for the 2020 to 2022 presidential initiative to leverage our expertise in our 102 centers to understand and mitigate cancer health disparities.

Cancer disparities in SKCC's catchment area

This focus on disparities includes, but is not limited to addressing the needs of diverse populations, as well as diversity in our home institutions. This is something I really think quite a lot about here in this large city of Philadelphia and our surrounding region that we serve. So, I thought I might just take a minute to give you a little bit of an introduction to my center and the kinds of challenges that I face as a cancer center director. I very much look forward to hearing similar stories from all of you.

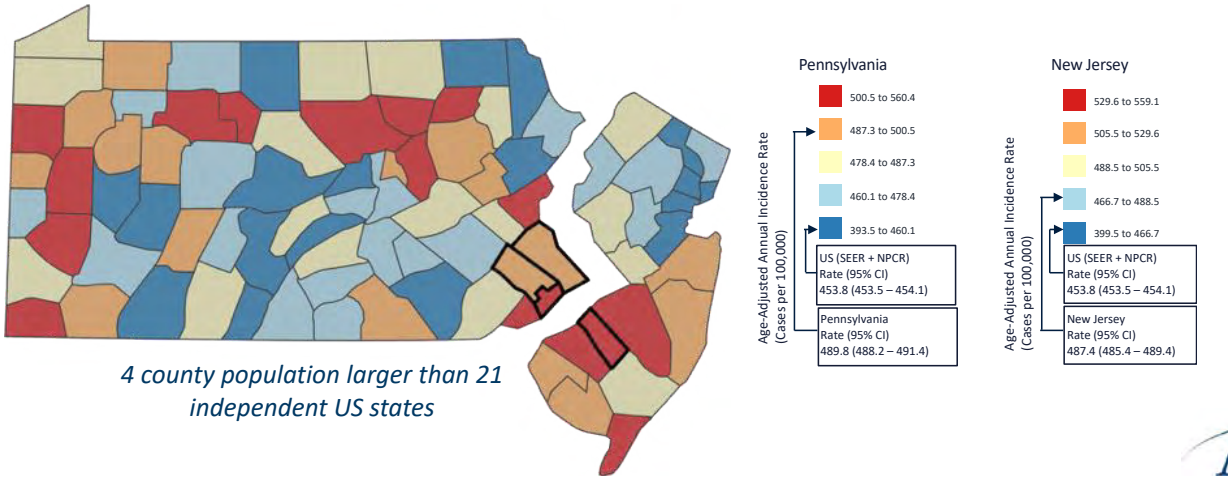
We serve a very large population, with an unacceptably high cancer incidence. Those four counties that are outlined in this heat map of incidents are counties where we actually have a Sidney Kimmel Cancer Center at Jefferson operation. It's a dense, heterogeneous county with a number of different challenges that are underpinning this high cancer incidence and high cancer mortality. The density of these four counties together actually is larger than 21 independent United States. So, it's quite a lot of diversi-

Presidential Initiative

SIDNEY KIMMEL CANCER CENTER CATCHMENT AREA

SKCC serves a population with an unacceptably high cancer incidence…

Heat Map of Incidence per 100,000 residents



4 county population larger than 21 independent US states

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…and unacceptably high mortality rates

Tumor Type	Incidence Rate (Rates per 100,000)			Mortality Rate (Rates per 100,000)		
	National	State (PA, NJ)	SKCC Catchment	National	State	SKCC Catchment
All sites	449	485, 486	**501.7**	159.3	166.2, 151.4	**175.2**
Breast	125.9	132.2, 136.6	**134.8**	20.3	21.2, 21.3	**23.8**
Cervix	7.6	7.3, 7.7	**8.4**	2.3	2.1, 2.0	**2.6**
Colorectal	38.4	41.1, 40.8	**41.9**	13.9	14.9, 14.1	**15.8**
Pancreas	12.9	14.3, 14.4	**14.8**	11	12, 11.3	**12.6**
Prostate	104.5	130.7, 131.3	**129.6**	19.1	18.8, 17.8	**23**
Leukemia	14.2	15, 15.7	**12.9**	6.4	6.6, 6.2	**5.8**
Non-Hodgkin Lymphoma	19.3	21, 21.8	**21**	5.5	5.9, 5.4	**5.9**
Cut. Melanoma	22.3	24.3, 22.2	**19.6**	2.4	2.5, 2.2	**2.2**
Lung	58.3	63.5, 55.3	**67.7**	40.2	42.3, 35.2	**44.4**

■ = rate exceeds national and/or state

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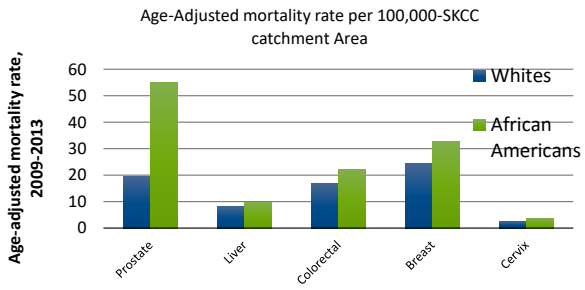
…with significant cancer disparities

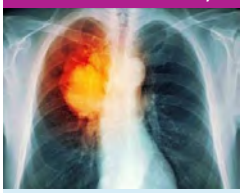
Disparities across demographics

Catchment Area Priority: Cancer Disparity



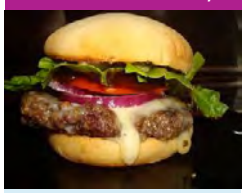
Behavior/Lifestyle & Exposure Disparities

Catchment Priority



High incidence smoking (top 10 city) and tobacco-related cancers

Catchment Priority



Obesity rates far exceed national averages; poor nutrition

Access Disparities

Catchment Priority

Lack of transportation (16% of SKCC patients)

Others disproportionate in the SKCC Catchment:

- Health Literacy
- Digital Access
- Viral infection (HIV, HPV, HepB/C)

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ty just within that small four-county geography.

We have unacceptably high incidence and mortality rates, and I won't go through the data. And I know you all have tables like this, that you look at within your own centers. I'd like to see them, and part of our first step for this initiative is to understand what are the cancer disparities and challenges that you're seeing within your own geographies. In red is where our catchment area outpaces either the state of Pennsylvania, the state of New Jersey, or the nation with regard to cancer incidence and cancer mortality.

Like many of you, we focus our efforts on understanding this high incidence or high mortality and attempting to prevent and mitigate. We think a lot about this, given the cancer disparities that are in my own geography. These are just a small sampling of the things we're challenged by in the greater Philadelphia area.

We have disparities across demographics. If you look at the graph on the left, it's very significant, and I've just shown an example of whites versus blacks in the Philadelphia region. Just looking at prostate cancer and age-adjusted mortality, you know we have a problem. It's one of the reasons why we have a large prostate cancer program.

We also have behavior and lifestyle and exposure disparities. We're a top-10 city for smoking incidence and tobacco-related cancers. We have obesity rates that far exceed national averages, accompanied by food deserts and poor nutrition. And also other types of disparities that we've worked very hard to control, like lack of transportation—16% of our patients report missing a cancer care episode due to having lack of transportation.

Other things that are disproportionate in our area are health literacy challenges, digital access challenges, even though we are an urban location and high levels of viral infection—in particular, HIV, hepatitis, and HPV. So, these are the kinds of things that my team and myself are wrestling with on a daily basis. And you're doing the same in your own centers.

So, this initiative is about sharing what those understandings are and determining how we might work more closely together. We know from a number of reports, and I'm just picking an example here from AACR, that disparities exist in many, many forms. Some of the ones I've talked about: racial and ethnic minority groups, socioeconomic status, the elderly, across a lifespan, particular geographies, being in a rural geography, individuals of different ancestry. There's quite a lot for us to tackle and understand in our own catchment areas. And we also

CANCER DISPARITIES EXIST IN MANY FORMS

American Association of Cancer Research (AACR) Annual Progress Report

know that many of these are associated with an increased risk of either acquiring disease or death from disease.

We know, for example, that men living in Kentucky have lung cancer incidence and death rates that are about 3.5 times higher than those of men living in Utah. We know that Hispanic children who have ALL are 2.6 times more likely to relapse than non-Hispanic children. These are the kinds of things that are being considered in each of the major cancer centers that are part of AACI.

Goals of the presidential initiative

So, phase one of the presidential initiative is to increase awareness and understanding of each other's challenges. Asking first, what are the priority disparities that have been identified in each of the major cancer centers? And which geographies are in the gap, potentially not yet studied? The mechanisms by which we'll go after that are to survey cancer centers through AACI with your participation, on the geographies that are already covered in disparities identified. The deliverable here will be a coalescing report on what geographies are covered, what gaps exist if any, and what disparities have been identified. What's common amongst our catchment areas? What's distinct?

The next phase of this will be to increase awareness and understanding through discovering currently implemented mitigation strategies. So, I'm happy to report out on what it is that we do in Philadelphia and share notes. I might learn something from what happens with Dr. [Cheryl] Willman in New Mexico or Dr. [Michelle] Le Beau in Chicago. These are the kinds of things that we'd like to consider and share.

The mechanisms here will be surveys of strategies, as well as podcasts with cancer center leaders, as well as key stakeholders, including those from the community, the communities that we serve, elected officials and others. The deliverable will be a report out on the progress of AACI cancer centers to date. What's worked and where are we struggling? What are best practices and what are the common pain points and gaps? It goes without saying we'd like to engage NCI as well in both the generation of these surveys and reports as well as in their discussion.

Finally, what I'd like to get to in this presidential initiative is converting knowledge into action. I call this phase two. This would be identifying collective AACR, AACI cancer center priorities, aligned to accelerating progress in mitigating cancer disparities. My

Presidential Initiative

GOALS: PRESIDENTIAL INITIATIVE

PHASE 1: INCREASE AWARENESS/UNDERSTANDING

- What are the priority disparities identified in each of the major cancers, and which geographies are not yet studied?

MECHANISMS:

- Survey cancer centers on geographies covered, disparities identified

DELIVERABLE:

- Report on :
  1. Geographies covered
  2. Gaps analysis
  3. Disparities identified (commonalities, distinctions)

PHASE 1B: INCREASE AWARENESS/UNDERSTANDING

- Discover currently implemented mitigation strategies, opportunities for improvement

MECHANISMS:

- Surveys of current strategies
- Podcasts with cancer center leaders, key stakeholders (community, elected officials, etc.)

DELIVERABLE:

- Report on
  1. Progress of AACI cancer centers to date
  2. Best practices
  3. Common pain points and gaps

PHASE 2: CONVERT KNOWLEDGE INTO ACTION

- Identify collective AACI cancer center priorities, aligned to accelerating progress in mitigating cancer disparities

MECHANISMS:

- Breakout accompanying 2021 AACI Annual Meeting to review Phase 1a/b materials, initiate action plans for advocacy

DELIVERABLE:

- Initiate actions intended to reduce disparities
  1. Awareness materials
  2. Advocacy strategy
  3. Partnerships with stakeholders

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goal for all of us is to have a breakout accompanying next year's meeting, which I hope will be in person, to review phase one A and phase one B materials and initiate action plans for advocacy.

The deliverable, I hope here, will be real actions planned out and intended to reduce disparities in a realistic way—including awareness materials, advocacy strategies, and identification of key partnerships with stakeholders that we'll need in order to be successful and make a dent in reducing cancer disparities. This is a perfect project, in my opinion, for all of us to work together as AACI members, as the centers are the members.

We know that AACI has a proven track record as a catalyst to affect change. And in this case, the change we're asking for is to reduce cancer disparities. So, I would ask all of us that are watching this presentation, if not the 102 leading cancer centers in North America, then who? We are well positioned to work together, to play a major part in reducing cancer disparities across North America and beyond.

And I'm going to thank you in advance for participating in this process. I'll be reaching out to all of you and I look forward to your input, your partnership, and your objective feedback along the way. So, I'm really excited about getting started the second that this meeting is over. And in the meantime, there are some related projects and initiatives I'd like to relay to you, and let's get started with those.

The Cancer Letter - AACI leadership survey

The first question is something that we addressed in partnership with *The Cancer Letter.* Again, with the idea of key stakeholder partnerships, and it's a question about our own diversity. A large number of you responded, so, thank you very much—78 of the directors responded; 61 were from NCI designated cancer centers. Only one identified as Black, 15 identified as either Hispanic, Latino, or Spanish, Middle Eastern or North African, Asian, American Asian, or multiracial. Sixty-six were men and 12 were women.

> The deliverable, I hope here, will be real actions planned out and intended to reduce disparities in a realistic way—including awareness materials, advocacy strategies, and identification of key partnerships with stakeholders that we'll need in order to be successful and make a dent in reducing cancer disparities.

So, this just gives a depiction of what our own ethnic diversity is within the cancer center director sphere. And I think that's probably known to all of us, as is the gender disparity within the cancer center director pool. And that's certainly an improvement over what would have happened 15 or 20 years ago. So, we're definitely moving in the right direction.

The question that we were asked to consider was, what about the pipeline? This is, again, distinct from the presidential initiative, but clearly gives us an opportunity to get self-awareness about our own research units. What we asked with regard to focusing on the pipeline is, what does the diversity look like within the deputy and associate director pool?

And this is what the data really tell us. It's something that is an opportunity for improvement for us, and you're going to be hearing a lot about this in the official report of this survey, which will come out in *The Cancer Letter* or has already come out by the time this presentation will go through. In which case, the deputy and associate directors, there are many more women in this pipeline pool than underrepresented minorities in the pipeline. And that's something for us to consider.

We also asked the directors what's happening at their own institutions. We know that across North America, there's an intensive focus on diversity and inclusion. And so, what's working? What's not? Again, with the best practice concept. We asked whether or not everyone's institution has programs to address diversity in recruiting. And the good news here is that over 50% did indeed say yes, that there was not only a program, but that had some moderate success.

The challenges here though, were very much appreciated in that, in scoring how difficult it is to recruit a diverse workforce in the research pool, in the oncology care pool, in the biomedical workforce pipeline compared to other institutions. I think everyone

is feeling the strain of how to get it done. So again, not the presidential initiative, but an important component potentially for cancer centers to come together and match the types of programs that they have at their institutions to those that may be seeing greater success.

50 years since the National Cancer Act

In addition, another initiative I wanted to raise your awareness about that you're going to be hearing more about during this meeting, is celebrating 50 years of progress. So, if you've looked at your calendar or you know that 2021 is coming soon, and that will be the 50th anniversary of the National Cancer Act, which established the National Cancer Institute and our network of world-class cancer centers in the U.S. Throughout the year NCI and other cancer centers will be looking back at five decades of progress against cancer.

And this is, again, because the centers are the members, a very important role for AACI and are our voices in this process. So, in part through the presidential initiative, but definitely through the AACI mechanism and the board and the members, we plan to accelerate and highlight progress by showcasing cancer centers' accomplishments, and improving access to cancer research and care, in honor of individuals such as Mary Lasker, who was instrumental in assisting in passing the National Cancer act and has had a long lasting effect on all of us.

So, in sum, what to expect from AACI, from myself as president, from Dr. Lerman as vice president and president-elect, from Dr. Jensen as the past president, from the board and from all of you, is convening cancer center leaders towards our shared mission to accelerate progress against cancer, through advocacy, iterative refinement of best practices, consideration of major issues that are affecting the center's goals for cancer care and cancer discovery—including, but not limited to the COVID pandemic—and conversion of our ideas into measurable, impactful actions.

Most importantly, we will continue to be nimble and serve as the unique single voice of North America's 102 leading cancer centers. And I know I speak for all of us when we say that we do this because of a passion for doing the right thing and a passion for improving the lives of cancer patients and their families.

I know that all of us will work together toward this end, and we'll be inspired by each other, but also by those that came before us in other disciplines. And I'll close with a quote from Ruth Bader Ginsburg that I think is highly suited to what it is that we do at AACI, which is "To fight for the things that you care about, but to do it in a way that will lead others to join with you." So, thank you for joining me. Thank you for joining AACI. I really look forward to continuing to work with you, and I'm happy to take questions. Thank you.

Q&A session

I would just like to reiterate what I said in the presentation, I'm really looking forward to the participation from all of the 102 AACI centers, as we bring about greater understanding with regard to mitigating cancer disparities. And I'm very excited about what we will achieve in working together. So, the floor is open for questions, and I have a few that have come across already that I will just go ahead and start to address.

Question: "Dr. Knudsen, what are some initiatives or programs that Jefferson is pursuing to address cancer disparities?"

Thank you for asking. Certainly, we still have a long way to go to mitigate cancer disparities in Philadelphia. I'll mention just a couple and they come in two different flavors. One is associated with changes in care delivery and access, and the other is through research. And they're both equally important in our center.

One of the things that we recognized in assessing our population is that we had a large number of patients who would miss cancer care, because they were on hourly wage or feared that they would lose their job if they were taking too much time off for chemotherapy, or to come to the infusion center.

So, one of the ways that we were able to mitigate that cancer disparity, I would argue successfully, is by changing our business practice. Staying open nights and weekends has really been revolutionary for us in terms of reducing the number of cancer patients who miss therapy because of that challenge. We've now extended that off as well to mammography and find that offering mammograms on the weekends or early in the morning or after work hours are some of the most popular times for us to do that. So, that's an example of changing business practice.

I talked in the presentation about transportation. Having our cancer center work with key partnerships with other industries to try to provide transportation for our cancer patients who have none was anoth-

er way that we were able to mitigate that disparity.

But the research component is really quite important. So, first we have to understand why the disparity exists and then decide what to do. I'll pick up on prostate cancer. We talked about that in the presentation and the deep disparity in prostate cancer incidence and mortality within our city.

So, we're really proud to be one of the first centers to open a men's genetic risk clinic. We know little about the genetic risk of prostate cancer with regard to the demographic that is around Philadelphia. And Dr. [Veda] Giri is really a phenomenal leader of our men's genetic risk clinic. That clinic exists to not only understand cancer disparities, the genetic basis of cancer disparities in our region, but also to educate men and their families about variant screening modalities that are important for someone with a genetic risk or with a family risk of cancer.

We're really proud to host the Philadelphia Consensus Conference every other year, which sets the stage for genetic testing for prostate cancer that's been adopted nationally. So, those are some of the things that we're doing, but there are many more efforts underway and areas where we still have yet to make a dent. That's where I think this initiative will be very helpful for us to learn best practices from each other.

Question: "Can you talk a bit about unconscious bias and how it's being addressed at cancer centers?"

Great question. This is a really important one for us. I actually can't speak with authority about what's happening at all of the other centers, and that's a useful conversation for us to have.

There was a phenomenal session yesterday. I had invited Melissa Wilson on, but it did address unconscious bias, and I would encourage all of you who did not get a chance to see that, to go back and look at that set of presentations. I thought it was really phenomenal. For us, I feel like our journey here is really just beginning to try to understand and do something about unconscious bias.

At least at Jefferson, we have a diversity and inclusion officer that, like myself, reports to the CEO. She's very well positioned within Jefferson. She's added core competency learnings for all of us at all ranks of Jefferson throughout the clinical side, and as well as the university side of our institution. And really, I think self-awareness is the first step.

Question: "Are there any measures that have been shown to be effective in recruiting minority candidates for research positions at cancer centers?"

So, this is something that I think will certainly come as a much deeper discussion based on the data that came out from the AACI-*The Cancer Letter* survey.

So, from my perspective, at first blush, looking at those data, I think that we have a real challenge here. There just aren't enough underrepresented minorities in the pipeline. And so, clearly, we need to start at an earlier stage to try to understand how it is that we can enhance underrepresented minority individuals from desiring and sustaining a career in both research, but also oncology care. Both sides there would require some mediation.

And so, I've had some great discussions in different panels with some of the directors about this. I think we need to understand what it is that we can control and what it is that we can do. If there are effective strategies, I hope this is the place that we as directors share them. I think this is really an opportunity for us at AACI to take on this challenge. So, more to come.

Question: "Will AACI advocate against the executive order preventing DEI training?"

So, again, great question. Something that we'll need to wrestle with with the board and leadership. And we'll get back to you on that one.

Question: "Is it enough to just recruit diverse leadership and workforce pipelines? The conversation should also include retention and promotion."

I can't say enough about that. I think that is absolutely true. I think that an essential component is not just getting someone. And I think this is true for all leadership, but not just getting them into a leadership position, but ensuring that they have the right tools in order to be effective.

So, this includes things like mentoring programs and really setting up someone who's coming in for success by nature of the package, by nature of things that are planned ahead of time. Not being reactive to someone who is questioning whether or not they want to stay in the pipeline, but being proactive. And so, understanding what those strategies look like from centers who've been particularly successful will be incredibly important.

There's a comment as well, saying that, "For retention and promotion, it's important to include in the conversation changing internal culture, so the diverse faculty and staff are supported and included."

I think this is all completely correct. It's on point. I can't remember a time when the directors have come together under the umbrella of any format. Other meetings that we go to, meetings that we attend specifically just as the directors of the centers in the U.S., where this has really been the major focus of discussion. So, we're off to a good start.

"We learned from other industries. It's also the case that other industries who have more diverse workforces have higher engagement with their employees. Better retention, better performance, irrespective of what metric you'd like to look at."

We have raised this as something that we need to understand. Because of our own workforce, because we know it's the right thing to do. Also because this is important for achieving something that is the presidential initiative, which is reducing cancer disparities. So, diversity in our workforce, on the research and on the clinical side really only has an upside.

We wrote about this a little in *The Cancer Letter* article that Dr. Jensen and I penned. We learned from other industries. It's also the case that other industries who have more diverse workforces have higher engagement with their employees. Better retention, better performance, irrespective of what metric you'd like to look at.

It's unequivocal, we're all scientists and clinicians, we're data driven. And I think we need to let those data drive us. It's the right thing to do. We know that this is some place that we need to go and start the deep discussion and AACI is a perfect platform for us to start to have those discussions.

So, I'm going to close with the following. We have a lot to accomplish, and I'm very much looking forward to working with all of you. For the presidential initiative, the first component is the survey to understand what are the areas that you are covering as these 102 cancer centers.

The next component is then to understand what mitigation strategy you're using in those various regions. And that will be completed by survey, by podcasts, by interview, and that's beyond just the centers, it's as well using key stakeholders.

So, I'd like to get started, literally tomorrow, with the first phase. I've heard from some of you already in the chat and beyond who have expertise in surveys, who have expertise in catchment area delineation. And I would absolutely count on and rely on your expertise.

So, if you or someone in your center would like to be involved in this effort, and I have not yet heard from you, please reach out to me directly and I'll be very enthusiastic about bringing you along. I think that the more that we have key stakeholders and leaders from diverse areas of North America, participating in this process, including Canada, the more apt we are to develop success.

In the end, I don't want this project to be overly aspirational. I said this at the board meeting yesterday, it's without question we will find more cancer disparity mitigation opportunities than we as AACI will be able to accomplish. And that's okay.

It's at that point, where this time next year, I hope that I'm standing in front of you in person. And we're talking about that list—what are the things that we think that are most appropriate for us, the leaders of the 102 centers, to address? And which are the things that we think would be better addressed through partnership or through working with key stakeholders in our communities?

At this time next year, I hope that we'll be making strategic priority decisions about what AACI can do together to reduce cancer disparities. Thank you very much for joining us. I look forward to the rest of the meeting and from hearing from all of you. And again, I'm going to thank you in advance for your participation. So, thank you everyone.

NCI DIRECTOR'S REPORT

Ned Sharpless: "Nothing will stop us"—NCI commemorates 50th anniversary of the National Cancer Act

By Alexandria Carolan

NCI plans to mark the 50th anniversary of the National Cancer Act of 1971 with an effort to build a coalition of support for cancer research, including raising the payline to 15% by 2025.

"With your help, this commemoration can become a movement to coalesce support around our common goals," NCI Director Ned Sharpless said Oct. 13 during the virtual annual meeting of the Association of American Cancer Institutes and Cancer Center Administrators Forum. "We'd like you to use this framework to talk about your own episodes of progress—how your own cancer centers have contributed to cancer research throughout the decades."

NCI's tagline for the campaign—"Nothing will stop us"—will be made available to cancer centers, professional societies, and others. *The Cancer Letter* will take part in this initiative.

"When I say 'us,' I really mean all of us," Sharpless said. "I really think this is an opportunity for all of us across the research community to clearly say to people with cancer, and the many more whose lives have been touched by cancer, that nothing will stop us in this regard."

The 50th anniversary of the National Cancer Act is an important opportunity to sustain public support for cancer research progress, Sharpless said.

"We are commemorating this anniversary by reflecting on our progress for the last five decades and how we got here, and also look at the needs before us—in ways that build our understanding and inspire the next generation of cancer researchers, to see the promise and the potential in continued investment in cancer research really pay off for patients," he said.

The National Cancer Act made it possible for leaders at NCI to launch game-changing scientific programs.

"I think many people are not aware of the role of the National Cancer Act in creating SEER, which I would argue is the most important set of cancer statistics in the world—or the Frederick National Lab, which is the national lab that NCI's used to administer programs like the Cancer Genome Atlas, or the Cancer Centers Program," Sharpless said. Most recently, the COVID-19 and Cancer Con-

sortium, which "has reported some of the most important and earliest findings on the pandemic with regard to cancer patients," was established in response to the public health crisis.

"I think that has been a great effort—when the National Cancer Act created the Cancer Centers Program 50 years ago, this was the kind of thing it was hoping the Cancer Center Network would do and has been one of those real successful sort of initiative and swift, nimble initiatives that the Cancer Centers Program can take on," he said.

NCI is also taking steps to address the discrepancy in funding for underrepresented populations in oncology. Specifically, Sharpless was asked how funding can be increased for Black cancer researchers, who receive grants at a lower rate than other investigators.

"It's well-documented in literature. We heard about one of the papers in the prior session. I don't think anybody sees the data and says, 'That's wrong.' I think we probably all agree it's probably right," he said. "We have a success rate problem and we have a pipeline problem, and we have to work on both."

Last week, *The Cancer Letter* published the results from a survey that assessed diversity in the leadership of academic cancer centers. The survey, conducted in collaboration with AACI, found that—of the 78 directors of cancer centers who responded—two in nine are non-white, and two in 13 are women (*The Cancer Letter*, Oct. 10, 2020).

"This is a problem that's been with us for a long time, it is going to defy an easy solution, and that's why I said in my talk that we have to create this enduring structure to look at metrics continuously and make sure this is going in the right direction," Sharpless said.

Sharpless's remarks at the virtual annual meeting follow:

I'd like to thank the AACI for inviting me to speak today, and I would like to thank their events team for all the work that it takes to put on a meeting like this. Unfortunately, we're all in the Zoom chat era, learning how hard it is to carry on these virtual online meetings.

I've been to this meeting several times in the past as a cancer center director and as an NCI director, and through the years, it really has been one of my favorite meetings. It's such a great venue for catching up with old friends—and I've always learned so much at this meeting.

It's also been a time to talk with the other cancer directors, the administrative staff. One could really learn how the other centers operate and really find out about best practices. I think it's really important to the vitality of the Cancer Centers Program.

Honestly, some of these most important conversations occurred over dinner and occasionally over drinks. I remember, one year, I got dragged out for sushi by, not the cancer center directors, but by the associate directors for administration of several of the cancer centers, and that was extremely educational. That was one year when I learned, in particular, a lot about how cancer centers work.

Suffice it to say, I miss this meeting in real life and I miss you guys, but virtual is better than nothing—I'm surprised by how effective and how much we can actually get done by this format. But I do look forward to seeing everyone in this group in person again someday soon.

In my remarks today, I'll report on NCI's budget situation and annual plan, some of our activities related to COVID-19 as it relates to cancer—and I'll highlight some other NCI efforts. My colleague, [NCI Office of Cancer Centers Director] Henry Ciolino, will be speaking later this afternoon and I think he'll also cover some of the specific aspects around the Cancer Center Support Grants Program, although I'm happy to talk on that topic as well. I do plan to take some questions at the end, so please chime in with questions if you have them.

I have no financial relationships to disclose and I will not be discussing any off-label use.

Appropriations

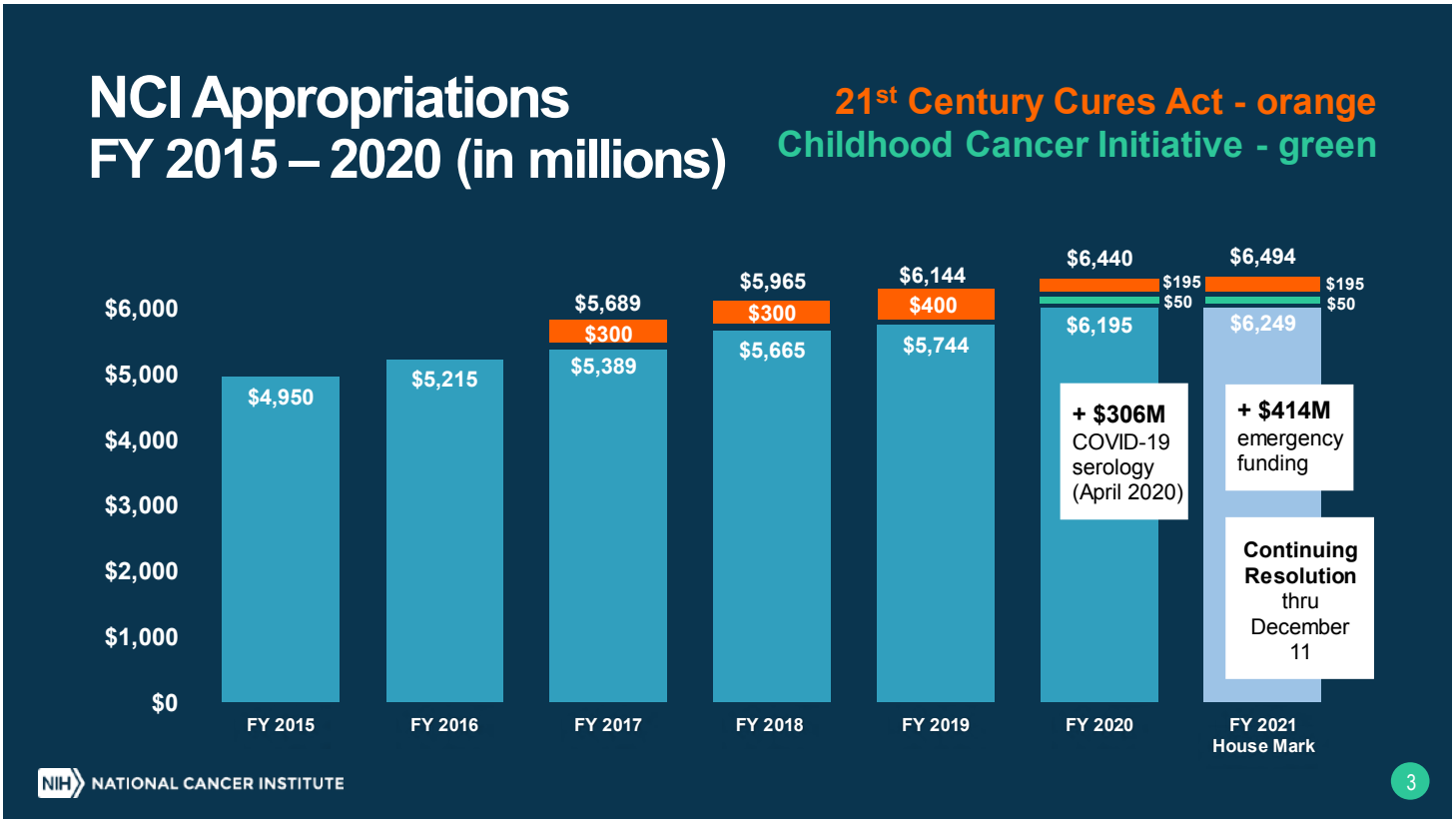
As a backdrop to my remarks today, here are the last several years of NCIs appropriations.

You can see several things here. What's most pertinent is that we've seen a steady increase in our funding since 2015, and that is really a reflection of a bipartisan congressional support for the mission of the National Cancer Institute. I would argue it really also reflects increasing appreciation for the challenges and opportunities in biomedical research in general, and particularly in cancer research.

As many of you are aware, we are currently in a new fiscal year and operating under a continuing resolution that is presently set to expire on December 11.

We are not expecting a budget in 2021 anytime soon, frankly—for current events-related reasons. The full year appropriation is, I would say, uncertain at the present.

This is not a problem for the NCI. Many years, the budget comes late in the year, and we have experience



dealing with that, but from my point of view, the sooner, the better.

You'll also see on some of the slides, over some of the years that Congress has increased our base budget, while also providing funding for some specific initiatives. Shown in the orange is the 21st Century Cures, or Cancer Moonshot funding, and in green, starting in 2020, is the Childhood Cancer Data Initiative.

I'll say a little more about these. In particular, in 2020, we actually got report language. We had a special instruction for Congress to provide additional funds for the RPG pool, the funds of the pool of monies that supports R01s and P01s. I suspect many of the cancer center directors, and their talking to members of Congress, was important in that decision by Congress to support the NCI RPG pool.

As many of you may recall, the National Cancer Institute has the opportunity, almost unique at the NIH, each year, to provide the White House and Congress with a professional judgment budget or so-called bypass budget, describing the scientific opportunities that lie ahead and the resources that the NCI would need to achieve those goals.

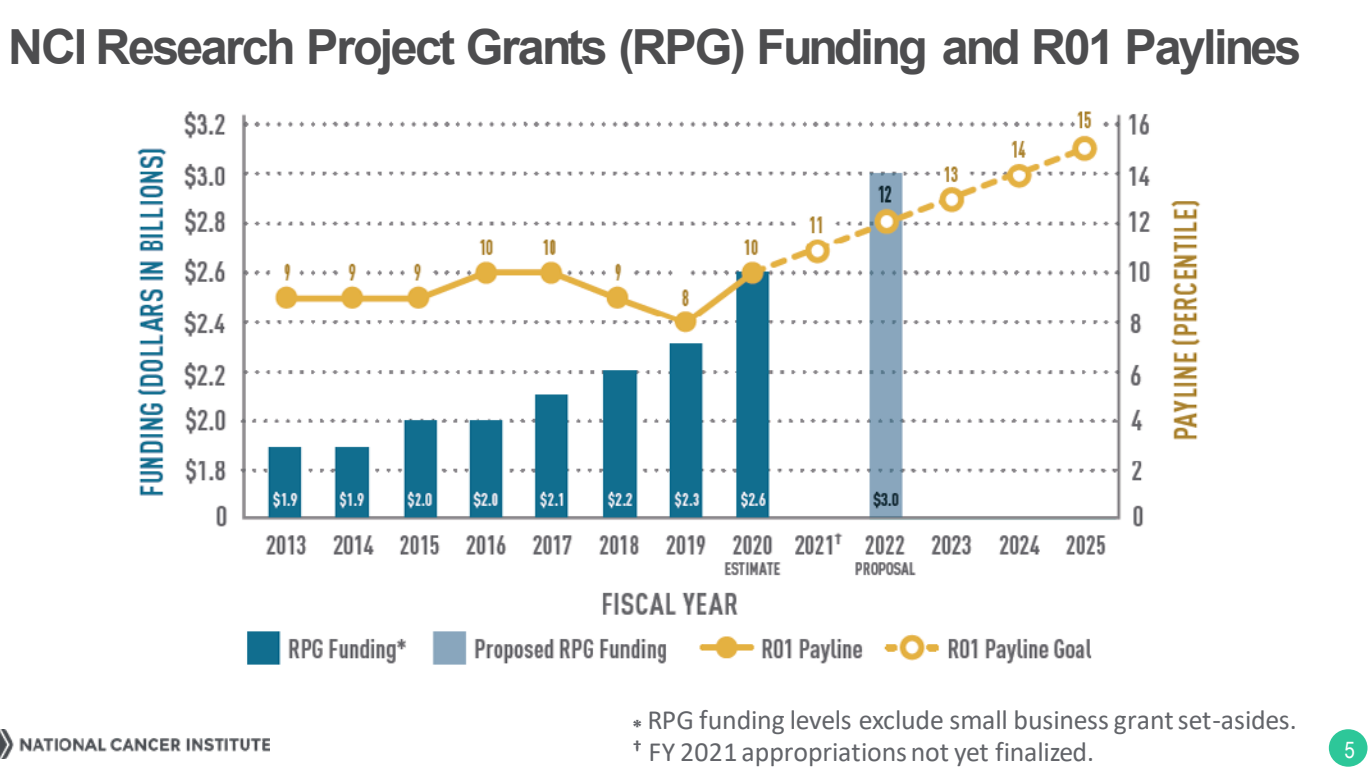
This is always for the next, next year. We just finished the 2022 bypass budget, for example, shown here.

We released this last month. The report is comprehensive and interesting and highlights some specific areas where the NCI thinks there's particular research opportunity, but I really wanted to focus on one part.

From my perspective, this is really the most important graphic in the plan, showing our request for 2022, FY2022, in relation to the RPG pool and paylines. It really shows the NCI's explicit goal of reaching a payline of the 15th percentile by fiscal year 2025.

Please note the leftward y-axis, which shows a rather large increase, a greater than $200 million increase in the RPG pool for 2020, which was a huge influx of funds. And that brought us from 8% to 10%. To get to 15%, we really would require significant additional investment over the next few years into the RPG pool.

For comparison, the entire Cancer Centers Program, which is clearly one of NCI's most popular programs—and I don't think anyone would argue is an over-resourced program—but the entire Cancer Centers Program cost something in the order of $300 million. This kind of investment in the RPG pool would be very substantial—and



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really, getting to this level would only be possible with help from Congress.

But we think this is a worthy goal as it provides support for investigator-initiated science, which we think has really been the linchpin of success for cancer research over the years. And I think this is probably a view shared by most cancer center directors.

COVID-19 and cancer

Let me now turn to a few updates about how or we're weathering the pandemic. As many of you are aware, NCI has been tasked by Congress to work on COVID directly, but we've also been very concerned about the impact of COVID on patients with cancer and cancer research.

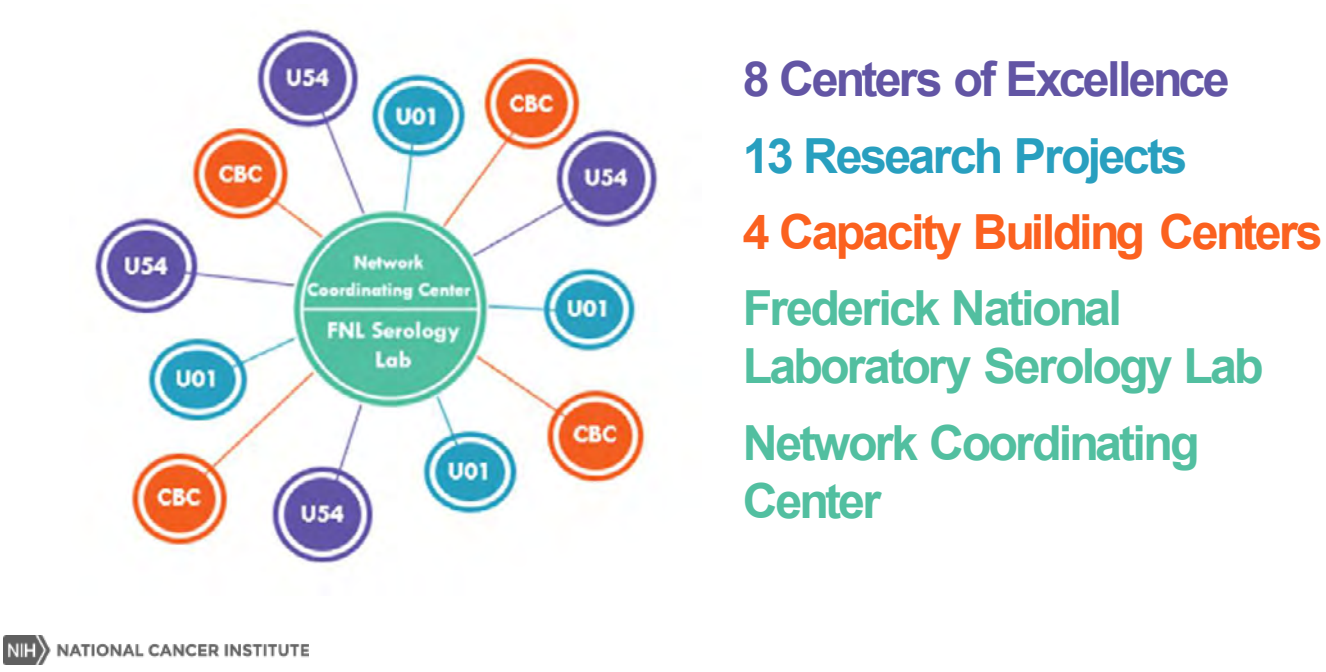
To remind you all, we were appropriated serology funds for COVID research by Congress in the fourth supplement last year to the tune of $306 million. It's important to emphasize, this is an appropriation that's separate from our base appropriation. These are special monies provided by Congress in an emergency way to help to let the NCI run some serology-related COVID research.

One of the things we used some of that funding for was this entity called SeroNet, which was launched last week—and this includes 21 grants, U54s and U01s, as well as four contracts to create a very sophisticated network with an overarching goal to increase our national capacity for serological testing, while also increasing the foundational scientific understanding of all aspects of the immune response to SARS-CoV-2, both humoral and cellular, and to use that knowledge to develop therapies and tests for immunity and vaccines, etc.

The research conducted through SeroNet will begin to answer fundamental questions expected to have a significant impact on the public health, and I would argue, also to be useful in cancer research.

Among those kinds of questions that SeroNet will try to answer, are what kinds of an immune response is necessary to gain immunity from vaccination versus a prior infection? Does disease severity correlate with long-term immunity? Do people with health conditions such as cancer have worsened outcomes? And what is the prevalence of SARS-CoV-2 infection in the U.S. across different groups, different racial and ethnic groups, or urban or rural populations?

Lessons learned from SeroNet research could be applied immediately and may prove valuable to the public health beyond the current pandemic. SeroNet Coordinating Center at the



Frederick National Lab, will coordinate and foster collaboration across all SeroNet components so that it functions as an interactive and collaborative network, with each component pursuing their own work, but also collaborating across the network in terms of sample sharing and best practices and new expertise.

In addition to NCI's funding of basic science related to serological research, we were also very interested in the problems the pandemic is creating for cancer patients. And we really have seen, and I would argue, appropriately, quite a drum beat of media coverage related to the effects of the pandemic on cancer and cancer patients. In June, *Science* ran an editorial that I authored where I shared modeling data provided by [Branch Chief in the Surveillance Research Program within the Division of Cancer Control and Population Sciences at NCI], Rocky Feuer, and colleagues from NCI CISNET.

I think many of you know CISNET—it's an intramural, extramural network that does modeling, and this work was done throughout that network involving external investigators. The estimate is that for breast and colon cancer, where the NCI has the best models, where CISNET that has the most sophisticated and validated models, we think over the next decade, we're likely to see around 10,000 excess deaths from these two cancers alone because of disruptions of screening and deferral of care related to a pandemic.

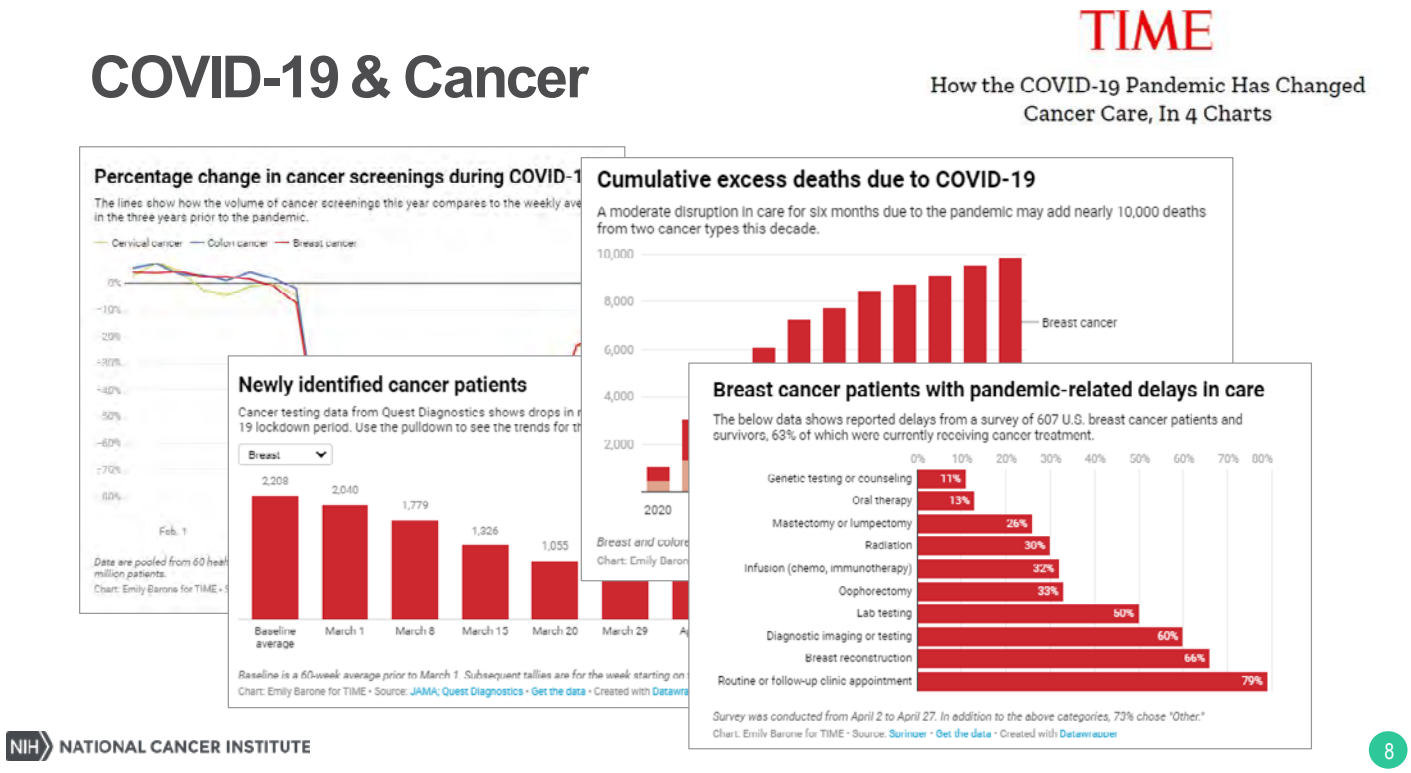
We believe this is a very conservative estimate, obviously. There's no reason to think that these disruptions and delays in diagnosis are unique to breast and colon cancer. We think this will affect other cancers like lung cancer, pancreas cancer, and create extra mortality for those diseases as well.

Additionally, when we made these guesses back in March and April, as to how bad the disruptions for the pandemic would be, I think we estimated the disruption actually wouldn't be as bad as it's turned out to be.

We thought, for example, you might only see a reduction in screening colonoscopy or mammography on the order of 75%—but in some datasets, the reduction in screening procedures has been much greater, 95% for a while.

And also, we thought deferral of—delays in diagnosis and treatment might last—a worst case scenario, six months, and now we're seeing that it may be longer in some cases as well. I think this estimate provided several months ago is, if anything, a conservative low-ball estimate.

Since June, we've really seen other analyses from a variety of kinds of data using EHR, medical records data



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> I also think we should be talking more about cancer morbidity. Mortality has gotten, I think, most of the initial focus, but morbidity, from pandemic-induced disruptions, could be a big deal as well.

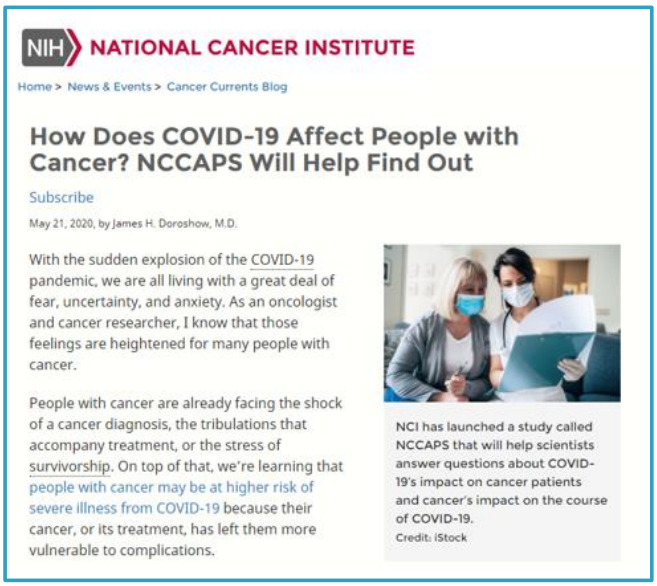
and claims data and analyses from other countries like the United Kingdom. And they're really converging to show a very similar sort of story, which is sort of illustrated in four parts from this *Time* magazine story. It is massive decreases in cancer screening, massive decreases in diagnoses, delays in care, delays in procedures, translating into excess death eventually over the next several years.

Time crafted visuals to tell the story in four parts, and I commend it to you if you haven't seen it. But I really find, most concerning here, the well-documented, greater-than-50% decrease in new diagnoses of cancer that has happened throughout the United States over the last few months. There's no real reason to believe the incidence of significant cancer has declined to this degree with the pandemic—and I believe these cancers will just become obvious in a few months at later stage, and with a worsened prognosis.

I've seen a few researchers voice the optimistic hope that this decrease in new diagnoses really may not be such a big deal—maybe it's just reduced diagnosis of indolent cancers—the cancers that would not have been so clinically significant, and that perhaps these delays may not be so bad. And this was maybe even a natural experiment to help the NCI understand the importance of overdiagnosis and overtreatment.

I do agree this is a clear research opportunity for the NCI to study these sorts of topics, but I don't believe that just non-diagnosis of indolent cancer can really explain these data. I think that view is misguided and perhaps naive. While no doubt, some diagnosed cancers are indolent and their delay in diagnosis may not be problematic, this is certainly not 50% of

NCI COVID-19 in Cancer Patients Study (NCCAPS)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Home > News & Events > Cancer Currents Blog

How Does COVID-19 Affect People with Cancer? NCCAPS Will Help Find Out

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May 21, 2020, by James H. Doroshow, M.D.

With the sudden explosion of the COVID-19 pandemic, we are all living with a great deal of fear, uncertainty, and anxiety. As an oncologist and cancer researcher, I know that those feelings are heightened for many people with cancer.

People with cancer are already facing the shock of a cancer diagnosis, the tribulations that accompany treatment, or the stress of survivorship. On top of that, we're learning that people with cancer may be at higher risk of severe illness from COVID-19 because their cancer, or its treatment, has left them more vulnerable to complications.

NCI has launched a study called NCCAPS that will help scientists answer questions about COVID-19's impact on cancer patients and cancer's impact on the course of COVID-19.

Credit: iStock

786

TRIAL SITES ACTIVATED IN

49

STATES AND PUERTO RICO

DC pending.
No site in WV.

197

PATIENTS SCREENED

143

ENROLLED

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Figures as of October 7, 2020. 9

cancers. Importantly, we're seeing decreased diagnosis of certain kinds of cancer, like lung cancer and pancreatic cancer, where indolent disease is pretty rare. I think we should all be worried about these statistics, and I think we should be collectively sounding the alarm.

I also think we should be talking more about cancer morbidity. Mortality has gotten, I think, most of the initial focus, but morbidity, from pandemic-induced disruptions, could be a big deal as well. We can expect this to be worsened for many reasons, including the fact that patients are worried about exposing themselves to COVID-19.

So instead of seeking care, they tough it out at home with symptoms and side effects that could otherwise be alleviated. Also, we're very worried about the racial disparities in cancer, and the outcomes. This is a topic where the NCI has fought against cancer health disparities, very diligently, for a long time. But now we see that COVID-19 is exacerbating some of these disparities and really having a disproportionate impact on communities of color.

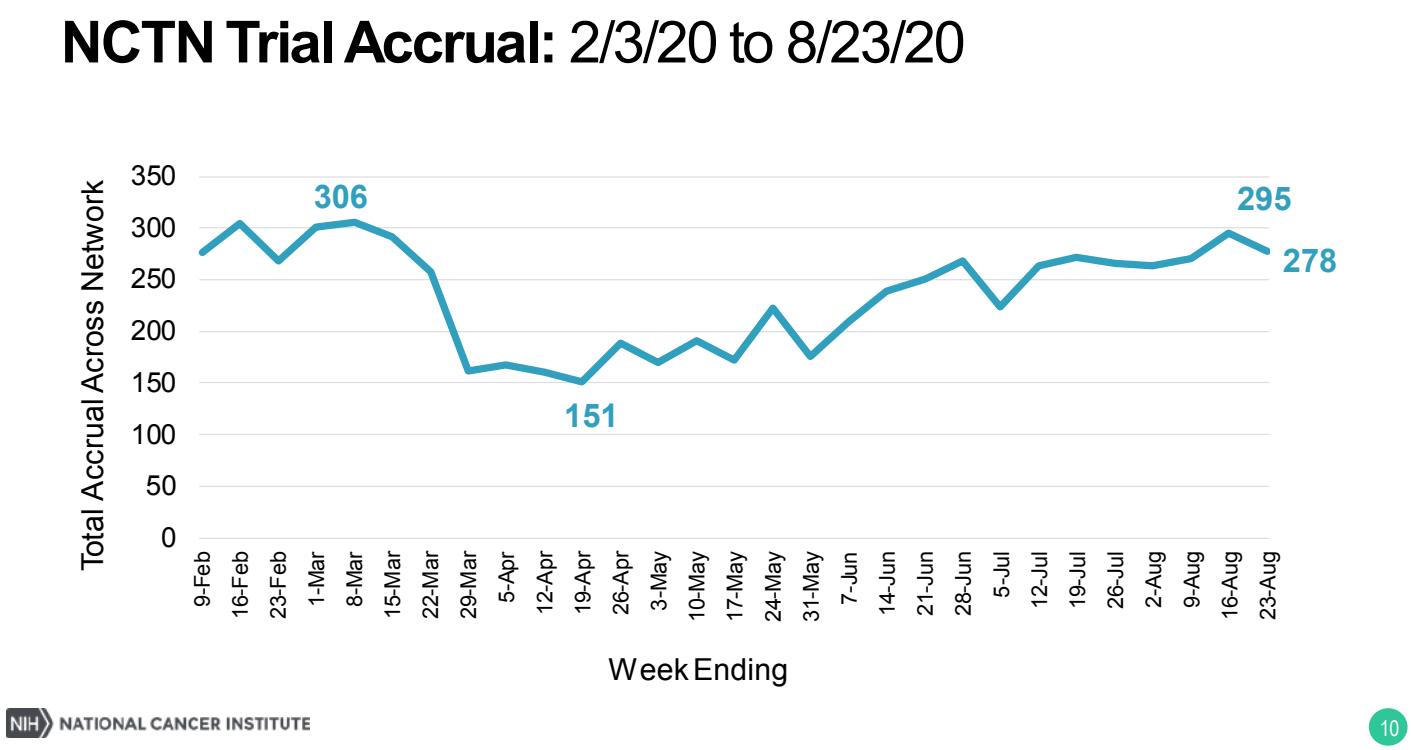
Across the cancer community, we must be creative, and we really have to find ways to prioritize care while doing so safely in a way that provides safety for our patients and our caregivers. I'm aware this is very hard to do, and there is a risk of sending out mixed messages, but I think we really have to get back to business in this regard. Cancer kills 600,000 Americans per year, including being the leading cause of death from disease for Americans under the age of 60.

Here, I would also like to point out the work would be COVID-19 and Cancer Consortium, which has been an important observational registry to collect clinical information on COVID patients, that really sprung up as sort of an organic initiative from the cancer centers, and now it's collected information on thousands of patients.

This initiative, which the NCI is very happy to support, has reported some of the most important and earliest findings on the pandemic with regard to cancer patients, resulting in these kinds of papers in the *Lancet* and *Cancer Discovery*.

I think that has been a great effort—when the National Cancer Act created the Cancer Centers Program 50 years ago, this was the kind of thing it was hoping the Cancer Center Network would do and has been one of those real successful sort of initiative and swift, nimble initiatives that the Cancer Centers Program can take on.

The NCI has also launched a clinical trial throughout our networks to understand how COVID-19 infection



affects people with cancer. This is the NCCAPS trial. It was activated in late May, really, six weeks after conception.

That included writing a protocol and getting it through a central IRB, and activating it at now close to a thousand sites, with 750 sites. The study has been very comprehensive, it includes longitudinal data collection, sample collection, biomarker analysis. And I think it will really be critical to helping us understand the effects of coronavirus in patients with cancer—patients who are enrolled at our clinic trials networks, the NCTN, the NCORP, and ETCTN. As you can see, we now have 786 sites accruing in 49 states and Puerto Rico. The trial was originally only open to adults, but now can enroll children as well.

And because this trial has the ability to totally collect patient data and samples, I think it will be especially important to address some of the long-term outcomes of COVID infection in patients with cancer. I think it will really be an important set of results for this population in the future.

Clinical trial accrual

The pandemic, of course, has also had an impact on accrual to clinical trials. Here are the numbers for accrual of trials across the National Clinical Trials Network.

This is phase III trials. The lowest weekly average accrual was 151 patients during the week of April 13, down from a typical weekly patient accrual rate of around 300. That was a roughly 50% drop at the nadir of accrual to the NCTN trials. You can see also, accrual is recovering but slowly, and it is still not fully recovered yet.

We are particularly worried about the effect of the pandemic on accrual for these very long, large trials that require extensive accrual over a long period to be successful. As stewards of federal funding, I think we have to monitor this problem closely, given that these types of trials are particularly resource-intensive.

As many of you are probably aware, we have convened a new working group under the auspices of the Clinical Trials and Translational Research Advisory Committee, or CTAC, to look at our large screening trials to help us advise us on managing this portfolio strategically.

As I said before, if there is a silver lining to be found in this pandemic, it may be in the rapid adoption of telehealth. This has clearly been a boon for patients to have an option that is more convenient than an office vis-

Telehealth & Cancer Care Delivery

Request for Information – July 2020

Scientific Gaps and Research Needs Related to Delivery of Cancer-related Care via Telehealth (Notice NOT-CA-20-080)

Webinar Series

October 30, 2020

COVID-19 Pandemic: Natural Experiment in Rural Cancer Care Telehealth Capacity

Dr. Anna Tosteson
Dartmouth-Hitchcock Norris Cotton Cancer Center

Dr. Kevin Curtis
Dartmouth-Hitchcock Connected Care and Center for Telehealth

Additional events to follow.

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it. And at the same time, this rapid uptake across the nation presents a really unique research opportunity for health services researchers and implementation scientists, to really assess what approach works best for patients.

We issued an RFI, a request for information on telehealth in July to help identify gaps in research needs, and are now considering how best to support the relevant research. Our Division of Cancer Control and Population Sciences is also hosting a webinar series, and one is scheduled later this month to discuss this topic.

A lot of interesting stuff going on in the policy arena here including new CMS guidance and an executive order, and some discussion on new legislation. Stay tuned. I think this will be a really important sort of next thing to come out of the pandemic that would really affect care of cancer patients. Let me now move on to some non-pandemic news.

Decline in lung cancer mortality

Shown here is a slide from a recent *New England Journal [of Medicine]* paper led by researchers at the NCI, Harvard and in University of Michigan to really try and understand national population statistics related to lung cancer.

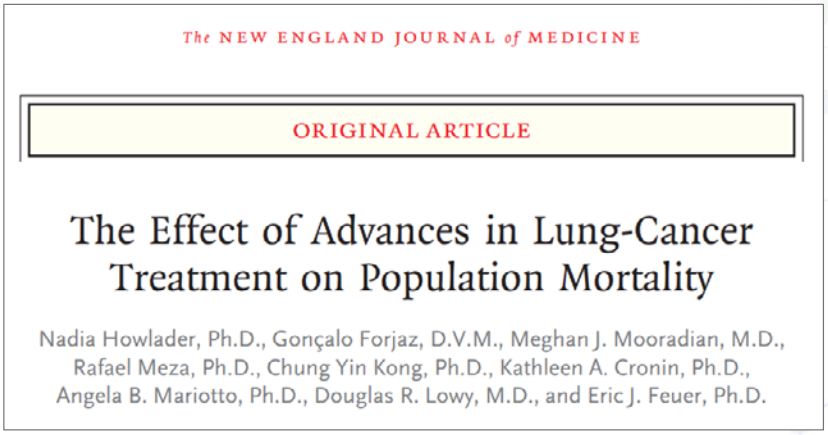
We already knew about the declines in lung cancer mortality from reports like the Annual Report to the Nation on the Status of Cancer, this is an annual report that the NCI puts out with other federal agencies to really look at cancer incidence and mortality.

By looking at how mortality rates have differed through the years across lung cancer subtypes, this analysis, which used novel analytic techniques, sheds important light on what accounts for those long-standing declines in non-small cell lung cancer mortality. In a nutshell, the analysis shows that advances in treating non-small cell lung cancer account for a significant portion of recent mortality declines for this disease.

And since this analysis really only included data through 2016, I believe we can expect further improvement in non-small cell lung cancer mortality in the years ahead as the positive effects of other treatments—so greater penetrance, for example, of immuno-oncology, as well as lung cancer screening. As these other trends become more evident in national statistics, I think that we will continue to see good progress in non-small cell lung cancer for a while.

As I wrote in an editorial for *Stat*, the progress made in non-small cell lung

Lung cancer mortality

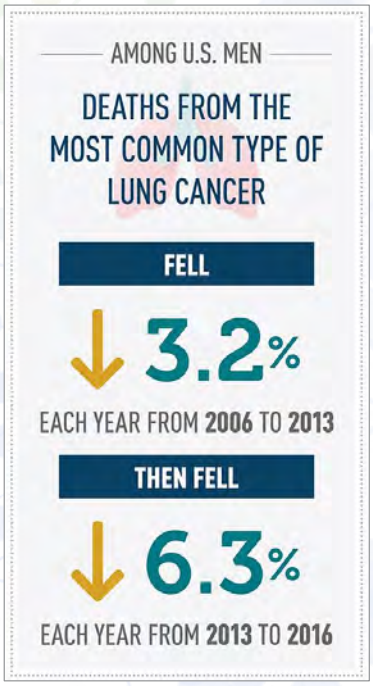

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

The Effect of Advances in Lung-Cancer Treatment on Population Mortality

Nadia Howlader, Ph.D., Gonçalo Forjaz, D.V.M., Meghan J. Mooradian, M.D., Rafael Meza, Ph.D., Chung Yin Kong, Ph.D., Kathleen A. Cronin, Ph.D., Angela B. Mariotto, Ph.D., Douglas R. Lowy, M.D., and Eric J. Feuer, Ph.D.

AUGUST 13, 2020



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cancer and also in melanoma illustrates what is possible even for cancers that long ago had really terrible prognoses for most patients. When I started in oncology, I thought melanoma and non-small cell lung cancer were two areas where we almost would never hope to make progress, and now we have really great mortality decreases at the population level related to treatment.

But I really see our job at the National Cancer Institute as keeping that research engine going and building on these important successes to fill remaining gaps, to ensure that the progress we've seen in those diseases can be realized for other types of cancer, like glioma and pancreas cancer, etc.

That is really both the hope and the expectation for the NCI now, is to translate success from other areas into these resistant recalcitrant malignancies.

NCI partners with CRUK

Last month, we kicked off a partnership between the National Cancer Institute and CRUK, Cancer Research UK, to support the Cancer Grand Challenges program. This program is similar to the NCI's Provocative Questions program, but it adds an international, multidisciplinary element to that. The teams must include international teams, and they must include patient involvement.

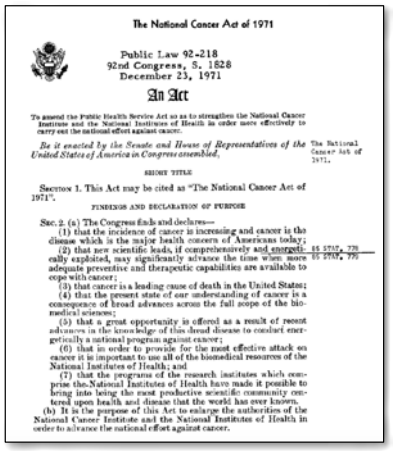
I want to be clear. This does not represent a diversion of resources from other NCI programs but, rather, a repurposing every other year of the PQ funds. So we will have PQ funds in even years, and Cancer Grand Challenges in odd years, using the same funds, for example, in alternating years. This includes significant UK funding as well.

To date, American scientists have competed very successfully in the UK Grand Challenges program, and we have every expectation that American scientists should compete very successfully for this program in the future as well.

The challenges framed as questions will be published tomorrow [Oct. 14], so stay tuned. The first stage in the competition involves expression of interest from teams, which will be accepted through April 2021.

I see Cancer Grand Challenges as a way to encourage and support high-risk innovative cancer research on a large international scale and, really, as a complement to our investigator-initiated portfolio that I discussed earlier. I think this will also stimulate some truly innovative ideas to overcome barriers and further advance

The National Cancer Act of 1971 — A Watershed Moment



The National Cancer Act of 1971

Public Law 92-218
92nd Congress, S. 1828
December 23, 1971

An Act

To amend the Public Health Service Act so as to strengthen the National Cancer Institute and the National Institutes of Health in order more effectively to carry out the national effort against cancer.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

The National Cancer Act of 1971.

SHORT TITLE

SECTION 1. This Act may be cited as "The National Cancer Act of 1971".

FINDINGS AND DECLARATION OF PURPOSE

SEC. 2. (a) The Congress finds and declares—

(1) that the incidence of cancer is increasing and cancer is the disease which is the major health concern of Americans today;

(2) that new scientific leads, if comprehensively and energetically exploited, may significantly advance the time when more adequate preventive and therapeutic capabilities are available to cope with cancer;

(3) that cancer is a leading cause of death in the United States;

(4) that the present state of our understanding of cancer is a consequence of broad advances across the full scope of the biomedical sciences;

(5) that a great opportunity is offered as a result of recent advances in the knowledge of this dread disease to conduct energetically a national program against cancer;

(6) that in order to provide for the most effective attack on cancer it is important to use all of the biomedical resources of the National Institutes of Health; and

(7) that the programs of the research institutes which comprise the National Institutes of Health have made it possible to bring into being the most productive scientific community centered upon health and disease that the world has ever known.

(b) It is the purpose of this Act to enlarge the authorities of the National Cancer Institute and the National Institutes of Health in order to advance the national effort against cancer.

The Act united patients, scientists, doctors, industry, and government in one vision.

- Created the nation's clinical trials network, leading to practice-changing trials for patients.
- Established the NCI-designated Cancer Centers Program of world class institutes, driving research and patient care.
- Built SEER and improved cancer registries.
- Created Frederick National Lab, providing the NCI with a government lab for targeted, high priority cancer projects.
- Accelerated research on prevention, screening, diagnosis, and treatment of cancer.
- Increased support for basic research, providing a critical underpinning to our cancer progress.
- Assured high-level access of the NCI to the President.
- Appointed advisory committees, allowing the NCI Director to explore new issues and opportunities.

fundamental biological knowledge, and its clinical application to cancer.

Increasing diversity in oncology

As we heard this morning in a great session on equity, inclusion, and diversity—this is really an important job for the NCI, and an area where I think the National Cancer Institute can really make a difference.

I commend the AACI on their work in this area and the important data they've gathered recently through a survey and editorials just published in *The Cancer Letter.* Just as AACI's undertaking new efforts in this area, at the NCI, we are in early stages of a new equity and inclusion program as well.

Cancer research really can't solve systemic racism and injustice by itself, but we can certainly look at our own work as individuals and as a community of practice and commit to taking action to make things better where possible. One of the clear goals here is to create an enduring structure to take these pernicious problems on in a systematic and enduring way, so not just write a single report and say, "Okay, now we're done with racism," but, rather, create a process of continuous monitoring, learning, and improvement.

At NCI, we've created a structure shown here. It includes an equity council, which serves a steering committee role, which I chair, and then these three working groups with the titles that are shown.

One addresses the topic of cancer health disparities, one addresses the topic of training the scientific workforce, and one addresses the culture

“Cancer research really can't solve systemic racism and injustice by itself, but we can certainly look at our own work as individuals and as a community of practice and commit to taking action to make things better where possible.”

Why is it important to commemorate the 50th Anniversary of the National Cancer Act?

within the NCI with regard to creating an equitable and inclusive community.

To be clear, I think that these are areas where the NCI has some success and some good things going on. I would argue the disparities research portfolio of the NCI is among the strongest in all of biomedical research, probably in part because of the Cancer Centers Program, in fact—an interesting thing to discuss. But that doesn't mean it couldn't be better. I think that we need to look at the portfolio of cancer health disparities research and make sure we're funding the right things in the right amounts and the right time.

Similarly, with training, we heard in the prior session about some of the great things the NCI's done in this regard, with the CURE [Continuing Umbrella of Research Experiences] Program, the iCURE [Intramural Continuing Umbrella of Research Experiences] Program, the YES [Youth Enjoy Science] Program.

I think those are really exemplary programs that are really admired by all of biomedical research in the rest of the NIH—but that doesn't mean they couldn't be better, and it's important to continue to think on that topic as well.

Lastly, the culture at the NCI is good. This is a great place to work, and we have great mission and passion. But, again, as I've done my internal listenings, where we're going to talk to people across the NCI—clearly, we still have some work to do, and we can make it better. So, that's really the goal here, is to tackle these problems head on.

The NIH is making a similar set of efforts, and our efforts at the NCI mesh well with those at NIH. We're already seeing some exciting things happen from both the NCI and NIH efforts. I will highlight one.

One example that I'm very excited about is the FIRST [Faculty Institutional Recruitment for Sustainable Transformation] initiative, and this is an NIH Common Fund program, meaning the funds come from the NIH Common Fund—but administratively, this program is led by the National Cancer Institute with a related Coordination Center grant program led by the National Institute on Minority Health and Health Disparities.

So NIH, MHD, and NCI have worked closely in crafting this program—and this effort seeks to create cultures of inclusive excellence at NIH-funded institutions by implementing a set of well-integrated, evidence-based strategies and evaluating their impact on

pre-specified metrics of institutional culture, inclusion, and diversity.

This term, inclusive excellence, really was chosen as it is a philosophical approach to higher education administration and processes. That means attending to both the demographic diversity of faculty and students, as well as the need for developing a climate and culture at institutions that will have a chance to succeed everyone interested in STEM disciplines.

We anticipate issuing the U54 funding announcement very soon—hard at work on that, and I hope that all of you will pay attention to it. I believe the cancer centers have long been interested in the topic of training a diverse workforce and I think are well prepared to play a role in these first initiative grant proposals.

Now, let me close my presentation today by taking a moment to focus on a really historic moment in cancer research.

Nothing will stop us

Next year will mark the 50th anniversary of the National Cancer Act. The legislation didn't, as many of you know, create the National Cancer Institute, but it did authorize or accelerate a number of programs that now really form the backbone of the nation's investment in cancer research.

These are efforts that are, I think, probably well-known to cancer center directors, but not the general public. I think many people are not aware of the role of the National Cancer Act in creating SEER, which I would argue is the most important set of cancer statistics in the world—or the Frederick National Lab, which is the national lab that NCI's used to administer programs like the Cancer Genome Atlas, or the Cancer Centers Program.

The National Cancer Act made the NCI director a presidential appointee. It also gave us the opportunity to present the bypass budget, so it improved access of the NCI to the White House and to Congress to talk specifically about the needs of cancer research.

So it's been really important, and it was really important for patients. It took cancer out of the shadows, and made it a diagnosis one could talk about, and it led to a real movement in patient advocacy related to cancer. We'll be commemorating the anniversary in a variety of ways in 2021, and we'll be looking to partner with you and others across the cancer research community to reflect on what

has been accomplished since 1971 and what opportunities still lie ahead.

As I see it, more important than what the National Cancer Act provided in terms of new funding is what it meant, what it really did for cancer research, and what it meant for patients—transforming how we think about cancer as a diagnosis. The act really drew the nation's attention not just to the tragedy of cancer, but to the hope and promise of research.

Now, there are two obvious potential critiques of commemorating this anniversary, and I will address those directly. First, the notion that 50 years is a long time, and cancer is still a painfully large problem with us today. Won't we be drawing attention to this milestone, simply for people who want to say that cancer research hasn't been a successful endeavor? Second possible criticism is it sounds like we might be doing a victory lap at a time when still, 600,000 Americans die from cancer a year. Clearly, no one wants to send that signal as well.

My answer to both those concerns is contained within this critique. Yes, we have a long way to go, but not because we failed. Actually, we've been quite successful, I would argue. But, rather, because cancer is a far more complex problem than we understood back in 1971.

Some of you will remember that the expectation was cancer would be cured by the country's bicentennial birthday, by 1976. So, the expectation was a pretty rapid solution to cancer, and cancer turned out to be a much harder problem.

To continue to make progress depends on inspiring and sustaining public support for that mission—and, really, the anniversary is an important opportunity to build on that collectively as a group.

Second, we are not celebrating. We are commemorating this anniversary by reflecting on our progress for the last five decades and how we got here, and also look at the needs before us—in ways that build our understanding and inspire the next generation of cancer researchers, to see the promise and the potential in continued investment in cancer research really pay off for patients. Ultimately, this is all about patients. We've made a lot of progress, but we can't rest on our laurels, and we really have to declare as a community that nothing will stop us.

That is the tagline for the educational efforts we want to release around the National Cancer Act. When I say us, I really mean all of us. I really think this is an opportunity for all of us across the research community to clearly say to people with cancer, and the many more whose lives have been touched by cancer, that nothing will stop us in this regard.

With your help, this commemoration can become a movement to coalesce support around our common goals. For example, as I mentioned earlier, 15 by 25, the 15th percentile by 2025, will require help from Congress. That's a story we'll tell. That's an argument we'll have to make.

NCI will be talking about 50 years of progress, and we'd like you to use this framework to talk about your own episodes of progress—how your own cancer centers have contributed to cancer research throughout the decades. I look forward to a very busy year, joining with all of you to recognize this incredibly important milestone.

Thank you for inviting me to speak. I look forward to discussion. I hope there'll be a lot of questions, and I can't wait to see you all again in person someday soon.

Roy Jensen, immediate past president of AACI, professor of pathology and laboratory medicine, anatomy and cell biology, cancer biology and molecular biosciences, director of The University of Kansas Cancer Center, director of Kansas Masonic Research Institute, and William R Jewell, MD Distinguished Kansas Masonic Professor:

Thanks, Dr. Sharpless. That was a fantastic talk and a great message to get us revved up for the 50th anniversary of the National Cancer Act.

We have a number of questions that have come in on the chat line. First one is actually from my successor, Karen Knudsen, who's going to be our president next year, as you know.

She said she very much agrees with the sentiment that we should be collectively sounding the alarm, but as individual centers, it can be difficult to rise above the noise and COVID news. What can NCI and AACI centers do to increase penetrance of our voices?

I think this came in around the time you were talking about the decrease in screening and prevention efforts.

Sharpless: It's a good question. I think there are a lot of things. Maybe one of the most important, I think, is really, to continue to talk about this and to educate the public on this. I think there is a lot of fear around COVID-19, and it's changing patient behavior, and it's limiting people from being willing to come in for necessary medical treatment or necessary medical appointments.

So we really have to explain to patients that deferral of care, non-diagnosis of

symptoms, ignoring screening, these kinds of things—are not good for them in the long term. It's, of course, nuanced. It's safe to miss a mammogram for several months or maybe a little longer—but it's not safe to put up evaluation of a new onset dysphagia, or a new serious symptom for very long. So we have to help our patients balance the risk of various kinds of medical procedures.

I still get called by a lot of journalists on the topic, there's still a lot of interest in this, and I think there's still a lot of common misunderstanding. We as a community can probably do a better job of explaining to patients why they need to seek cancer screening.

We can also make sure our hospitals are fully open. I've heard many stories of, "My hospital's mostly open, but one radiologist won't come in for the mammography clinic, so we can't do that"—that kind of stuff. I think we just need, as I said, to get back to work and really do right by our patients.

I think another thing that we should do is embrace best practices, to try and make care as safe as possible in our clinics and hospitals, but also for the caregivers and for the patients.

Now, it's helpful because a number of societies like ASCO and the American College of Surgeons have started to put out guidelines for appropriate care in the pandemic era, and how you can really do both. And, of course, the NCI has a real interest in the research opportunities this provides about how to do this safely.

But suffice it to say, it's not one silver bullet, it's many, many things that we have to do together—both the NCI and the caregivers and the researchers—to really communicate this need to our patients and make sure that we don't just change one public health emergency for another.

Jensen: A number of questions have come in in regards to the payline issue and the proposal to increase the RPG pool. How likely is it, do you think, that this will go forward and be executed on, by Congress? What can we do to facilitate that?

Sharpless: Right. The bad news about the National Cancer Institute is our funds are appropriated year to year, and no Congress can compel a future Congress on how to spend the funds. We don't really know what our budget's going to be every year, other than we know that people in Congress admire the NCI and think it's a good use of federal monies.

Generally, on both sides of the aisle, there's an interest in increasing the funding for the National Cancer Institute when funding allows, but—of course, Congress, the appropriators, have many other concerns, and so the NIH and NCI is just one of many things in any given budget year. We have no future crystal ball on how funding is going to go, other than the trend in the last five years has been pretty good and we hope that will continue.

The NCI is really saying that if Congress helps out, if it does its part and provides modest increases, maybe even large increases, to our base funding—then our top priority would really be to try and do the payline issue, because that's I think, now, something that Congress understands.

It's an important cause I think we can all get around. It's easy to explain. But it's also very, very important. It's particularly important for junior scientists, who are really considering what career they want to take on, if they want to be cancer researchers, or some other kind of scientist. So it's really important that cancer look like a welcoming field where one could make a living as a scientist.

I mentioned funding from Congress is one variable—the other variable is how many new grants are we going to get. As I think many of you are aware, the NCI, since going back to about 2008, but particularly since 2013, has seen this massive increase in the number of grants. More new grants have come to the NCI than to the rest of the NIH as a whole.

Our delta, since 2013, has changed more than the entire NIH. That's a really interesting question why that happened. I think part of the answer for that, by the way, spoiler alert, is probably cancer center programs have been very successful of leading junior scientists in cancer research.

In any event, that's a good thing. I think many, many scientists bringing their new training and their new ideas and their new ways of thinking into cancer research and trying to make new ideas for our patients is really great for cancer patients, and is really one of the reasons why the engine of therapeutic discovery in cancer has been so strong of late.

But it does create a problem for paylines because paylines are just grants funded divided by applications received, and if the applications continue to increase at that tremendous pace, then it's hard to keep up with, even with more funding from Congress.

That was really why paylines went down to 8%. It wasn't the NCI was spending less on R01—in fact, it was going up. It's just the rate of new applications increased so dramatically that we couldn't keep up.

And we don't know what's going to happen there. The pandemic is a big

unknown. I think a lot of people were unable to work for several months, in the lab, at least, and presumably some of those people wrote papers and grants, and we may see our grant applications go up at some future date. We have not yet. So, for our first round in '21, the data I've seen look about flat. We may see grant numbers go up in the second round, and that would also have an impact on paylines.

It's a real unknown, but it's very, very important. I think the entire National Cancer Institute is committed to this goal. We have uniform buy-in. I think the cancer community is committed to this goal and understands it's important and is good at talking to Congress about it. I think if we keep making it known this is what we want to do, then that really will increase our chances for success.

Jensen: Well, I've heard from a number of our junior investigators in particular, and they're very appreciative of the fact that the NCI has basically heard their cries. They recognize that you have set a plan up for future success there, so thanks.

Sharpless: By the way, one important point to make, that even before paylines started going up, one of the first things we did was try and increase the paylines for early stage investigators and also length of the awards—so we introduced this R37 award. We did a few things for ESIs, early stage investigators, before we could really even—but that wasn't good enough, we felt, and so now we've tried to have all boats rise by increasing the general R01 payline.

That correspondingly further drives up the early stage investigator payline, which is now getting to a number where, if you're an ESI, you can look at that and say, "Well, I might be able to get a grant at the NCI." That is an achievable goal, as opposed to some of the lower numbers we had before that were really a turn off for these scientists.

Jensen: You mentioned the increase in utilization of telehealth for cancer patients in your talk. A number of cancer center directors have been talking about, how can we foster and preserve this option for our patients? Because, frankly, our patients love it.

Every single appointment with a physician does not have to be in person if you're just checking up on them, or they're getting more medications or whatever. But we're already beginning to see the advent of insurance companies dialing this back, and frankly, it would be a real tragedy if we don't utilize the lessons we've learned in being able to take care of people in their homes. So, what can we do to make sure that this continues on?

Sharpless: Roy, I totally agree. I think that this has been really great for patients. It's been great for cancer care. It's been great for clinical trials accrual. We can consent people over the phone now with telehealth. It's good for cancer research. It's a win-win-win for patients, for caregivers, and for scientists.

Really, the question is how do we prevent the loss of momentum—and I totally agree with what you said. I hear almost daily from someone telling me about some effort to roll back some aspect of telehealth, whether it be state line licensure, or covering certain kinds of visits, or increasing copays or all kinds of stuff.

A lot of the important driver here will be the federal behavior, particularly what CMS decides to do. As a federal employee, I am not allowed to tell CMS what to do. That's not my job. But I will say that I think [CMS] Administrator [Seema] Verma has been very outspoken on this topic in a really good way.

She's very carefully articulated the successes of telehealth and her desires that CMS preserve some of the things that are working, at least, for future patients. I think that's a really good message and also was accompanied by an executive order from the president, making some of the same noises. I think that's positive, and that tells you that there's support within this administration for continued success, continued preservation of this ability to do certain things by telehealth, which would be really good for patients.

I think this is a message that the private payers are going to have to hear from the doctors and the clinicians and the hospital executives and the patients themselves. They're going to have to hear that if they try and roll these things back, that may compromise care. They will listen. They will be convinced by argument.

Right now, as you're aware, there really aren't a lot of data on what's good and bad for telehealth. We just kind of changed. Payers are rightly going to ask, "Is this really working for patients? Are they getting as good care, and should we pay the same amount for these kinds of visits?"

So that, I think, is where the NCI does have a role. We really can fund grants and fund science to address that topic of what is best for patients by telehealth. As you can see, DCCPS, as I mentioned, is working on this—really, at amazing breakneck speed, because they realize these issues are coming to the fore immediately in national life.

I think the most important thing that cancer centers can do, really, is talk to the payers and talk to Congress about this, because it would be so ironic to go through this terrible pandemic and have all this loss of life, and the one kind of good thing that came out of the pandemic was better telehealth and then to have that go away. That would be just very frustrating.

Jensen: One possibility in the way that NCI could support this might through the Supplement Program, where the NCI could ask specific questions around the applicability of telehealth in the outpatient setting. I don't know if you've considered that or not.

Sharpless: Well, let me tell you, DCCPS [Division of Cancer Control and Population Sciences] is, as you know, a well-worn user of the supplement—they had seven supplements in 2020 or something.

That's the part of the NCI that does supplements really well. But there might be other ways to fund this kind of science, too. But, yes, providing some funds to important research questions in this topic, as quickly as possible, is a stated goal of the NCI. That's why [DCCPS Director] Bob Croyle, led that RFI to get data on this topic to really make sure we had the right questions. As I said, it's a real interest there, now.

Jensen: Another question has come in, and this relates to the issue of health equity and attempts to diversify the workplace. As you're well aware, there's been data generated, actually—a number of KU [Kansas University] investigators have looked at this issue, that underrepresented minorities, particularly African American investigators, seem to be funded at a lower rate than other investigators of some of these grants. What are your thoughts on this, and what potential things can be done to mitigate this and improve this, if you will?

Sharpless: Since I've been at NCI, we've really taken a careful look at these data. We try to get various sources to really get the right information, and I think we now have those data in hand, and they paint a pretty clear story.

It's a long-winded answer, but I'd like to describe this, and maybe the comparison with female investigators is illustrative. There are not enough female investigators funded by the NCI. I think that about 30% of R01s, maybe a little more, go to women—and that number has been gradually increasing, but I think at a rate that is frustratingly slow and not high enough and is even worse for certain mechanisms, like the SBIR [Small Business Innovation Research] Program, for reasons I don't understand—has particularly not done a great job of recruiting women scientists.

But when you really look at those data, the numbers are improving, and have been for more than a decade. When you look at the success rate of women who are PIs under R01, their grant is as likely to get funded at any score as a male investigator. The problem there, really, is a pipeline issue. There are too few women applying for these grants, and we have to think about how we can increase that number. But if they do apply for grants, their chances of getting funding are not much different from for male investigators.

So, then we look at the underrepresented minority population, particularly Black scientists, and there, the data are different. There, the data haven't improved in 20 years. There's really kind of a flat number, where we have a low number of R01-funded Black scientists.

Data are a little better for Hispanic, Latinx scientists—but, really, the African-American population of cancer researchers hasn't improved markedly in a while. Then, if you also look at the chances of funding success, they're lower. So, a Black scientist is less likely to have their grant funded than a white scientist, or an Asian scientist. It's well-documented in literature. We heard about one of the papers in the prior session. I don't think anybody sees the data and says, "That's wrong." I think we probably all agree it's probably right.

It's a real problem, and there are not a lot of explanations for this. One possible explanation is there is some sort of structural bias built into the review process, or in the awarding of grants process, and I think the NCI has to seriously consider that possibility and look carefully at how grants are obtained and even called for.

How do we create funding opportunities and disseminate that knowledge? How do they come in? How are they reviewed and scored, and who do we choose to fund? That three buckets I showed, that's one of those buckets—is really looking at this workforce problem. By the way, I will mention, not only, though, is there a problem with the funding success rates for Black investigators, but there aren't enough of them.

The number of submissions is very low and clearly an area where we'd like to do more. So, we have both problems. We have a success rate problem and we have a pipeline problem, and we have to work on both.

The most visible efforts that the National Cancer Institute has made with

regard to the pipeline is really stuff that I think is familiar to most of the cancer center directors related to the CRCHD's [The Center to Reduce Cancer Health Disparities] efforts, the CURES program, the iCURES program, YES program, which is a little newer.

These are efforts to really identify talented young scientists, in some cases, going back to middle school or high school, but get them interested in cancer and then get them in the pipeline and then keep them advancing at every stage.

As I said, that program is the envy of biomedical research. I think it is a good thing the NCI does. But as successful it is, we still aren't seeing enough scientists come through the pipeline, so what can we do to increase that number? We're talking about that a lot, and [CRCHD Director] Sanya Springfield, who runs CRCHD, has a lot of great ideas on this topic.

I'll tell you one other thing we did in 2020, which is we, as I'm sure many of you are aware, are not allowed to condition an award on race or gender. So we can't say, "Here's an R01 program just for women or for Black scientists," or something like that.

But we are allowed to use select pay to promote diversity of thought within the RPG pool, to make sure that we really are getting grants funded that really cover the waterfront of cancer research needs. We used select pay, meaning picking up grants outside the 10% payline, to pick up some awards for scientific areas that we thought we really needed to be funding that also had a particularly diverse group of PIs. I don't think that is a long-term sustainable solution, or that by itself isn't enough, but I think it was a measurable thing we could do immediately in 2020.

The luxury of the NCI, the good news, bad news of the NCI—is that we have so many good grants that we can pick up an 11th percentile—I mean, a 13th percentile is still a smoking good grant. That is a really good proposal, and that's outside our payline, so we have the real luxury of picking up things when we want to. So, those are the things we've done, but we're really working to address both the pipeline and the success rate issues.

This is a problem that's been with us for a long time, it is going to defy an easy solution, and that's why I said in my talk that we have to create this enduring structure to look at metrics continuously and make sure this is going in the right direction.

Jensen: Well, one other thing I want you to make sure you take credit for is the change at the NCI in terms of the T32 program and the ratio of postdocs to graduate students in that. While this is not going to be an immediate solution, I think, longterm, that's going to have a significant impact on the number of diverse investigators that get in that pipeline. So, thank you for doing that.

Sharpless: Thank you for that comment.

Jensen: One other question has come in around access to data, and, specifically, how can the NCI and AACI members get access for cancer centers to their state's SEER data? Many centers struggle with this due to state requirements around the data. Is it possible for there to be some kind of congressional mandate to free up this data in a more timely fashion?

Sharpless: That's an interesting idea. I think there's unlikely to be a congressional interest in this topic unless it's reported out to Congress. I think that, often, Congress, I don't think it really understands the importance of SEER and national data.

Maybe the pandemic will have changed people's minds on that topic. I think the pandemic has shown national data networks are very valuable. So maybe, with the times, people will be a little more receptive to this topic. But I can tell you, in the past, when I have gone to talk to legislators about big data it's kind of—the eyes glaze over, and it's a hard thing to sell legislators on. So I just say, "data's very expensive and we need to do it," and don't go into the details.

But I think it's a really important question. First thing to say, is part of the answer may be a little weedy, and if I don't get to the right answer, feel free to contact me and I will refer you to people in SEER who may be able to help with some of the data transfer.

As I think probably many of you are aware, NCI's recently expanded SEER. SEER used to cover—I'm kind of making up the numbers—but it was around 35% of the nation, and now it's more like 45% of the nation through creating some new contracts in new states to pick up additional parts of the U.S. population. I think that will further enhance national data collection, particularly of certain populations that weren't well-represented in the old SEER. This is really under [SEER Associate Director] Lynne Penberthy and Bob Croyle's leadership.

SEER, by the way, is a phenomenal program. It has really undergone substantial changes. This is not your grandfather's SEER. If you think of it as a list of cancer death rates from 1970s, it used to be that—but now it's got linkages to Walgreens, and EHR data, and very interesting linkage technologies across multiple datasets.

It's a really exciting big data effort, and for those of you that haven't used SEER in a while, I would recommend you look back at it. Under Lynne's leadership, SEER's taken on new capabilities, it's grown, and one of the things that Lynne has made a real focus is to try and get a more rapid turnaround of the data. In certain states that don't have a SEER registry, they rely on the state to collect a CDC-run registry that, frankly, we don't think collects as much data as we would like and takes longer, which is one of the reasons why we're so proud of SEER. But we use data from both kinds of registries for our national cancer statistics.

One of the problems with SEER, as you can imagine, is it gets on the order of 600,000 pathology reports for cancer every year, and to read 600,000 pathology reports is really hard.

One of the things Lynne has been trying to do is disseminate new tools, natural language processing tools, for example, to help abstract the documents that come into SEER. That's part of the delay.

If it used to be two years from the incident diagnosis to the getting in the data, they are trying to get that down to a matter of months. But it is a formidable data challenge and certainly an area where the NCI's made significant investment and will continue to do so.

But it's working. I think, even though SEER has its flaws and there are things about it that we wish worked more quickly, as I said, it really is the most important set of cancer statistics in the world—and the linkage to Medicare and other databases has really provided real advances for cancer research and cancer care. It's a vitally important thing the NCI needs to continue to innovate and reinvent and do well.

Jensen: Another question relates to what areas of basic research do you see as being particularly exciting, or having the potential to make great advances going forward over the next few years?

Sharpless: One of the reasons why I'm a big believer in the RPG pool is I don't think federal officials are very good at predicting. If I knew, we'd just have a funding announcement on that topic, but the cancer research has taught us that these assistant professors with crazy ideas at institutions you've never heard of—they come up with immunotherapy, and that was Jim Allison, when he started his career, right? They have really inventive ideas that are much better than the NCI director's ideas, and that's why funding the RPG pool and investigator-initiated science is really, really important.

Having said that, areas where I see obvious opportunity for the NCI really are—I think our experience with The Cancer Genome Atlas has taught us that if the NCI creates great datasets and makes them available to the community, they'll get used for really innovative purposes that we never even envisioned.

The TCGA has been so successful for that reason. So now we're trying to do that at greater scale, so creating the CPTAC [Clinical Proteomic Tumor Analysis Consortium], which has proteomic as well as genomic data and some clinical information to make those data available. We now have a canine research data commons to provide a whole different kind of data on cancer outcomes, that I think is interesting and useful.

I didn't talk a lot about the Childhood Cancer Data Initiative today, but that is really an effort to do this at scale, to get data, really, from every child with cancer in the United States, some genomic data, some claims data, whatever data we can get from whatever source, and try and make that linked in a common way and make that maximally useful.

So, creating large sets of interoperable data that are proteomic, genomic, cancer imaging archives, and then use novel analytic techniques like machine learning, etc., and high-performance computing is really a good opportunity for the NCI.

Another, I'll mention, that we're really starting to think through in a big way, is the advances in the interesting technologies related to early detection of cancer using blood-based tests, so liquid biopsies, if you will.

This is technologies like the one developed at Johns-Hopkins, or the GRAIL technology, a very fascinating topic with a real potential to diagnose a lot of cancer earlier stage, and clearly in need of some critical clinical research to understand how to use these technologies in the general population or if we can do that.

They have the potential to really be very important. They could substantially reduce cancer mortality if they sort of live up to the early studies, and, of course, that's a great unknown at present. But I think this is an area that really bears watching.

Many other topics—immuno-oncology continues to be impressive. Cell-based immunotherapy continues to be very impressive. Novel chemistries that are coming up with new drugs that inhibit RAS for the first time. Medicinal chemistry is creative and innovative. That's the great thing with NCI. Our portfolio is so diverse, and these areas are so interesting. So we'll see

what comes out from investigator-initiated research over the next decade.

Jensen: One more question, and I'll combine a couple of questions here. What can cancer centers and the NCI do to help diversify the population that gets enrolled on interventional clinical trials? Are there best practices that could be fostered? What are some of the things that the NCI is doing in particular?

Sharpless: I think probably some of you heard [Community Oncology and Prevention Trials Research Group Chief] Worta McCaskill-Stevens' presentation on our data on this topic. It tells a good story, but it's certainly an area where the NCI still can do better.

It shows, going back to the '90s, an increase in minority accrual to NCTN and ETCTN, NCI-sponsored trials, particularly a nice increase in Hispanic patients but also a modest increase in African American patients.

We think that clinical trials accrual is really important for a lot of reasons. It's important to have a diverse real-world treatment experience for the agent being investigated, but it's also important because I think it's really a marker of good care.

I think data from several NCI cancer centers has shown that access to clinical trials is sort of a proxy for good care, and centers that do that well, that enroll patients, all take good care of their patients. I think if we want to be fair and equitable in our care, minority accrual is something we should watch.

I think one of the reasons why the NCI—and I will stipulate—I don't think it's a matter of dispute, I think it's a fact that our numbers in this regard are considerably better than industry's, which is still under-accruing massively underrepresented minority patients.

I know both at the FDA, when I was there, and here at the NCI, we're really worried about that, and we talk to industry a lot about—why is that happening, and what can they do differently. Again, COVID may have changed this a little bit, too, because I think they have gotten that message related to vaccine trial accrual. So, we'll see if any of that transfers over to other therapeutic areas in the future.

But the reason I think the NCI's done a better job than industry is that we have made this a priority. We've said this, we want to do this. We have talked about it for a long time. I think, cleverly, we created the National Community Oncology Research Program, NCORP, that has a lot of sites in the community, including sites that predominantly serve underrepresented minority patients.

So, places that take care of underrepresented minority patients are more likely to enroll them on clinical trials, and if you look at where a lot of our accruals in specific populations come from, it's from some of those NCORP URM sites. This is an area where I think the trends are good under Worta's leadership, but clearly an area where we continue to need to do more.

Jensen: Well, we've reached the end of the hour. I want to thank you, Dr. Sharpless, for that wonderful and inspiring talk.

GUEST EDITORIAL

AACR conference examines how societal framework of racism drives cancer disparities

Steven R. Patierno, PhD
Deputy director, Duke Cancer Institute;
Professor of medicine, pharmacology and cancer biology,
Professor of family medicine and community health,
Duke University School Medicine,
Conference co-chair, AACR Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved

The global coronavirus pandemic has torn the veil that dimmed the nation's awareness of the breadth and depth of health disparities, including cancer health disparities.

Cancer disparities span the continuum of cancer care and adversely impact risk, prevention, screening, early detection, diagnosis, interception, treatment, progression, survival, and survivorship.

Cancer disparities are driven by a complex intersection between social, psychosocial, lifestyle, environmental, health system, and biological determinants of health.

This framework of intersectionality must contend with the interplay between ancestry-related individual-level genetics and biology, neighborhood-level social and physical environments, institutional-level systems (health care, workforce, legal, political), and societal-level cultural frameworks (racism, poverty, discrimination), including policies that perpetuate such frameworks.

In 2007, the leadership of the American Association for Cancer Research was prescient enough to call for a Cancer Disparities Think Tank to explore how to harness the AACR's considerable influence to address this issue. I had the privilege of co-chairing that Think Tank along with my colleague Dr. Olufunmilayo (Funmi) Olopade.

Our two-day discussions focused on the critical need for cancer health disparities research, including basic, translational, clinical, behavioral, and population-level research, to identify the determinants of cancer health disparities among racial and ethnic minorities and the medically underserved, to develop evidence-based interventions at every level toward achieving cancer health equity, and to address disparities in the cancer research workforce.

These topics were rigorously revisited and expanded in the second AACR/NCI Cancer Disparities Think Tank in 2018, and are elaborated in detail in the newly released inaugural AACR Cancer Disparities Progress Report.

At least two important deliverables emerged from the 2007 Think Tank: 1) a road map for the NCI for investment in cancer health disparities research, and 2) a plan to inaugurate an annual national conference on The Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved.

The 13th annual installment of that conference took place Oct. 2-4 using a virtual format, corresponding to the 20th anniversary of the founding of the AACR Minorities in Cancer Research. The conference was chaired by Dr. John Carpten and co-chaired by Drs. Gerado Colon-Otero, Marcia R. Cruz-Correa, and Lisa A. Newman, and me.

The meeting was kicked off with a tribute to MICR by Dr. Carpten and a distinguished lecture by Dr. Lourdes Baezconde-Garbanati on optimizing engagement to reduce disparities among Hispanic/Latinos/Latinx and other underserved communities.

This was followed by a keynote address by Dr. Francis Collins, director of the National Institutes of Health, who also gave the keynote address at the inaugural meeting in 2008. Dr. Collins reiterated the NIH's recognition of and commitment to mitigating health disparities and achieving health equity.

His address was followed by a lively panel discussion on a forward-thinking agenda for cancer disparities research moderated by Dr. Robert Winn, and panelists Drs. Patricia LoRusso, Clayton Yates, Chanita Hughes-Halbert, Mariana Stern, and Brian Rivers.

Major focal points of the discussion included the need for "convergence science" to more rigorously explore the intersectionality between the various determinants of cancer health disparities and to address the ongoing problematic workforce challenges that contribute to the lack of diversity and inclusion at every level of employment from graduate student to cancer center director.

“The conference did not shy away from addressing some of the most difficult questions, including the impact on cancer of structural racism and implicit bias within our health systems, at the local, regional, national levels, and embedded state and federal policies and the political fabric of society.”

One of the major emphases of the conference was on addressing the issue of advancing diversity and inclusion in participation in oncology clinical trials, and exciting advances were presented by academic, industry and governmental participants.

Several speakers pointed out exciting results from innovative oncology clinical trials stratified by race, showing that although Black patients entered the trials with worse disease, they responded better to treatment, compared with their white counterparts.

This powerfully underscores not only the importance of increasing diversity, but also of conducting clinical trials that are stratified by race and/or ethnicity.

The conference did not shy away from addressing some of the most difficult questions, including the impact on cancer of structural racism and implicit bias within our health systems, at the local, regional, national levels, and embedded state and federal policies and the political fabric of society.

Throughout the conference the attendees also heard impassioned presentations by patient advocates who shared their personal stories and inspired us to work harder to mitigate cancer disparities and achieve cancer health equity.

Special sessions also addressed global cancer health disparities, disparities in treatment and survivorship care of young and adolescent cancer patients, and disparities in cancer care for LGBTQ cancer patients.

Other major topics of discussion included public health-level disparities in environmental exposures, cancer prevention and screening, and disparities in psychosocial health of specific populations.

Towards addressing cancer disparities in precision oncology, the conference also focused attention on the com-

parative genomics, epigenomics, transcriptomics, proteomics, metabolomics, immune-genomics, and microbiomic aspects of multiple tumor types and the intersection of these biological contributors to other drivers of cancer disparities. This framework of intersectionality was deemed "convergence science," an exciting area that will undoubtedly attract more attention and research funding.

Finally, the conference cast light on the ongoing challenge of disparities in the cancer research and cancer care workforce, and the importance of focusing attention to the matter of inclusion and diversification in these areas.

Dr. Samuel Broder, former director of the National Cancer Institute, was known for his emphatic statement "Poverty is a carcinogen."

What this year's conference underscored is that societal-level cultural frameworks of racism and discrimination, reinforced by policies that relegate vulnerable members of society to social and physical environments and institutional systems, can both promote and exacerbate factors that influence cancer, particularly in medically underserved populations.

These factors can be extrinsic (e.g., socioeconomic status, diet, pollution), intrinsic (e.g., age, physiology, genomics), or both (e.g., allostatic load). Many of these factors can be related to race and ethnicity.

Although race and ethnicity are sociocultural constructs rather than genetic or biological constructs, they are influenced by the genetic and biological diversity that evolved as part of the human diaspora. External features and internal physiology (phenotype) changed as a function of human migration patterns, whether voluntary or forced through slavery.

Many of these phenotypic changes are passed from generation to generation, indicating that they are encoded in our genotype, illustrating that diaspora-driven ancestry impacts our cultural and biological diversity and therefore our physiology and pathology, including our risk for disease, biology of disease, and response to therapy.

> "Societal-level cultural frameworks of racism and discrimination, reinforced by policies that relegate vulnerable members of society to social and physical environments and institutional systems, can both promote and exacerbate factors that influence cancer."

Cancer is no exception to this, and in fact may be most emblematic of both the scourge of health disparities in our nation and around the globe, and the moral and ethical imperative for the cancer research community to focus its attention on achieving cancer health equity.

AN APPRECIATION

"Political oncologist" Helene Brown dies at 91

By Paul Goldberg

A cancer pioneer, Helene G. Brown had coined the name for her peculiar subspecialty: political oncology.

For at least six decades, if you were trying to get something done in cancer, Brown was someone you needed to have on board. She had served on many boards—the National Cancer Advisory Board, the board of the American Cancer Society, to name two big ones—and she opened many doors, sometimes to let good people in, sometimes to throw the rascals out.

Brown, who died on Oct. 4 at age 91, had no medical training. Her cancer education began when she was 16 and her father was stricken by lymphosarcoma. Helene learned to administer morphine.

"I'd always been interested in science," Brown said in a 1997 interview with the *Los Angeles Times*, but "I was a child of the Depression, and accounting was something that could get you a job."

As a young woman, she was horrified to learn that Pap smears were available for screening women in the 1930s, but mass screening efforts began a quarter-century later. This discovery got her interested in public health.

Helene knew everyone, referring to movie moguls, billionaires, NCI directors, and politicians (including one former U.S. president) as "good friends." People drop names; Helene didn't. These really were good friends, either because they wanted to tap into her deep connections and her vaults of knowledge—or because they liked her.

Helene was a four-foot-something-tall human internet, an exchange of presumably reliable information. Moral outrage blasted like a big tuba through the drumbeat of her brutal observations. Betrayal of public trust made her blood boil.

Many of Helene's stories focused on the American Cancer Society, a charity with which she had a life-long love-hate relationship. Dinner with Helene meant hearing about ACS in the bad old days.

There was a story about the wife of a former executive who was known to shop at Saks Fifth Avenue as a chauffeur, an ACS staff member, waited for her in an idling limo. She loved telling the story of a trip to the Vatican, where top-tier ACSniks—executives of a secular charity, no less—received a papal blessing.

She told stories of debauchery, malfeasance, payoffs, and non-disclosure agreements. A rumor had it that at one point Helene had files documenting all that. I hoped she did, but Helene would neither confirm nor deny. (Decades have passed, people have died, statutes of limitations have run out, but it's never too late for something that juicy to see the light of day.)

There were also stories of Helene and her husband Bob barnstorming in their single-engine Cessna across the U.S. to promote screening for cervical cancer.

A Jewish Amelia Earhart, Helene sported a white silk scarf, or so her story went. The purpose of these trips was to promote cervical cancer screening—and ACS. To Helene, a small-d democrat, ACS was all about the grassroots.

Also, she believed that the society had the potential to bring together the disparate interests that make up the cancer field. Once united, cancer groups would be in a position to ask for more money, or so she seemed to believe.

When I met her in the early 1990s, Helene seemed convinced that dark days were over at ACS, almost certainly with the help of her deft political oncology maneuvers, and that the new CEO, John Seffrin, a good friend, would do a fabulous job at the charity's helm.

In the end, Helene would be disappointed, but we are getting ahead of the story.

In February 1994, I was writing an obit of Mary Lasker, the philanthropist who made the National Cancer Act of 1971 happen. Of course, I called Helene. Did Helene know Lasker? She did. Mary was a good friend; what else?

So, I quoted Helene:

"Mary used to say, 'You can get more money out of the government in one day than you can get by going door-to-door for 10 years."

I remember making an effort to work in Helene's recollection of Lasker oft-repeated pronouncement about Republicans: "There's some good ones." I seem to have failed to weave that into the Lasker obit (*The Cancer Letter*, March 4, 1994).

Two weeks later, *The Cancer Letter* started reporting the beginnings of a scandal that ruined the career of one of cancer's greats—the surgeon Bernard Fisher. Scientific fraud committed by another surgeon, in Canada, seemed to have tainted the breast cancer data collected by the National Surgical Adjuvant Breast and Bowel Project, the cooperative group Fisher ran (*The Cancer Letter*, March 18, 1994).

Facing scrutiny from congressional investigators, NCI fired Fisher, touching off a massive scandal that concluded years later with an apology to Fisher (*The Cancer Letter*, Nov. 1, 2019).

Back in February 1994, having rotated off NCAB, Helene was in no position to help Bernie.

So, to cheer up her good friend, Helene went to a hardware store, bought the biggest screw she could find, had it embedded in Lucite and scribbled a note—I believe it was a poem, but wouldn't swear to that—about Bernie being a true gentleman who didn't deserved to get screwed.

She placed the object and the note in a FedEx box and sent it off to poor Bernie.

It's not publicly known whether Fisher was cheered up or driven deeper into despair by this emanation of Brownian humor.

About a year later, Helene told me about another good friend, the financier cancer survivor Michael Milken putting together a strategy for a new war on cancer. How did Helene happen to meet Mike?

Well, it's a good story. She met him well before his conviction, before he went to Wall Street, before he went to college.

Here is what I wrote at the time (*The Cancer Letter*, Nov. 24, 1995):

> It appears that from the start of this intellectual journey, Milken realized that he needed a political road map, a way of distinguishing the white hats from the black hats.
>
> To that end he recruited Brown, a long-time cancer activist who describes herself as a "political oncologist."
>
> Over four decades of cancer activism, Brown has offered many a word of advice to a long line of NCI directors as well as activists including Lasker and Armand Hammer.
>
> To sundry others, she has delivered an ultimatum or two. Brown is a member of the board of directors of the American Cancer Society and the advisory board of the NCI Division of Cancer Prevention and Control. She is also the director of Community Applications of Research at the University of California at Los Angeles Jonsson Cancer Center.
>
> Brown first met Milken when he was a student at Birmingham High School in Van Nuys. Brown's children were attending the same school. The two were re-introduced years later by Hammer, then chairman of the President's Cancer Panel.
>
> As Milken was starting CaP CURE, he invited Brown to serve on the board.
>
> My decision was simple," Brown said. "Here is a man who has the courage and conviction and the need to do something.
>
> Enormous advances come from people who think differently. What Michael did in financial markets was astounding. He came up with a new way to finance business. If there is a new way to get at the cancer puzzle a bit faster, Michael has the kind of mind to be able to do that."
>
> As Milken's interest in cancer grew, Brown acted as a guide, opening doors, steering the foundation toward the mainstream, and preventing gratuitous conflicts with other groups.
>
> Brown said that now that Milken's interest has broadened to all cancers, he finds himself in the advantageous position of having the support of virtually all major cancer interests while incurring none of the logistical problems of maintaining a membership-based organization.
>
> "He is extremely interested in working with every stake-holder in the cancer program," Brown said. "He doesn't need his own constituency, and the existing constituencies need a leader. It's a beautiful exchange."

Milken's appearance in cancer politics stirred up the calcifying field. Milken put together a march on Washington, which was modeled on the original Earth Day. The objective was to build a massive constituency for cancer research.

At the same time, NCI Director Richard Klausner asked NCAB member Ellen Sigal to reach out to the film industry.

This is what I wrote at the time (*The Cancer Letter*, Oct. 31, 1997):

> "We got cancer politics out of Washington and took it to the community," Sigal said to The Cancer Letter.
>
> Exclusive reliance on scientists as advocates for science did not strike Sigal as an effective strategy. Something else had to be thrown onto the battlefield. "I thought it was very clear: you need to combine research, survivorship and high-visibility people in a high-visibility business," Sigal said.
>
> With the help of Helene Brown, a self-described "political oncologist" and an official at the University of California at Los Angeles, Sigal met Sherry Lansing, chairman of Paramount Pictures Motion Picture Group. As a result, actors and motion picture executives have been making regular appearances on Capitol Hill, and following up by writing letters on appropriations for cancer research.

The working relationship between Sigal and Lansing ultimately led to creation of Stand Up To Cancer, SU2C, an organization that brought in new funding for cancer research.

Alas, my working relationship with Helene took a hit when I started reporting a story about the emergence of an ACS-led coalition called the National Dialogue on Cancer, which sought to unify all cancer groups and redraft the National Cancer Act.

The PR firm ACS had hired to put this coalition together also represented tobacco companies (*The Cancer Letter*, Jan. 21, 2000). And NCI viewed this ef-

A UCLA holiday party, (left to right): Bahar Navab, Patricia Ganz, Barbara Kahn, Helene Brown

fort as an attempt at usurpation of the cancer agenda by broadening it beyond research.

You can hear Helene's anger in the quote she gave me when I reached out to her for my first story on the Dialogue:

> "Any time you have an organization like General Motors, the small automobile maker is going to complain about them. Any time you have an organization that has the life-long series of accomplishments that the Cancer Society has had, you are going to hear people complaining.
>
> "If there is somebody else out there that wants to take this on their shoulders, and wants to fund it, and wants to organize it, I am sure they are welcome to do it. But there isn't anybody else that has that kind of freedom, because of the constituency and the size of the purse."

I wrote the story, and I stand behind it. Helene dropped me a scathing personal note. My coverage was wrongheaded and unkind to her good friends, she wrote. There was more to it, but I seem to have blocked it out. It stung, but a journalist's loyalty is to the reader.

Helene and I were not in touch as she deliberated within the Dialogue's structures as the organization produced clouds of words. The National Cancer Act hasn't been rewritten. Cancer groups haven't been corralled into speaking with one voice, and the "dialogue" was ultimately renamed and continued to grind into irrelevance.

At roughly the same time, Helene was growing disenchanted with ACS. Though initially a good friend, Seffrin, who became the CEO in 1992, was making the place more efficient, true, but efficiency has a tendency to extinguish meaning and kill the soul.

First, under Seffrin's leadership, the society stripped power from two grassroots levels of the divisions—"units" and "areas"— making them purely advisory. Then, over the years, the divisions were merged, shrinking from 57 to 12.

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Next, Seffrin attempted to create "one organization," but that effort was shot down by the assembly in mid-1990s.

The society entered a relentless decline after the recession of 2007, ultimately deciding to centralize control, giving greater authority to the CEO, stripping divisions of self-determination, and taking over their real estate holdings. That effort was called "transformation."

I was told that Helene, then an 82-year-old nonvoting honorary life member of the National Assembly, was emerging as a strong critic of this transformation, which she saw as both anti-democratic and a suicidal business move. She was, after all, a grassroots activist. So, I decided to give her a call (*The Cancer Letter*, Nov. 18, 2011).

"If you have royalty and a castle in Atlanta, it can be totally efficient, but that is not the way we do things," Helene said to me. "I don't think that you can continue to raise funds if you have volunteers who cannot vote."

Helene said she had spoken against the changes at the meeting of the ACS assembly, but her words of caution were ignored.

"I don't believe there was anybody truly listening for new information," Helene said. "There is no longer check or balance on that board. It would be a self-perpetuating board."

I asked several of Helene's friends and associates to share their Helene stories:

Patricia A. Ganz

Distinguished Professor Health Policy & Management and Medicine
UCLA Fielding School of Public Health
David Geffen School of Medicine at UCLA
Director, Cancer Prevention & Control Research
Jonsson Comprehensive Cancer Center

For those in the cancer community who knew Helene Brown, her passing occasions much sadness, but her memory brings a smile to our faces.

When I think about cancer control, cancer advocacy, speaking truth to power—all done with incredible grace, no small amount of sass, and a bold sense of humor—I can think of no one other than Helene Brown.

As a young medical oncologist in the early 1980s, I was in awe of her knowledge of the cancer research environment and its associated politics, including her extensive engagement in the highest echelons of the oncology world—she was a presidential appointee to the National Cancer Advisory Board, a board member of the American Cancer Society, and national leader in the NCI cancer communications effort through the Cancer Information Service.

She had helped to implement community-based cancer control screening programs in Los Angeles in the earliest years after the signing of the National Cancer Act in 1971, and later focused on local and national efforts in tobacco control. She spent almost 50 years continuing to serve the cause in various ways, with the ultimate goal of reducing morbidity and mortality from cancer.

Helene was a gifted communicator, talented reader of human character, and a prodigious connector of people. In Los Angeles, she used her social skills to advance the cause of cancer control whenever possible, serving in leadership roles in many public and lay organizations.

She worked very hard at UCLA's Jonsson Comprehensive Cancer Center to raise funds for cancer research, and was instrumental in other Los Angeles charitable foundations with similar goals (Armand Hammer's STOP Cancer).

Long before the advent of professional cancer center fundraisers, Helene and her army of friends (including a rabbi's wife) single-handedly orchestrated the annual cancer center gala, stuffing envelopes, arranging for entertainment, and making everyone feel at home once they were settled in at the event.

She was glamorous, but down-to-earth, and she made everyone feel special, from stuffy academics to leaders of community-based organizations.

When Helene observed that cancer centers were insulated from the real-world experience of cancer patients and their families, she led the NCAB to require that to be designated "comprehensive," cancer centers would have to demonstrate their reach into their communities.

The definition of "comprehensive" expanded over time, but initially it mandated that a cancer center be visible in the community through facilitation of cancer screening, enrollment in clinical trials and providing outreach and education.

Locally, our cancer prevention and control research group benefited from being surrounded by people like Helene, as well as other luminaries—Joe Cullen and Lester Breslow—who were the founding parents of cancer control at the Jonsson Cancer Center.

Ellen Gritz initially, and then I, were tasked to follow in their footsteps. Achieving "comprehensive status" at UCLA was a piece of cake because of the environment they had created for us. Helene capably supervised the NCI contract for the Cancer Information Service into the 1990s, and then assisted our former center director, Dr. Judith Gasson, in community and philanthropic engagement while serving on the cancer center board.

Personally, I am very grateful to have had Helene Brown as a role model, mentor, and friend. She was the most skillful and dedicated advocate and she taught us all how to do it.

Helene gave so much to us locally at UCLA, even as she was busy with leadership tasks at the national level. She was the consummate impromptu speaker and entertainer.

We always relied on her to emcee our many social gatherings in our research group, which she continued to attend up to this past year. Our holiday parties will never be quite the same.

The cancer control community has lost a pioneer and great leader.

Jerome Yates
Former ACS National Vice President for Research

Helene Brown was passionate about every effort she addressed. This included politics, cancer prevention, equal access to optimal therapy, her family, and piloting an aircraft.

She was equally comfortable when interacting with senior political office holders, respected and talented research scientists, California-based movie moguls and the officers and board members of the American Cancer Society. She brought insightful, intelligent understanding to those discussions, often with solutions to major problems, which usually required action and accountability for the other discussants.

I first met Helene in the early 80s, as a member of a contract review committee sent by the National Cancer Institute to either cut or eliminate the funding for a major cancer control effort at UCLA, which she led.

We met in offices located on the mid-level floor of a building in downtown Los Angeles. Early presentations were in progress when the building started to sway, and most of us, from other parts of the country, were visibly concerned about our safety.

Helene assured us it was only a "little earth-quake" and not to be alarmed. Because the committee started with an overt adversarial objective, there were jokes from committee members familiar with Helene, who said that she had probably arranged the tremor to show who was in control.

Over the years, I came to understand this was a jest which recognized her ability to make things happen. The committee shifted from being a threat to the project to recognizing the benefit and supporting Helene's efforts.

Both Helene and I were long-term volunteer supporters of the American Cancer Society, often served on policy and review committees for the NCI, and shared a love of flying single-engine aircraft. Out of the initial adverse relationship grew a friendship and respect for honesty and enthusiasm, as we both sought ways to improve the leadership, operations and outcomes from major prevention and early detection cancer control endeavors.

Helene was instrumental in the success of early tobacco control efforts, programs for the early detection of both cervical and breast cancer, genetics as a tool for the individual risk of developing cancer, and the dissemination of credible, relevant health-related information to the public.

She would laugh when others, mostly men, would describe her as "formidable", "pushy", "difficult," or "aggressive". Some called her "that woman," which she took as a symbol of respect. Among friends, she shared one personal incident that many would be reluctant to talk about.

One day, she decided to treat her husband Bob to a romantic surprise

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by greeting him at the door naked when he came home from work. When she thought he was to appear at the door, she flung it open and saw a very surprised United Parcel Service man delivering a package. It says a whole lot about Helene that she could tell this story without embarrassment.

Helene had no formal medical training, but she proved to be one of the most effective public health promoters in the past 50 years. She was not intimidated by famous celebrities, politicians or scientists as she applied pressure to increase funding for cancer control from both government and non-governmental agencies. She was an early believer in the adverse health effects imposed by both poverty and poor education.

Through most of her life, Helene was a staunch supporter of ACS. She became critical of the leadership when she saw changes buffering the delivery of local programs and the perceived diversion away from research support and local control over the dissemination of public cancer control information.

When I was the National Vice President for Research for the ACS, she goaded me to fight harder against the diversion of research funds to new "showcase" efforts, like renting headquarters space in downtown Atlanta or the centralization of the cancer information activity to Austin, Texas.

Her objective criticism of selected changes in the ACS in recent years caused her some personal pain, because of her love for the society for most of her life. That did not stop her from expressing her opinions directly to the top executive staff.

My life is richer for having known and worked with Helene in a variety of settings. I will miss the twinkle in her eye when she was pushing us to the edge of our comfort level for a cause she knew was right.

"That woman" Helene Brown made a difference in many lives. We will all miss her enthusiastic honesty that caused some discomfort while she was getting things done.

Susan Love

Surgeon, author,
Founder of Dr. Susan Love Foundation for Breast Cancer Research

While many will relate stories describing Helene Brown's influence which far surpassed her height, there was another aspect of her personality which was critical to her success—and that was her generous spirit.

When I was recruited to UCLA to head the Revlon UCLA Breast Center, there was a mixed reception. I was an out Lesbian surgeon with a wife and young daughter. I had written a popular book on breast cancer in 1990, and I spoke my mind.

Despite the controversy, or maybe because of it, Helene immediately reached out to me and invited us all to her Passover Seder. What I did not know at the time was that Helene invited everyone to her Seder.

She specialized in finding the residents, graduate students and visiting faculty who had never participated in this wonderful holiday. We all had copies of the Haggadah and left with new understanding of this wonderful tradition.

Our daughter was so well versed in the Passover story that when the teacher asked her grammar school class who could explain it, she was the first one to raise her hand. But the gatherings were more than just religious as the wine and stories flowed.

We reciprocated, by including Helene in our Christian tradition of Christmas morning breakfast of steak followed by opening of presents. She loved being part of the festivities.

Later, when I took over Otto Sartorius's nonprofit to focus on determining the anatomy of the human breast and ways to access it, Helene cheered me on and became a member of our board of directors.

Her enthusiasm and support were unflagging!

The world is certainly a better place because of the life of Helene Brown.

IN BRIEF

OSUCCC – James receives $7 million Program Project NCI grant renewal

The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) and the Ohio State College of Pharmacy have been awarded a five-year, $7 million competitive Program Project grant renewal from NCI.

This multidisciplinary project grant is the only PPG funded by NCI that is led by a pharmacy investigator, and will allow teams at Ohio State, the University of Illinois – Chicago and University of North Carolina – Greensboro to continue investigating potential anticancer drug leads based on compounds from tropical plants, coastal lichens, cultured cyanobacteria and filamentous fungi.

The grant renewal extends through 2025 and is led by principal investigator A. Douglas Kinghorn, professor and Jack L. Beal Chair of the Division of Medicinal Chemistry and Pharmacognosy at the College of Pharmacy. He is a member of the OSUCCC – James Molecular Carcinogenesis and Chemoprevention Program.

"We are so appreciative of this renewed funding. It will enable us to continue our momentum of discovery in the lab, including further investigation of natural products identified as having potential for anticancer activity," Kinghorn said in a statement. The grant was initially funded in 2007.

The grant, which initially received funding in 2007, is organized around three projects and three cores:

Project 1 – Isolation Chemistry of Tropical Plants and Biological Evaluation
(Ohio State; Project Leader, Dr. A. Douglas Kinghorn)

Project 1 involves the isolation chemistry of bioactive tropical plants to be collected by Project 2, inclusive of extraction, dereplication, compound purification, structure elucidation and scale-up isolation stages. More recently, work has begun in screening U.S. coastal lichens and their fungal mycobionts (H. Liva Rakotondraibe). Biological screening is offered for Projects 1-3 using a selection of secondary cell-based and mechanism-based assays (Esperanza J. Carcache de Blanco and Jack C. Yalowich).

Project 2 – Isolation Chemistry of Cultured Cyanobacteria and Plant Acquisition

(UIC; Project Leader, Jimmy Orjala)
Project 2 entails cyanobacterial collection, culturing, genomic evaluation (Alessandra Eustaquio), extraction and dereplication, as well as plant collections from tropical rainforests (Djaja D. Soejarto). Extracts from the plants are further investigated in Project 1.

Project 3 – Isolation Chemistry of Filamentous Fungi and Biological Evaluation
(UNCG; Project Leader, Nicholas H. Oberlies)

Project 3 works on new lead compounds from fungi obtained from Mycosynthetix, Inc. (Hillsborough, NC; CEO/CSO Dr. Cedric J. Pearce), and comprises culturing, extraction, dereplication, compound purification, structure elucidation, scale-up isolation/yield optimization and biosynthetic manipulation. Some biological testing is carried out at Columbia University as part of Project 3 (Brent R. Stockwell).

Core A – Administrative and Biostatistics Core
(Ohio State; Core Director, A. Douglas Kinghorn)

Core A carries out overall administrative functions (aided by Amanda S. MacFarlane) and offers biostatistics support (directed by Xiaoli Zhang) to Projects 1-3 and Cores A, 1 and 2.

Core 1 – Biological Correlation and Analysis Core
(UIC; Core Director, Joanna E. Burdette, assisted by Leslie Aldrich)

Core 1 provides in vitro testing (screening assays using a small cancer cell line panel; HDAC and proteasome inhibition assays) for samples submitted by Projects 1-3. Promising compounds are evaluated mechanistically and evaluated in mouse hollow fiber and xenograft bioassays.

Core 2 – Medicinal Chemistry and Pharmacokinetics Core
(Ohio State; Core Director, James R. Fuchs)

Core 2 conducts medicinal chemistry (synthesis/analogue development, SAR evaluation) and pharmacokinetic-related functions (e.g., solubility, stability,

formulation, metabolism, protein binding; supervised by Mitch A. Phelps and aided by Chris Coss) for selected compounds of promise from Projects 1-3.

Co-investigators from the Ohio State College of Pharmacy include: Esperanza Carcache de Blanco, Christopher Coss, James Fuchs, Mitch Phelps, H. Liva Rakotondraibe, and Jack Yalowich.

Walther Cancer Foundation to invest $11 million to expand IU-Purdue bioinformatics collaboration

The Walther Cancer Foundation plans to invest $11 million to advance collaborative cancer research at Indiana University and Purdue University by supporting scientists through bioinformatics.

"Sometimes you have so much data, it's hard to comprehend where it's leading you. I hope the data-driven analysis will uncover nuggets of opportunity that would otherwise never be seen," Tom Grein, president and CEO of the Walther Cancer Foundation, said in a statement.

Income from the new Walther Cancer Foundation Bioinformatics Fund will support bioinformatics personnel, technology, and other tools shared by the cancer research programs at both universities. IU and Purdue will also make their own investments into the fund.

Since its founding in 1985, the Walther Cancer Foundation has invested more than $165 million in cancer-focused medical research and in research and education aimed at supporting cancer patients and their families.

John Glaspy named inaugural chair in integrative oncology at UCLA

John Glaspy was named the inaugural Simms/Mann Family Foundation Endowed Chair in Integrative Oncology at David Geffen School of Medicine at University of California, Los Angeles.

Glaspy is professor of medicine and hematology/oncology at the David Geffen School of Medicine at UCLA and chair of scientific protocol review at the UCLA Jonsson Comprehensive Cancer Center.

The chair is funded with a $2 million gift that is part of an $18 million endowment commitment from the Simms/Mann Family Foundation. Led by Victoria Mann Simms and Ronald Simms, the foundation helps support UCLA's integrative psychosocial care for people with cancer and their families who are dealing with the emotional, psychological and physical burdens of cancer and its treatment.

Psychosocial treatment at Simms/Mann includes individual, family and group therapy, as well as educational programs in nutrition, spiritual care, qi gong and meditation; and workshops.

Glaspy is also the medical director for the Simms/Mann UCLA Center of Integrative Oncology.

SKCC refines NCI-supported research programs

The Sidney Kimmel Cancer Center–Jefferson Health and Thomas Jefferson University has said its cancer research programs will be clustered into four key areas: Cancer Risk and Control; Molecular Oncology Regulation and Approaches; Translational and Cellular Oncology; and Immune Cell Regulation and Targeting.

Each program prioritizes distinct cancer research focus areas and clinical trials that address the specific needs of cancer patients in the greater Philadelphia region. Members of each program include researchers from Thomas Jefferson University and SKCC's consortium partner, Drexel University.

The Cancer Risk and Control Program concentrates on intrinsic and extrinsic risks for cancer, including genetic, environmental, physiologic, and molecular alterations; cancer control, in which novel methods of treatments are being evaluated to address cancer risks for patients both during cancer therapy and extending into survivorship; and novel paradigms to reduce health disparities.

Nicole Simone, Margaret Landenberger Professor of Radiation Oncology at SKCC; Meghan Butryn, associate professor in the Department of Psychology at Drexel; and Andrew Chapman, chief of cancer services at SKCC, will lead the Cancer Risk and Control Program.

The Molecular Oncology Regulation and Approaches Program is focused on precision oncology, particularly as associated with targetable nuclear gene regulation and genome stability-DNA repair mechanisms, and developing new clinical interventions to reduce cancer mortality through early phase clinical trials.

Josep Domingo-Domenech, associate professor in the Departments of Medical Oncology and Cancer Biology; and Russell Schilder, director of the Early Drug Development Program, and chief of gynecologic medical oncology at SKCC, will lead the Molecular Oncology Regulation and Approaches Program.

The Translational Cellular Oncology Program is focused on novel signaling and metabolic pathways that are crucial in supporting malignancy at the cellular and intercellular levels, with the potential of impacting both clinical and progression therapy. The program also aims to uncover tumor cell crosstalk among heterogenous cancer cell populations and translate newly acquired information into means for precision medicine by preventing or counteracting tumor progression.

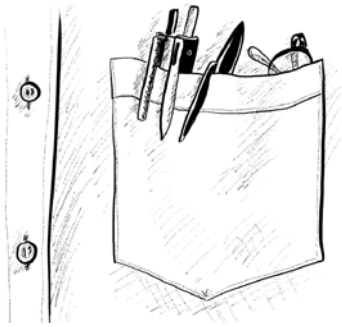
Mauricio Reginato, professor and director of the Graduate Program in Cancer Biology at Drexel; Alessandro Fatatis, professor of pharmacology and physiology at Drexel; and Ubaldo Martinez-Outschoorn, associate professor in the Department of Medical Oncology at SKCC, will lead the Translational Cellular Oncology Program.

The Immune Cell Regulation and Targeting Program focuses on cancer-associated immune cell function, transformation and targeting. This program houses exceptional leadership in immune-oncology, and translation of strategies to harness anti-tumor functions for cancer therapy in both solid tumors and hematologic malignancies.

Christine Eischen, professor and vice chair in the Department of Cancer Biology at SKCC; and Pierluigi Porcu, director of the Division of Hematologic Malignancies at SKCC, will lead the Immune Cell Regulation and Targeting Program .

Until 10 years ago, most women diagnosed with cancer had to terminate their pregnancies, or give birth prematurely, in order to start treatment. Since then, studies have shown that it is possible to start treatment during the early stages of pregnancy.

THE CLINICAL CANCER LETTER



TRIALS & TRIBULATIONS

COVID and lung cancer: How experts in cancer and virology joined forces in a challenging time

By Fred R. Hirsch, MD, PhD
Executive director, Center for Thoracic Oncology, Mount Sinai Cancer, Mount Sinai Health System; Professor of medicine and pathology, Icahn School of Medicine; Joe Lowe and Louis Price Professor of Medicine; Associate director, Tisch Cancer Institute

Researchers from Icahn School of Medicine at Mount Sinai was recently awarded a U54 grant ($3.9 million over the first two years as a part of a five-year research proposal) to establish a NCI/SeroNet Center for Serological Excellence at Mount Sinai with a focus on lung cancer.

The Center of Excellence at Mount Sinai for lung cancer will be led by Fred R. Hirsch, MD, PhD, executive director for the Center for Thoracic Oncology at the Tisch Cancer Institute and professor of medicine and pathology at Icahn School of Medicine, and Professor Adolfo García-Sastre, PhD, an expert in virology at Icahn School of Medicine, Mount Sinai.

From different registries throughout the world, it was clearly demonstrated that patients with lung cancer, who contracted infection with SARS-CoV-2 virus, and particularly those who were hospitalized for COVID-19, had a very aggressive course of the COVID-19, leading to a high mortality rate due to COVID-19.

New York was the epicenter for the COVID-19 pandemic over several months, and the Icahn School of Medicine at Mount Sinai has been in the forefront of research related to COVID-19.

Dr. Hirsch and Mount Sinai in New York have also been a significant contributor to the global Lung Cancer-COVID database study, TERAVOLT, which recently, at the European Society of Medical Oncology Annual Meeting, presented results from more than 1,000 lung cancer

patients with COVID-19 from more than 20 countries. Mortality rate for patients with lung cancer and COVID-19 was reported to be at 32%.

During the pandemic, international experts in lung cancer research and virology research at Mount Sinai came together and established research collaborations with a focus on lung cancer patients. A COVID-Lung Cancer Consortium (CLCC) was established by Dr. Hirsch, Dr. John D. Minna at UT Southwestern, and Dr. Paul A. Bunn Jr. at University of Colorado, which was described in a guest editorial in *The Cancer Letter*, April 24. 2020.

The CLCC was established in order to gather a forum of key-opinion leaders in academia, leaders from NCI and FDA, as well as patient advocacy organizations, to discuss emerging clinical issues for patients with lung cancer during this challenging time, and to facilitate scientific collaborations.

The research program proposed for the NCI-SeroNet was a result of this collaboration.

SeroNet is a major component of NCI's response to the pandemic, and is included in an emergency congressional appropriation of $306 million to NCI to develop, validate, improve, and implement serological testing and associated technologies.

Through the involvement of more than 25 universities, cancer centers, and laboratories working in partnership with NCI, the National Institute of Allergies and Infectious Diseases and the Frederick National Laboratory, members of SeroNet will work to rapidly deploy serological testing to the American public and to improve our understanding of the immune response to SARS-CoV-2 and mitigate the pathogen's spread.

Dr. Hirsch and Dr. García-Sastre, together with other investigators at Mount Sinai and in collaborations with UT Southwestern (Dr. Minna, and Beatriz Fontoura, PhD), and the University of Colorado (Dr. Bunn).

The collaboration also includes a partnership with the large patient advocacy organization, GO2 Foundation for Lung Cancer, and they were awarded the NCI U54 grant to establish a Center of Excellence for Serological Sciences at Mount Sinai in New York.

The focus of the research program is to study antibody response in lung cancer patients compared to "healthy" individuals through a large case control clinical study and through pre-clinical model systems.

The hypothesis is that lung cancer patients have a weaker antibody response to infection with SARS-CoV-2 compared to "healthy" individuals, which can contribute to explain the very aggressive course of COVID-19 in this particular population.

During the study period, it is anticipated that many of the lung cancer patients will undergo vaccination for SARS-CoV-2, and embedded in the study is a comparison of antibody response to the vaccination for patients with lung cancer, compared to the control population.

The hypothesis is that lung cancer patients have a weaker antibody response to infection and the vaccination, and this might lead to the need for a specially designed vaccination program for patients with lung cancer, which could differ from a program for a "healthy" population.

The Center of Excellence at Mount Sinai will also study which biological factors might influence the aggressiveness of SARS-CoV-2 infection based on preclinical model studies. Basis for the antibody studies are a very sensitive antibody assay (the first one developed by an academic group to be approved for Emergency Use by FDA) led by Florian Krammer, PhD, professor in microbiology at the Icahn School of Medicine at Mount Sinai.

The extended research group at Mount Sinai will follow 1,000 newly diagnosed lung cancer patients with antibody test at time of diagnosis, after 3-, 6-, 12- and 24 months, and compare the results with 1,000 "healthy" individuals.

The studies will focus on the magnitude of the antibody response, the quality- and the duration of the response in lung cancer population, compared to the control group. Dr. Hirsch and the investigator group is also planning to add other research proposals to the awarded program, which also includes a partnership with the largest patients' advocacy group in thoracic oncology, the GO2 Foundation for Lung Cancer, which will also include patients to the studies.

As mentioned, the Center of Excellence for Serological Sciences with a focus on lung cancer at Mount Sinai is a part of a larger scientific network established by the NCI—the SeroNet. Seven other U54 grants were awarded with different focus, although all related to COVID 19, and thirteen research projects were awarded (*The Cancer Letter*, Oct. 9, 2020).

As one of the four SeroNet Capacity Building Centers, Mount Sinai will also receive more than $3.46 million from the NCI, so a multidisciplinary team of Mount Sinai researchers and clinicians can assist with SeroNet's effort to rapidly deploy and expand SARS-CoV-2 serological testing capacity and practice in the community.

The Capacity Building Center at Mount Sinai will led by Carlos Cordon-Cardo, MD, PhD, professor and chief of the Department of Pathology at Mount Sinai. Mount Sinai's serology testing platforms and operations are uniquely poised to provide a solid translational engine capable of the capacity building SeroNet is committed to accomplishing, said Cordon-Cardo, MD, PhD, Irene Heinz Given and John LaPorte Given Professor and Chair of Pathology, Molecular and Cell-Based Medicine at the Icahn School of Medicine at Mount Sinai.

CLINICAL ROUNDUP

Genomic study of 6,000 NCI-MATCH cancer patients leads to new clinical trial benchmarks

Data from the NCI-MATCH precision medicine trial established a new benchmark for next-generation sequencing in clinical trials.

"Our exhaustive efforts to enlist all of the promising agents in NCI-MATCH established a new benchmark for the utility of next-generation sequencing in the conduct of clinical trials," Keith T. Flaherty, a medical oncologist at Massachusetts General Hospital Cancer Center, and ECOG-ACRIN study chair for the overall NCI-MATCH trial, said in a statement. "With time, the efficiency of using tumor genetic testing for broad-based clinical investigation will only increase."

NCI-MATCH, jointly run by ECOG-ACRIN and NCI, is the largest precision medicine cancer trial to date. The trial sought to match genetic abnormalities driving patients' tumors with approved or experimental drugs targeting those defects. The type of cancer did not matter. Nearly 6,000 cancer patients joined the trial and contributed their tumor specimens for genomic testing.

The data was published in the *Journal of Clinical Oncology*. The study provides an in-depth look into the tumor gene make-up of patients in the trial. It is the largest data set ever compiled on patients with tumors that have progressed on one or more standard treatments, or with rare cancers for which there is no standard treatment.

Four in 10 patients had tumor gene abnormalities that matched to targeted drugs studied in the trial. The gene abnormalities studied in the trial were already known to drive cancer growth. The chosen treatments were either new drugs in development that had shown promise in other clinical trials or ones that were FDA-approved in at least one cancer type.

What was not known before this trial was how often the tumor gene defects happen across cancer types. Based on the NCI-MATCH data, the individual patient has a high likelihood (a 40% chance) that there is a defect in their tumor for which there is a drug available or in development.

This discovery tells patients and their physicians that there is value in having tumor gene testing. The 40% match rate was for a limited number of targeted treatments--between 10 and 30 in the trial at that time. The rate may increase as more drugs become available, especially ones that target common gene defects.

"The 6000-patient analysis from NCI-MATCH describes the genetic complexity that is characteristic of relapsed, refractory cancers," Peter J. O'Dwyer, a medical oncologist at the University of Pennsylvania and group co-chair of ECOG-ACRIN, said in a statement. "This publication represents an important milestone in the oncology field's efforts to translate a genetic understanding of cancer into improved treatments."

While the overall match rate was 40%, it varied across cancer types. Over 25% of patients with either melanoma, bile duct, prostate, uterine, gastroesophageal junction, urinary tract, central nervous system, or cervix cancer, had tumor gene defects that matched to trial treatments. Only 6% of those with pancreas cancer did. The average match rate was 17% for the four most common cancers—breast, colorectal, non-small cell lung, and prostate.

NCI-MATCH researchers compared the tumor gene make-up of patients with seven cancer types against The Cancer Genome Atlas. The seven cancer types were breast, bile duct, cervix, colorectal, lung, pancreas, and prostate. The researchers were surprised to see that there was not much difference between the primary and metastatic databases.

Until NCI-MATCH, the research community did not have a database of metastatic tumors to compare to TCGA. However, NCI-MATCH researchers cannot make any conclusions yet. They plan to compare the NCI-MATCH patients' primary and metastatic tumors.

In the trial, it was common for patients to have not just one but several tumor gene abnormalities that drive cancer growth. This discovery should encourage cancer researchers to shift their thinking and explore combinations of targeted and other therapies that address multiple defects at the same time.

Miami Cancer Institute analysis shows developments for brain metastases patients

Miami Cancer Institute researchers found that the overall median survival for patients with brain metastases has improved over time.

The analysis identifies that certain subsets of brain metastases have sub-

stantially better survival, leading to the creation of an algorithm to estimate patient survival, individualize treatment and stratify clinical trials.

Results of this analysis were recently reported in the *Journal of Clinical Oncology*, examining a database of 6,984 patients from 18 institutions in the United States, Canada and Japan. Among the key results is that the median survival for brain metastases patients has improved, but varies by subset: lung cancer, seven-47 months; breast cancer, three-36 months; melanoma, five-34 months; gastrointestinal cancer, three-17 months; and renal cancer, four-35 months. The findings led to an algorithm to assess a patient's survival.

"Our report evaluates the outcomes of patients with brain metastases in the modern era, identifying variables that can predict survival for a given patient," Minesh Mehta, deputy director and chief of radiation oncology at Miami Cancer Institute, and senior author, said in a statement. "We've found that there are subcategories of patients who have substantially better survival – we're talking survival in years compared to months. No longer is it appropriate to categorize all patients with brain metastases as having just one outcome."

Previously, the authors of the report developed and refined a Graded Prognostic Assessment , a diagnosis-specific index for patients with brain metastases. Those prognostic factors were weighted in proportion to their significance and scaled so that patients with the best or worst prognosis would have a GPA of 4.0 or 0.0, respectively.

The new findings gather updated GPAs into a single report to define the eligibility quotient, which would identify patients best suited for clinical trials. These updated GPAs are available as a free tool for clinicians to accurately estimate a patient's survival, individualize treatment and stratify clinical trials and can be accessed at.

In the United States, an estimated 300,000 patients are diagnosed each year with brain metastases. In the remote past, the average survival for brain metastases patients was poor at only about three to six months, and the majority of patients could not effectively be treated with most systemic therapies. It was not uncommon for these patients to be treated in a palliative manner and referred to hospice. The researchers said, it is recommended for enrollment to be encouraged and for the trials to be stratified to ensure appropriate comparisons are made.

"It becomes a self-fulfilling prophecy if we start assuming that brain metastases patients are going to have poor survival and therefore we don't enroll them in trials with agents that could be effective for their treatment. Instead, if we recognize that these patients can have better survival and enroll them on these trials, we might in fact identify newer agents that are more effective," Mehta said. "What's important to recognize is that we have to stratify clinical trials because patients with brain metastases have different survival rates. We have to have different categories, which will ultimately balance the arms of clinical trials."

Napo Pharmaceuticals initiates phase III trial of Mytesi for prophylaxis of diarrhea in adult cancer patients

Napo Pharmaceuticals Inc., a wholly owned subsidiary of Jaguar Health Inc., has initiated its pivotal phase III clinical trial of crofelemer (Mytesi) for prophylaxis of diarrhea in adult cancer patients receiving targeted therapy.

The phase III pivotal clinical trial (NCT04538625) is a 24-week (two 12-week stages), randomized, placebo-controlled, double-blind study to evaluate the safety and efficacy of crofelemer in providing prophylaxis of diarrhea in adult cancer patients with solid tumors receiving targeted cancer therapy-containing treatment regimens.

Crofelemer or placebo treatment will start concurrently with the targeted cancer therapy regimen. The primary endpoint will be assessed at the end of the initial (stage I) 12-week double-blind placebo-controlled primary treatment phase.

After completing the stage I treatment phase, the subjects will have the option to remain on their assigned treatment arm and re-consent to enter into the stage II 12-week extension phase. The safety and efficacy of orally administered crofelemer will be evaluated for the prophylaxis of diarrhea in adult cancer patients receiving targeted cancer therapies with or without standard chemotherapy regimens.

The assessment of the frequency of diarrhea will be measured by the number of loose and/or watery stools for the stage I treatment period.

Novel "targeted cancer therapy" agents, such as epidermal growth factor receptor antibodies and tyrosine kinase inhibitors, with or without cycle chemotherapy agents, may activate intestinal chloride ion channel-mediated secretory pathways, leading to increased electrolyte and fluid content in the gut lumen, which results in passage of loose/watery stools (i.e. secretory diarrhea). Diarrhea has been reported as one of the most common side effects of TKIs, including the recently approved irreversible pan-HER TKI neratinib (Nerlynx), with occurrence ranging from 86% to >95% in published studies. Diarrhea is also a common side effect of some CDK 4/6 inhibitors.

Mytesi is a non-opiate, plant-based, chloride ion channel modulating anti-

diarrheal medicine that is FDA approved for the symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS receiving antiretroviral therapy.

The only oral plant-based prescription medicine approved under FDA Botanical Guidance, Mytesi has a novel mechanism of action that works locally in the gut by gently and effectively modulating and normalizing the flow of water and electrolytes with minimal systemic absorption. Crofelemer was purified by Napo scientists and is sustainably harvested from the Amazon Rainforest.

Phase II EV-201 study demonstrates 52% ORR in urothelial cancer

The phase II clinical study EV-201 evaluating the antibody-drug conjugate Padcev (enfortumab vedotinejfv) for treatment of urothelial cancer demonstrated a 52% overall response rate in the second cohort.

The EV-201 study evaluates Padcev in patients with locally advanced or metastatic urothelial cancer who have been previously treated with a PD-1/L1 inhibitor and have not received a platinum-containing chemotherapy and are ineligible for cisplatin.

Padcev is sponsored by Astellas Pharma Inc. and Seagen Inc.

Results showed a 52 percent objective response rate (ORR) [95% Confidence Interval (CI): 40.8, 62.4] per blinded independent central review and a median duration of response of 10.9 months.

Padcev is a first-in-class antibody-drug conjugate that is directed against Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer. FDA previously granted accelerated approval to Padcev in 2019 based on results from the first cohort in this trial, which included patients whose disease had progressed during or following platinum-based chemotherapy and a PD-1/L1 inhibitor.

Virus-mimicking drug helps immune system target cunning cancer cells

Researchers at the UCLA Jonsson Comprehensive Cancer Center have found that a virus-mimicking drug, BO-112, may also make certain stealthy melanoma tumors visible to the immune system, allowing them to be better targeted by immunotherapy.

The findings, published in *Science Translational Medicine*, open up the possibility of using drugs that mimic viruses to overcome immunotherapy resistance in tumors with defective interferon signaling and help create more personalized therapies for people with hard-to-treat cancers.

"Most immunotherapy approaches rely on the ability of T cells to recognize and kill tumor cells," lead and corresponding author Anusha Kalbasi, assistant professor of radiation oncology at the David Geffen School of Medicine at UCLA and member of the Jonsson Cancer Center, said in as tatement. "But in some patients, tumors escape the immune system through mutations in genes involved in the interferon signaling pathway. This is a critical pathway because it normally allows tumors to increase their antigen presentation, an intricate machinery that makes tumors visible to T cells."

The team first attempted to overcome defective interferon signaling by using adoptive T cell therapy, a type of immunotherapy that involves extracting T cells from a patient and engineering them in the laboratory to recognize and kill cancer cells. The researchers found that these T cells remained ineffective against tumors with defective interferon signaling.

The authors then engineered mouse melanoma tumor cells with a gene called NLRC5. NLRC5 increased antigen presentation even in the absence of interferon signaling and restored the effectiveness of the T cells. While this approach was effective in mice, engineering tumor cells in humans was not as simple.

Instead, Kalbasi and his colleagues turned to a virus-mimicking drug called BO-112 that activates virus-sensing pathways in tumors. When the drug was injected directly into the tumor in the laboratory, the team discovered that the activation of virus-sensing pathways increased antigen presentation even when interferon signaling was defective. As a result, these tumors could be recognized and killed by T cells.

"This study helps us understand the interdependence between interferon signaling and antigen presentation, which gives us important insights into how tumor cells are recognized by the immune system," senior author Antoni Ribas, professor of medicine at the Geffen School of Medicine and director of the tumor immunology program at the Jonsson Cancer Center, said in a statement. "New strategies to promote antigen presentation to make tumors more visible to the immune system will allow immunotherapy to be effective for even more tumor types."

The findings also highlight the potential of other promising clinical approaches that bypass tumor interferon signaling and antigen presentation, like CAR, or chimeric antigen receptor–based T cell therapy, which can recognize and kill tumor cells even in absence of antigen presentation.

Kalbasi is now leading a human clinical trial of the combination therapy of nivolumab, an immune checkpoint blockade drug, and BO-112 in people with certain types of sarcoma who are undergoing radiation followed by sur-

gery. The idea is to activate the immune system against the patient's tumor while the tumor is still in the body.

The research is a collaboration with colleagues at Highlight Therapeutics, a biotechnology company based in Spain that has developed and tested BO-112 in early phase clinical trials in Europe. The work was supported in part by the Parker Institute for Cancer Immunotherapy and the National Institutes of Health.

DRUGS & TARGETS

Keytruda receives FDA approvals in Hodgkin lymphoma indications

Keytruda (pembrolizumab) has received an expanded label use from FDA as monotherapy for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma.

FDA also approved an updated pediatric indication for Keytruda for the treatment of pediatric patients with refractory cHL, or cHL that has relapsed after two or more lines of therapy.

Keytruda is sponsored by Merck.

The approval in adults is based on results from the phase III KEYNOTE-204 trial in which Keytruda significantly reduced the risk of disease progression or death by 35% (HR=0.65 [95% CI, 0.48-0.88; p<0.0027]) compared to brentuximab vedotin.

Median progression-free survival was 13.2 months (95% CI, 10.9-19.4) for patients treated with Keytruda and 8.3 months (95% CI, 5.7-8.8) for patients treated with BV.

Keytruda was previously approved under the FDA's accelerated approval process for the treatment of adult and pediatric patients with refractory cHL, or who have relapsed after three or more prior lines of therapy based on data from the KEYNOTE-087 trial.

In accordance with accelerated approval regulations, continued approval was contingent upon verification and description of clinical benefit; these accelerated approval requirements have been fulfilled with the data from KEYNOTE-204.

This approval was reviewed under the FDA's Project Orbis.

United Kingdom signs on to FDA's Project Orbis

The United Kingdom plans to join two international initiatives that will allow pharmaceutical companies to submit medicines to be reviewed by several countries at the same time, pooling resources and allowing patients to benefit from earlier access.

The two schemes are:

- Project Orbis: A program coordinated by FDA, which also includes Canada, Australia, Switzerland, Singapore and Brazil. The program allows these countries to review and approve promising cancer treatments. The scheme has already given the green light to treatments for breast cancer, lung cancer, liver cancer, endometrial cancer, and chronic lymphocytic leukaemia.
- Access consortium: A program involving Australia, Canada, Switzerland and Singapore to help secure improved patient access to high-quality, safe and effective medicines. The consortium has previously approved nine innovative prescription medicines, including five new cancer treatments.

The UK's Medicines and Healthcare products Regulatory Agency will participate as an observer of both groups before the end of 2020 and will be a full participant as of January 1, 2021 after the EU transition period.

MHRA will have the authority to make the final decision to authorise medicines onto the UK market and will have complete autonomy to streamline the approval processes even further if needed outside of both schemes.

MD Anderson and Allogene Therapeutics collaborate to advance allogeneic CAR T therapy

MD Anderson Cancer Center and Allogene Therapeutics Inc. have entered into a five-year collaboration agreement for the preclinical and clinical investigation of AlloCAR T candidates across Allogene's portfolio of hematologic and solid tumors.

Under the agreement, MD Anderson and Allogene will collaborate on the design and conduct of preclinical and clinical studies with oversight from a joint steering committee. Allogene will provide funding, developmental candidates, and other support. Responsibility for regulatory filings will be agreed upon by the joint steering committee.