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THE CANCER LETTER

Inside information on cancer research and drug development

Vol. 46 No. 26

JUNE 26, 2020

www.cancerletter.com

PARTICIPATION BY MINORITY RACIAL, ETHNIC GROUPS IN NCI-FUNDED TRIALS NEARLY DOUBLES IN 20 YEARS

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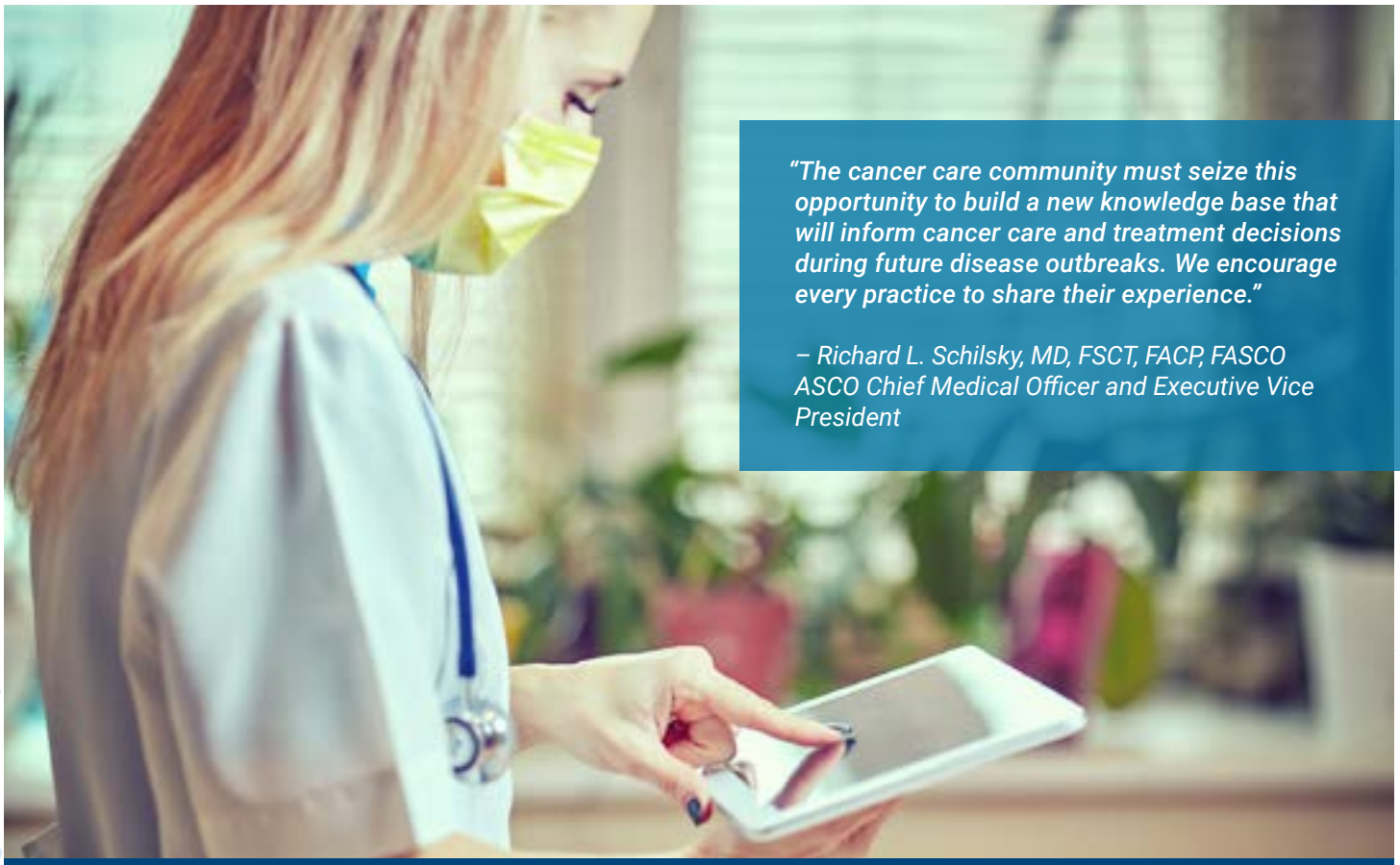
- Delivers periodic reports with key findings
- Provides insight to inform treatment now and in the future
- Qualifies as an accepted clinical trial registry for improvement activities under the Merit-Based Incentive Payment System (MIPS)



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– Richard L. Schilsky, MD, FSCT, FACP, FASCO
ASCO Chief Medical Officer and Executive Vice President

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Individual subscriptions $555 per year worldwide. Group subscriptions required for institutional distribution. To subscribe, click here.

ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

LETTER FROM THE EDITOR & PUBLISHER

The Cancer Letter's paywall is returning

Dear Reader,

When the COVID-19 crisis began, *The Cancer Letter* made the decision to take down our paywall, and provide coverage of the pandemic free of charge "until this crisis is resolved" (*The Cancer Letter*, April 3, 2020).

One crisis quickly expanded, as the disease attacked underserved communities—and a struggle for health equity expanded into a struggle for social justice. In these times of tumult, it's essential not only to hear the voices of scientists, physicians, and other leaders, but also the voices of those who have come to know injustice directly, through lived experiences.

Diversity is an indisputable prerequisite for any institution's relevance—not a lofty goal. In recent months, the issues of *The Cancer Letter* swelled to unprecedented heft as we provided authoritative, uncompromising coverage, conversations with experts, and guest editorials from leaders in oncology. And our readership numbers skyrocketed.

All of our coverage of COVID-19 and its impact on cancer patients, cancer research, and cancer care is available on our coronavirus landing page. These stories will remain accessible.

As this crisis persists, our goal is to inform. This mission includes providing a platform for voices that must be heard as America struggles to control a deadly virus—and fights for justice and equity in health care and in our society as a whole. We will be here, covering this "new normal" for a long time to come.

Subscriptions make up 90% of our revenue, and we cannot make *The Cancer Letter* open-access indefinitely. Starting next Friday, July 3, 2020, the paywall will slowly begin to return. Not all stories will be behind the wall, however. When we determine that a public-interest story is of overwhelming importance, we will make it open-access, as we have done in the past.

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Thank you for the good work you are doing on the front lines of this crisis, and for turning to *The Cancer Letter* for information about cancer and SARS-CoV-2.

Paul Goldberg
Editor & Publisher

THE CANCER LETTER | JUNE 26, 2020 | VOL 46 | ISSUE 26

PARTICIPATION BY MINORITY RACIAL, ETHNIC GROUPS IN NCI-FUNDED TRIALS NEARLY DOUBLES IN 20 YEARS

By Matthew Bin Han Ong

The proportion of racial and ethnic minority patients in NCI-funded clinical trials has nearly doubled over two decades—from 14% in 1999 to 25% in 2019, according to data from NCI's National Clinical Trials Network and the NCI Community Oncology Research Program.

"Individuals of diverse populations need access, and these two networks do provide access for patients to embark upon a journey into clinical trials or improved outcomes for themselves as well as others," Worta McCaskill-Stevens, chief of the Community Oncology and Prevention Trials Research Group in NCI's Division of Cancer Prevention, said in a virtual meeting of the Board of Scientific Advisors and National Cancer Advisory Board June 15. "And finally, diverse enrollment is a major aim of many national research policies."

In absolute numbers, participation by minority patients rose from 13,784 in the beginning of the studied period to, most recently, 21,125.

In a related study conducted by SWOG Cancer Research Network, a member of NCTN, researchers found that Black patients are better represented in taxpayer-funded clinical trials testing new cancer treatments, compared to trials run by pharmaceutical companies.

SWOG analyzed the data from a total of 358 trials—85 industry trials and 273 SWOG trials—that enrolled 93,825 patients being treated for 15 different cancer types. Enrollments spanned the years 2003-2018. In those 15 cancers, the rate of Black enrollment in industry trials was 3%, compared to 9% in SWOG trials. Blacks account for 12% of the U.S. cancer population.

Noteworthy improvements in representation of minority groups in NCI's NCTN and NCORP trials from 1999 to 2019 include:

- The percentage of African Americans patients enrolled increased from 8% to 11%,
- Hispanic or Latino representation have increased from 4% to 10%, and
- Accrual of minority patients to phase III trials increased from 14% to 27%.

"We too rarely, I think, see presentations like you've just presented, Worta. So, that was fantastic. While we see needs

for improvement, we have so much work to do, and we want to engage in that work and support you," Cheryl Willman, director and CEO of the University of New Mexico Comprehensive Cancer Center, said at the joint meeting.

"I think one of the barriers we see from a minority-serving institution has been the issue of eligibility criteria on so many clinical trials that limit eligibility due to comorbidities, and challenges that we too often unfortunately see in minority and underserved populations," Willman said. "I know the NCAB has tried to do a lot of work around that, but how deeply we've actually impacted changing eligibility criteria, for us, is a huge issue.

"And second is developing trials in areas where we have higher incidences, in certain populations. And I know when you visited us, we look at tribal communities who have some of the highest rates of liver and kidney cancer in the United States, and yet, the trial menus in those cancers are more limited."

Race is a sociological—as opposed to a biological—construct. It does not reflect the actual genetic admixture of many African Americans, said Otis Brawley, the Bloomberg Distinguished Professor of Oncology and Epidemiology at Johns Hopkins University.

"I think that this data speaks to access and fairness. And the question is: Do Blacks, do Hispanics, do Native Americans have access, and fair access to clinical trials?" Brawley said at the meeting. "And I speak to that because I've written about this 27 years ago, even, on the NIH Revitalization Act of 1993, the congressional mandate actually calls for subset analysis amongst the races as if Black is a biological category, different from white, different from Native American.

"I think the politicians got that totally wrong. I'd like to point out that the OMB Directive 15 that defines race in the United States, actually says that they are socioeconomic categories. And if you look at 23AndMe or Ancestry.com, most African Americans in this country have at least 10% Caucasian admixture, that actually makes sense that the category Black, is socioeconomic and not biologic, for example."

Studies designed to characterize groups according to risk may be more useful for targeting specific populations that are at high risk of certain cancers, Brawley said.

"In order to get the complete answer to the question of some disparities, we need to start thinking about certain very focused studies that look at very particular groups of individuals who do have an increased risk of a particular disease, because of—I will use the category—area of geographic origin, as opposed to race," Brawley said.

"For example, there are some Native American populations—and Dr. Willman may be able to better define the population than I—who have increased risk of gallbladder cancer; the African, sub-Saharan African, increased risk of prostate cancer. Again, I'm getting away from race and getting close to the area of geographic origin and asking the question, should we do some very defined studies on particular problems that are really significant problems?

"I'll just end by saying, the work that Dr. McCaskill-Stevens presented is very wonderful in my mind—11% of the American population is Black and 11% of people who are on NCI clinical trials are Black. So, from a national perspective, we're very representative of the population, but I'm thinking about these very specific targeted questions on specific areas of geographic origin."

NIH and cancer center directors need to be cognizant of preserving hospital funds for programs that may not be related to cancer—for instance, budgets for clinical trials in general, Brawley said.

"If I can just add one more thing, as a former cancer center director in a poor hospital, there is the tendency or the pressure on the cancer center director, especially in academic hospitals, to divert resources away from programs that can actually help the population and to build a program to put people on clinical trials. And that can actually hurt that hospital," Brawley said.

"We have to be careful that the NIH in general is not encouraging cancer center directors to take hospital resources that should be going into other things, maybe even other non-cancer things, that would help their community, in order to build a cancer research environment," Brawley said. "That just means that the federal government needs to pay more for this accrual from hospitals, especially hospitals that take care of a lot of poor folks, you have a lot of Medicaid coming in."

McCaskill-Stevens's remarks at the virtual NCAB-BSA meeting follow:

I'm going to present today the accrual of minorities in the NCTN and the NCORP clinical trials in 20 year view.

The scientific evidence gained from clinical trials provides the most important and reliable information for the effective care and management of cancer patients, as well as those individuals at risk of developing cancer. It is for these reasons that the trials must provide evidence that's both valid and generalizable to all populations. And hence, the frequent interest and frequent questions as to who really participates in NCI clinical trials.

Individuals of diverse populations need access, and these two networks do provide access for patients to embark upon a journey into clinical trials or improved outcomes for

Accrual to NCI's NCTN and NCORP Clinical Trials: All Phases

Minority Accrual (Numbers)								
	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	85,424	104,766	77,936	74,616	63,570	49,968	58,707	514,987
Minority	**13,784**	**20,947**	**16,020**	**18,610**	**17,098**	**15,235**	**21,125**	**122,819**
Black or African American*	**7,614**	**11,612**	**7,700**	**8,603**	**7,106**	**5,555**	**8,8,77**	**57,067**
Unknown/ Not Reported	2,044	2,247	2,276	2,887	1,912	2,878	3,110	17,354
Total	101,252	127,960	96,232	96,113	82,580	68,081	82,942	655,160
Minority Accrual (Percentages)								
	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	84%	82%	81%	78%	77%	73%	71%	78%
Minority	**14%**	**16%**	**17%**	**19%**	**21%**	**22%**	**25%**	**19%**
Black or African American	**8%**	**9%**	**8%**	**9%**	**9%**	**8%**	**11%**	**9%**
Unknown/ Not Reported	2%	2%	2%	3%	2%	5%	4%	3%

* Subset of Minority Accrual

5

themselves as well as others. And finally, diverse enrollment is a major aim of many national research policies.

Today's discussion will include accrual from 1999 to 2019 as reported using the Office of Management and Budget categories. Minority accrual in newer-generation trials are included. It allows us to take a look at the trials that have been completed, the current trials and how we should look at under-representation for future trials.

We use the Cancer Therapy Evaluation Program Enterprise System for abstracting the accrual. We looked at the cooperative groups from 1999, hence, we have the reorganization into the NCTN, and, similarly, for the Community Clinical Oncology Program and the minority-based CCOPS and its reorganization and transition to the NCORP. We looked at three-year intervals for accrual numbers and percentages and by age intervals for subsets of minorities, specifically African Americans and Hispanics.

Minority enrollment NCTN, NCORP trials

So, we first looked at all phases of trials. As you can see, in the circled number, over 355,000 individuals enrolled in clinical trials over this time period. Of those, 122,000 met the criteria for the racial and ethnic minorities. We started in 1999, somewhat arbitrarily, but it's six years after the NIH Revitalization Act, which mandated the inclusion of women and minorities in clinical trials. This is important, because institutions will have had time to think about how they were going to collect these data, but more importantly, to allow intervention so the patients could self-report the accuracy of this information.

You can see that the percentage of minority enrollment over time is 19%. You can see that there have been increases and there are actually variations that vary depending upon the availability of trials. Included over these years are the large adjuvant trials in breast and bowel, in particular. There were two large prevention trials for breast and prostate that affect some of the variations that you may see. But we had begun, about this period of time in the mid-2000s, to inform our investigators that we were going to utilize new technology and molecularly characterized trials, that would be smaller, and there would be less of the adjuvant trials.

As an example, TAILORx began in 2006 for it's accrual. So, you can see that as we get closer to the last two of the three-year intervals, that better reflects the transition to the new generation of trials.

Accrual to NCI's NCTN and NCORP Clinical Trials: All Phases

Minority Accrual (Numbers)

	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	85,424	104,766	77,936	74,616	63,570	49,968	58,707	514,987
Minority	**13,784**	**20,947**	**16,020**	**18,610**	**17,098**	**15,235**	**21,125**	**122,819**
Hispanic or Latino*	**4,099**	**6,650**	**5,475**	**6,687**	**6,485**	**6,051**	**8,235**	**43,682**
Unknown/ Not Reported	2,044	2,247	2,276	2,887	1,912	2,878	3,110	17,354
Total	101,252	127,960	96,232	96,113	82,580	68,081	82,942	655,160

Minority Accrual (Percentages)

	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	84%	82%	81%	78%	77%	73%	71%	78%
Minority	**14%**	**16%**	**17%**	**19%**	**21%**	**22%**	**25%**	**19%**
Hispanic or Latino*	**4%**	**5%**	**6%**	**7%**	**8%**	**9%**	**10%**	**7%**
Unknown/ Not Reported	2%	2%	2%	3%	2%	5%	4%	3%

* **Subset of Minority Accrual**

Accrual of African Americans

In this slide, we focused, as a subset, on minorities and African Americans. Over this time period, over 57,000 African Americans were enrolled into clinical trials. You can see that they pretty much mirror the enrollment overall for clinical trials and the total minority accrual is about 9%. But as you look through the years, we'd go up an 8% to the last three-year interval of 11%.

We looked at age. We're very interested in what was happening in the pediatric population, as well as the increasing interest in adolescents and young adults and, hence, selecting that age interval between the ages of 15 and 39.

We can note that for African Americans, the majority of the patients enrolled were in the age group of 40 to 69. We were also very concerned about the under-representation of minorities and the elderly patients, paying close attention to the chronic comorbidities that we know are significantly seen in these populations.

If we look at the younger populations, we can see that if you combine the younger children and the adolescents and young adults, the percentage is about 19%. African Americans do not have the highest distribution of younger populations within that group.

Accrual of Hispanics, Latinos

This again, all phases, we've focused our attention on enrollment of Hispanics, or Latinos. You can see that beginning from 1999, as we traverse over the years to the last three intervals, we've pretty much doubled the enrollment, such that over the period of time, over 43,000 individuals were enrolled into clinical trials.

Of note, when you look at the younger population, we can see that the Hispanic population, first, is the youngest of the racial ethnic populations throughout the country with about a third or 18% between the ages of one to 18, and another third or 15 million between 18 and 33. So, in contrast to what we saw in the African Americans, that the percentage, if you combine the younger children with the adolescents and young adults, you have a 42% representation as to 19% seen in African Americans. So, this population is much younger.

If one were to ask the question, "Well, what's the percentage of cancers in this group?", it's pretty much driven by leukemia. And the Hispanic population amongst the young has the

Accrual to NCI's NCTN and NCORP: Phase III Clinical Trials

Minority Accrual (Numbers)

	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	72,249	86,974	56,435	58,191	45,295	32,516	40,001	391,661
Minority	**11,514**	**18,204**	**11,458**	**15,197**	**13,098**	**11,596**	**15,552**	**96,619**
Unknown/ Not Reported	1,804	1,966	1,674	2,042	1,540	2,364	2,234	13,624
Total	85,567	107,144	69,567	75,430	59,933	46,476	57,787	501,904

Minority Accrual (Percentages)

	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	84%	81%	81%	77%	76%	70%	69%	78%
Minority	**14%**	**17%**	**17%**	**20%**	**22%**	**25%**	**27%**	**19%**
Unknown/ Not Reported	2%	2%	2%	3%	2%	5%	4%	3%

highest percent of leukemia among the younger population. So, we know that we looked at 2018 and it was reported and estimated that about 2,700 patients would be diagnosed with cancer in the zero to 14 group. So, depending upon the availability of leukemia trials, we can say that we're closely matching that age range.

We then looked at phase III trials, which represents about 87% of the total phases. We can see that over 500,000 patients were enrolled. And I wanted to direct your attention to the minority enrollment, because if you just focus on phase III trials, actually, in the last three years of enrollment, it was up to 27%. Not shown here are the phase II trials—we did not include them because we did not observe significant differences in the trends of enrollment of racial and ethnic minorities.

Accrual of other minority groups

We then looked at the other four categories in the OMB criterion, and the overall Asian enrollment is about 3%. So, it's a little less than what we're seeing throughout the U.S. Certainly, for American Indians, as well as in the Alaska natives, as well as the native Hawaiians and other specific islanders, there are less than 1%. You can see what has happened over the years, we haven't seen significant trends, but I know that there are significant efforts to engage these populations by various initiatives.

We then asked the question, what do we see in terms of enrollment from the community setting and the academic setting? So, what you see here, and we looked, we just started at the inception of NCORP in 2014 and looked at the similar time point for the NCTN groups. You see the total of 23,000 enrollments for the NCORP and 90,000 from the NCTN—the overall contribution being 26% on the right hand side, and the minority enrollment contribution 27%. Please note that the NCORP program has a specific component dedicated to minority underserved populations, to which the enrollment for racial and ethnic minorities is 55%. Next slide.

Additionally in 2014, we included the science of cancer care delivery research. The goal of this was to improve clinical outcomes and patient well-being by intervening on patients, clinicians and organizations, factors that influenced the delivery of care, which gave us an important insight as to other areas it might influence the enrollment of underserved populations, specifically in the organizations. You can see that over this period of time, 6,900 patients were enrolled; 26% of them were racial and ethnic minori-

Accrual to NCI's NCTN and NCORP Clinical Trials: All Phases

Minority Accrual (Percentages)								
	1999 - 2001	2002-2004	2005-2007	2008-2010	2011-2013	2014-2016	2017-2019	Total 1999-2019
Majority	84%	82%	81%	78%	77%	73%	71%	78%
Minority	**14%**	**16%**	**17%**	**19%**	**21%**	**22%**	**25%**	**19%**
Black or African American	8%	9%	8%	9%	9%	8%	11%	9%
Hispanic*	4%	5%	6%	7%	8%	9%	10%	7%
Asian	**2%**	**2%**	**2%**	**3%**	**3%**	**5%**	**4%**	**3%**
American Indian or Alaska Native	**0.3%**	**0.4%**	**0.5%**	**0.4%**	**0.6%**	**0.6%**	**0.5%**	**0.5%**
Native Hawaiian or Other Pacific Islander	**0.2%**	**0.3%**	**0.2%**	**0.2%**	**0.3%**	**0.3%**	**0.3%**	**0.3%**
More than one Race	**0.01%**	**0.1%**	**0.2%**	**0.2%**	**0.2%**	**0.3%**	**0.6%**	**0.2%**

ties. And over 60% of that came from the minority underserved NCORPs.

Enrollment in immuno-oncology trials

This was a picture taken from an article published in the *New York Times* in 2016. About the time when there was tremendous beginning of excitement about immunotherapy. And essentially, the article states that the participants were overwhelmingly white. And that researchers were looking at ways to enhance minorities enrolled into those trials.

We took a snapshot of two slides that had enough targeted therapy that we thought we could present to you. The first trial is one that utilizes the immunotherapy nivolumab in the perioperative setting, where patients who were going to undergo nephrectomy for renal carcinoma. What you see here is the overall minority accrual is 20%.

We thought of this in the context of the participation in the clinical trials that give the drug approval. For each of the categories that are shown here, at this particular time, the minority representation for all groups exceeds that of the representation and at the time of FDA approval, and with the exception of Asian populations because the Asian population actually have the highest number among racial minorities in the FDA approval clinical trials.

The second trial that we wanted to bring to your attention was a trial that was using pembrolizumab in the adjuvant setting with triple-negative breast cancer, in which patients will be randomized to the drug if they had residual disease after receiving neoadjuvant therapy. And importantly, here, you see the minority enrollment is 28%.

And if one looks at the populations in which we have the greatest incidence of triple-negative breast cancer, Blacks and Hispanics, we can see that one, they exceeded the enrollment into the FDA approval trials. But in addition, this is about equal to the African American population within the U.S. And importantly, it is consistent with the incidence of triple-negative breast cancer in the African American population, similarly for Hispanics.

Moving forward

The impetus for having these data presented to you was the question regarding disaggregation within race and ethnicity, which is a very important one. Currently, we have begun to [collect] NCORP information on Afri-

Minority Accrual to Immuno-oncology Trials

Minority Accrual, Actual and Percentages									
Protocol No.	**Actual Accrual**	**Overall Minority %**	Hispanic %	AI/AN %	Black/ AA %	Native HI/PI %	Asian %	Not Reported %	White %
EA8143 Renal	**366/766**	**20.6**	9.6	0.3	7.1	0.3	3.3	3.8	81.1
S1418 TNBC	**685/1000**	**28.3**	9.6	0.7	14.2	0.4	3.4	5.5	75.6

can Americans as to whether they are African American, whether they come from the Caribbean or whether they're from the sub-Sahara in Africa. We are going to begin to look at this in the Hispanic population, which is incredibly important as we see increased numbers throughout the country and estimated increases over time.

We have focused our attention on language, but we are also very interested in the country of origin, not only for the nuances of language and culture, but we want to have ways that inform strategies for enrolling. For example, we need to know whether that individual comes from a country that has had a registry, has had access to clinical trials or the existence of clinical trials, so that we can better understand ways to overcome barriers from those areas.

We have implemented a clinical child log for pediatrics, as well as adults, with a goal to expand the demographic collection of information, including education, socioeconomic factor, barriers, comorbidities that will help us at the NCI, at the site level, but also importantly in trial design as we think about that information.

We had a consensus when we began to enroll patients into the tissue acquisition studies, and this is important for minority populations, because most of these studies are focusing on advanced disease and then providing information to the treatment trials.

We have not, in the past, provided accruals for these. We are currently doing that at this time, moving forward, which will allow us to monitor the participation of these populations that are very, very important as we see that this is the direction which we're going to be going with our clinical research.

Quality of life studies expertise is within the NCORP, as well as the review. We have a number of quality of life studies that are embedded in treatment trials. And the quality of life of the populations for whom there's significant obesity, and other chronic diseases, and how they interact with the new drugs that are coming on board, is very important. And so accrual also is being monitored and given to the sites for participation.

And for those important tools that are included in the quality of life accruals, we have found that many of the tools are not translated, in populations, to languages that will be inclusive. We have Moonshot funding, to look and validate those tools for various languages, but that's led by Diane St Germain in the NCORP group.

And finally, we have the expertise and interest across the research bases and the NCTN groups, to look at other groups for under-representation, including the elderly, the adolescents and young adults, sexual and gender minorities, as well as rural populations, which was identified as an actual population eligible to participate in NCORP because of rurality.

AACR session on disparities points to the new consensus: Being woke is not enough

By Alexandria Carolan

The name of the session was a message in and of itself: "Racism and Racial Inequalities in Cancer Research."

Panelists at the AACR session "Racism and Racial Inequalities in Cancer Research.

Together, speakers at the panel convened by the American Association for Cancer Research expressed the ideas of the new consensus: that cancer is a cluster of molecular manifestations of a greater political malaise.

The problems that manifest themselves as cancer are interconnected, inseparable. The problems of disparities in patients who get cancer cannot be separated from the problems of a lack of balance among people who search for more effective treatment and those who make clinical decisions.

If the AACR session is an indication, oncology leaders from academia, government and industry agree that—to paraphrase Martin Luther King Jr.— injustice anywhere along the chain is a threat to justice everywhere.

It's one big thing: isolating discreet little injustices in today's George-Floyd-and-COVID-19 America is missing the point.

"Hopefully from this point forward, we are more than just woke. We are active in maintaining our health, not only just our personal health, but this racial equity. Putting that altogether—our health—on a daily basis," Robert Winn, director of the VCU Massey Cancer Center, said at the AACR session.

The murder of George Floyd prompted Winn, the only Black director of an NCI-designated cancer center, to reflect on his own close calls with police brutality. "I am almost certain that no other director of an NCI-designated cancer center can claim the distinction of having had a gun pulled on them by police," he wrote in this publication. (*The Cancer Letter*, June 5, 2020).

The killing of Floyd marked a moment of change for John D. Carpten, professor and chair of translational genomics, director of the Institute of Translational Genomics at the University of Southern California Keck School of Medicine.

"There have been a lot of events throughout history, but this one struck a nerve in me in a way that I've never had the feeling that I felt," Carpten, who is also chair of the AACR Minorities in Cancer Research Council, said. "It was the moment when I said to myself—no matter what I do, no matter what I accomplish in life, the first thing someone will see in me is Black."

The unified condemnation of racism has engendered hope.

"Black lives should matter when it comes to, for instance, education. Black lives should matter when it comes to the judicial system and inequalities in the judicial system," Carpten said. "Black lives should matter when it comes to employment opportunities. And, of course, from our standpoint, Black lives should matter when it comes to health equity."

Diversity in the oncology workforce

Carpten is working with Black trainees in his department to let them know they're not alone, even though a lot of the time, they are the only Black researcher in the lab.

"I've been doing everything I can to work with others at USC Keck School of Medicine to make sure that all of our trainees and early-stage investigators have the support they need going forward," Carpten said.

Russell J. Ledet is president and co-founder of The 15 White Coats, a group of medical students who work against racism and disparities, pursued his education in part because he hoped it could prevent him from being racially profiled.

"No matter how much education I have, I don't know right now whether that education will save that from happening to [my daughter] or my nephews," Ledet, a third-year MD-MBA student at Tulane University School of Medicine and A.B. Freeman School of Business, said at the session. "That's a numbing feeling. You almost feel hopeless, because you're not sure what is going to change it."

NIH has designed programs to enhance diversity, including the Diversity Program Consortium, national mentoring network, the Maximizing Opportunities for Scientific and Academic Independent Careers program, and the Faculty Institutional Recruitment for Sustainable Transformation program.

"We recognize that it's a vicious circle," said Hannah Valantine, chief officer of scientific workforce diversity and senior investigator in the Intramural Research Program at the National Heart Lung and Breast Institute. "If we're not successful in increasing the faculty level diversity in particular Black scientists, we will not make a difference, first in the demographics, secondly in the inclusion, and thirdly in the health disparities."

African American scientists get less funding than non-Hispanic whites, Valentine said.

"If we continue to speak with a despair that all of us are feeling this week, I don't see how any other of our Black trainees will join us in this work," Valentine said. "We have some hope. [Within] the career development awards, the K awards—that funding gap for Black scientists, has been completely eliminated."

NIH has programs in the works to address funding gaps within the R01 mechanism, Valentine said.

Early intervention to provide educational opportunities is also crucial, said Lola A. Fashoyin-Aje, acting deputy director of the Division of Oncology 3 in the Office of Oncologic Diseases at FDA.
The Oncology Center of Excellence Summer Scholars program at FDA

The #WhiteCoatsforBlackLives march in Washington, D.C. June 6. Photo courtesy of Pock Utiskul

helps to provide those opportunities for underrepresented populations in science, she said.

"The issue of the pipeline starts well before anyone is eligible for an R01 or K. It really starts quite early, and we can all play a part in helping to foster that," she said.

Academics have been vocal about disparities since the 1960s, VCU Massey's Winn said.

"The reality is many of us have been saying the same thing for—God knows—since the '60s, in the '70s, in the '80s. It's like a fugue state. We keep going back to the same information," Winn said. "This excuse that we need to re-study, we need to replan—what I suggest is we just need to do. And to have the will is the hardest part of this whole issue."

For years, cancer researchers have had the tools to eliminate disparities, Winn said.

"The truth of the matter is, I refute that we don't know how to get this done," Winn said. "And at some point during this issue around equity we felt just like an antibiotic that was prescribed for 14 days, when we took it for 8 days, or 4 days we probably felt good—so we stopped."

Health care disparities

Diversity in clinical trials is one area that needs to change, the panelists agreed

Immune therapeutics are often approved based on clinical trials that do not reflect diversity of the U.S. population, FDA's Fashoyin-Aje said.

"That is problematic on many levels, including the fact that there's decreased access—there's no access for a majority of patients to be on clinical trials, which in many diseases is still the best care that can be received for the patient," she said.

Drugs are also approved for diseases that vary by race and ethnicity, Fashoyin-Aje said.

"It's problematic that we're having to approve drugs that are not really appropriately characterizing safety effectiveness in those demographic subgroups," she said.

FDA is partnering with AACR and the American Society of Clinical Oncology to broaden eligibility in clinical trials, which is a barrier for minorities. Global clinical trials also need to be more inclusive to Black patients as well, she said.

"Subsaharan Africa, South, Central America are places that could also be explored as potential ways to enroll patients with ancestry that's similar to patients who are underrepresented in U.S. trials," Fashoyin-Aje said.

Minority patients can be discouraged from participation in clinical trials when those conducting the trials aren't diverse, said Kenneth C. Frazier, chairman of the board and chief executive officer of Merck.

"When people don't see people like them conducting these trials, they're not so sure whether we're doing something for them or doing something to them," Frazier said at the session. "We have to increase partnerships with minority investigators and those who serve communities of color to help improve the diversity of participants in clinical trials. Not just the patients, but the people conducting those trials themselves."

Black patients are better represented in NCI-funded cancer clinical trials than those funded by industry, according to a study published in *JNCI Cancer Spectrum*.

In the study by Joseph Unger et al., also presented at AACR virtual annual meeting II, Black patients accounted for 2.9% of pharmaceutical company-sponsored trials, and 8.3% for SWOG trials.

"Because pharmaceutical company-sponsored trials test the newest available therapies, limited access to these trials represents a disparity in access to potential breakthrough therapies," the authors concluded. "Pharmaceutical companies could improve racial/ethnic diversity in their trials—and

expand access to all patients—through increased outreach to community sites, as suggested by the findings for the NCTN trials." A related story about participation by minority racial and ethnic groups in NCI-clinical trials appears on page 6.

In the U.S., Black patients are less likely to have access to treatment, because they cannot afford it, either because of lack of insurance, or insurance that is too expensive and doesn't cover treatments.

A study by Anna Lee et al., "Changes in cancer mortality rates after the adoption of the Affordable Care Act," showed a 29% decline in age-adjusted overall cancer mortality rates in states with expanded Medicaid, falling from 65.1 to 46.3 per 100,000 individuals, from 1999 to 2017 (*The Cancer Letter*, June 5, 2020).

By comparison, in states that did not expand Medicaid, rates dropped by 25%, from 69.5 to 52.3 per 100,000 individuals. However, the same mortality decrease was not seen in Black patients.

"You get a system where, by innovating in a way that doesn't account for racism and doesn't account for other forms of discrimination, you actually perpetuate and exacerbate disparities," Christina Chapman, assistant professor in the Department of Radiation Oncology, University of Michigan School of Medicine, and Center for Clinical Management Research, VA Ann Arbor Healthcare System, previously said to The Cancer Letter (*The Cancer Letter*, June 12, 2020).

At Roche, race equity training can help to expand representation, said Levi A Garraway, chief medical officer, executive vice president and head of global product at Roche.

"One clear element there is to develop a plan for all of our officers in our company to make progress around diversity and inclusion in our organization," Garraway said at the AACR session.

Roche has hired a chief diversity officer to increase diversity.

"You can't just have a diversity office and expect these issues to go away," Garraway said. "If you really want to make a sustained change in this area, one needs to be willing to set goals and measure progress towards those goals, and have accountability for those goals."

COVID-19

COVID-19 has demonstrated the same inequalities that are pervasive within cancer, said Marcia Cruz-Correa, director of the Gastrointestinal Oncology Division at Dr. Isaac Gonzalez Martinez Oncologic Hospital, professor of medicine, biochemistry and surgery, and an affiliated investigator of cancer biology at the University of Puerto Rico Comprehensive Cancer Center.

Thirteen percent of Americans are Black, yet they account for 33-36% of those affected by COVID-19. How do you address this immediately?

"One of the aspects we cannot forget is that hospitals that take care of minority groups are disproportionately carrying the burden of this disease," Cruz-Correa said at the session. "Providing resources to those hospitals that take care of the patients is key."

African Americans, who are more likely to be economically disenfranchised, face the brunt of layoffs brought on by COVID, Cruz-Correa said. Expanding Medicaid coverage to these populations will help decrease the burden, she said.

"As the COVID pandemic starts to ease out, we need to go back to cancer prevention, early detection, minorities are by far the groups that present with cancer at an advanced stage," Cruz-Correa said. "And it's usually a direct response of simply not having the right test at the right time."

During COVID, telehealth has emerged as a way to equalize care for minority populations—barring technology barriers.

"If we could reduce the costly trips into the major medical centers by patients and their family members who have to take off from work, that in itself could be a boon," Judith Kaur, professor of oncology and medical director of Native American Programs at Mayo Clinic Cancer Center, said at the session. "We may learn whole new ways of efficiently and effectively including patients and families in our trials if we maximize that.

The COVID-19 pandemic has taught oncologists to think on their feet, Fashoyin-Aje said.

"Industry partners [and] government have mobilized to really expedite and collaborate on addressing the issues of the COVID pandemic," she said. "My hope really is that that same vigor and expediency will be applied to this issue."

Where do we go from here?

"I know one thing that will help—is a whole bunch of non-Black people speaking up, and not just being allies. We don't need allies, we need disruptors," Ledet said. "We need people who will shake up conversations that they know are racist instead of being complicit at the dinner table."

Marginalized people alone can't hold the burden of eliminating racism, Ledet said.

"It's the people doing the marginalizing that have to solve the problem. And that requires them doing some rethinking," Ledet said.

Institutions and organizations also need to act, Kaur said.

"Yes, we need allies, but we also need re-education and re-commitment to the values that AACR stands for," she said.

NCI seeks applications to build research capacity for COVID-19 serology and immunology

By Matthew Bin Han Ong

NCI has issued two Requests for Applications and a Request for Proposals focused on COVID-19 serology and immunology.

In April, Congress appropriated $306 million in supplemental funding for NCI to conduct research specific to COVID-19. Some of these funds will be directed toward the creation of a Serological Sciences Network for SARS-CoV-2, which will consist of Serological Sciences Capacity Building Centers, Serological Sciences Centers of Excellence, and other serological sciences projects (*The Cancer Letter*, April 17, May 8, May 15, 2020).

"The goal is to expand the testing capacity and practice in the community, implementing standardization for serology development, and using these tests and scale up as necessary for testing, and to acquire convalescent sera from recovered patients who are seropositive, and to conduct surveillance trials, and to pursue focused serological science," Douglas Lowy, principal deputy director of NCI, said at a virtual joint meeting of the Board of Scientific Advisors and the National Cancer Advisory Board June 15.

Other goals of the Serological Sciences Network include understanding "the mechanisms driving serological, humoral, and cellular immune responses to SARS-CoV-2 viral infection, and to inform the development of novel serological tests, to determine the serological correlates with disease, pathogenesis, and protection against future infection, and improve population-based models of outbreak and susceptibility through serological focused studies," Lowy said.

Following are the RFAs and RFP issued by NCI:

- Two RFAs to support research into the SARS-CoV-2 immune response (deadline for both is July 22):
  - SARS-CoV-2 Serological Sciences Centers of Excellence (U54) (RFA-CA-20-038)
  - Research Projects in SARS-CoV-2 Serological Sciences (U01) (RFA-CA-20-039)
- Another RFP issued earlier in June would support the SeroNet Capacity Building Centers (deadline is July 16).

More information is available here:

- NCI Seeks Applications for SeroNet COVID-19 Research
- Serological Sciences Network for COVID-19 (SeroNet)

Lowy's remarks at the virtual joint meeting of BSA and NCAB follow:

We have benefited from an incredible collaboration, primarily other parts of NIH and the Department of Health and Human Services, NIAID, FDA, CDC and BARDA, and also Mount Sinai, where Ramon Parsons, Florian Krammer and their colleagues have really been very helpful, and in addition, other cancer centers as well.

The shorter-term goals have been to characterize the performance of different serological assays, correlate them with neutralization, and understand possible cross-reacting sera from prior to the epidemic, and to correlate this with serological tests submitted to the FDA.

The longer term goals are to understand implications of being seropositive. Does this really mean resistance to reinfection and duration of seropositivity?

FDA and commercial serology devices

The FDA had issued a number of press releases, first on March 16. They permitted the sale of commercial laboratory-based, rapid lateral flow SARS-CoV-2 serology devices without actually assessing the performance. The serology devices, importantly, are not used to diagnose current infection. That's measuring the viral RNA or viral protein. This instead is measuring antibodies.

During this initial period, there was a lot of heterogeneity in the quality of the devices that were available, but at the beginning of May, the FDA gave emergency use authorization to several commercial devices and required that all other manufacturers would submit emergency use authorizations or EUA requests within 10 business days, and some of the Emergency Use Authorizations, they took advantage of data that had been developed at the Frederick National Laboratory and the serology laboratory.

> “Third, it's not currently known whether being antibody positive is associated with protection against re-infection, what antibody levels may be associated with protection, and how long protection and antibody levels will last.”
>
> *– Douglas Lowy*

Then about 10 days ago, the FDA gave emergency use authorizations for several additional devices. [Here are] the results of the initial 40 commercial serology devices that have been evaluated by the Frederick National Laboratory serology laboratory:

We have tested both IgM and IgG antibody tests, but I think that people should be focused more on the IgG antibody tests, because IgM and IgG in this disease become positive at about the same time, but IgM goes down faster than IgG.

What we have found in this analysis is that the sensitivity for the various devices, the ability to detect true positives, vary enormously. Some of them were extraordinarily good, being in the 90% to 100% range, but some of the devices were not very good and had sensitivity that was well below that, and one as low as 30%.

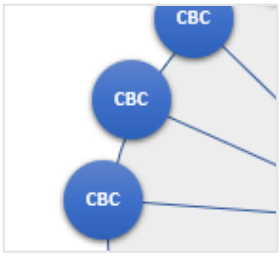
Specificity was also quite variable, and I'll have something to say about that in a subsequent slide. The specificity, it's the efficiency with which you don't detect false positives, and again, it varied from a high of 100% to a low of 87%.

The results, we then sent them to the FDA to help FDA determine suitability for Emergency Use Authorization, and as I mentioned, the FDA has made some of their NCI evaluation results publicly available, and others will be released in the near future, and my expectation is that because of the increased stringency of the authorizations, that in the very near future, only devices with high sensitivity and high specificity should be available in the United States.

Low rates of seroprevalence

The vast majority of the United States, with the possible exception of perhaps first responders or healthcare workers in New York and a few other places, the seroprevalence is actually quite low, well below 10% in virtually all areas of the United States, when you look on a state-wide level, rather than looking at specific populations, such as nursing homes or meat processing plants, but if you look at this slide, if a test has 99% specificity, which we would consider a very good test, and the seroprevalence is found to be at 5%, 20% of the positive will be false

Serological Sciences Capacity Building Centers



RFP (due July 22)

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

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

Goals

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

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positive. In other words, one out of five of the positives will be false positives.

If a test has 95% sensitivity, which you usually would think about as being quite good, and the seroprevalence was found to be 5%, at that point, 50% of the positives will be false positives, which means that there's a tremendous false error rate. That is why it's so important for the current tests to have very high specificity.

So, I want to go over with you some of the questions that currently are unknown and being addressed by research. First, being antibody positive means either the person is currently infected with SARS-CoV-2 or has been previously infected. Second, you can now use the test for seroprevalence studies. It should identify most people who had asymptomatic or symptomatic infection. However, a small minority of people, mainly those with asymptomatic infection, may remain antibody negative.

Third, it's not currently known whether being antibody positive is associated with protection against re-infection, what antibody levels may be associated with protection, and how long protection and antibody levels will last. And therefore, we think that antibody titers are likely to become important, and we are in the process of developing quantitative assays, and I think in the near future that the FDA will also be evaluating quantitative assays.

For candidate polyclonal antibodies, from convalescent sera and neutralizing antibodies, which are currently being initiated in clinical trials, will they reduce the risk of serious disease? It remains to be seen. If they do, it will imply that the candidate SARS-CoV-2 vaccines, which mainly we think will function by inducing neutralizing antibodies, would be more likely to confer protection.

The phase III trials for the vaccines will be starting sometime next month, as many of you have heard, but they will be randomized controlled trials that will look at evaluating whether there are enough events in the control group and the vaccine group to be able to identify a clear cut benefit.

I just want you to see how many different people have been involved in making this effort possible. I, of course, want to acknowledge the people at the Frederick Serology Laboratory, Ligia Pinto, Troy Kemp and Jim Cherry.

COVID-19 SeroTracker

This is setting up a data resource for strategic assessment of serology. It will be a COVID-19 sero-track. We are

Serological Sciences Centers of Excellence (RFA)

4-8 U54 awards (due July 22)

Up to $1.5M total costs per year for up to 5 years

Goals

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

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

Budget set-aside for collaborative projects proposed post-award

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setting this up with the strong collaboration with NIAID and CDC.

The reason we are doing it is that both the NIAID and CDC asked us if we could do it, they were so strapped for their various resources. So Tony Kerlavage and Stephen Chanock have been extraordinarily proactive in setting this up over a very recent period, and Neal Freedman from NCI is going to be the subject matter expert at NCI, and they will be subject matter experts from NIAID and CDC, and the idea for the warehouse is to collect and manage COVID-19 serological test results and serve as a research resource to NCI, NIAID, CDC and the broader research community.

The dashboard, the goal will be to be a summary of global serological studies, assay types and results generated, and antibody prevalence in the U.S. For the ability to filter results by geography and demographics. If you look on the right, the prototype would be in two stages. We hope that the summary dashboard will be able to be set up sometime this summer, and the larger prototype to be a prototype to be working in the fall. So stay tuned for this.

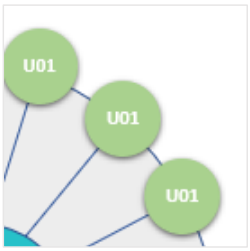
Proposed Serological Sciences Network

I want to now, for the remainder of the time, talk about the proposed Serological Sciences Network for SARS-CoV-2. The announcement for this network came out 10 days ago, and the due date is going to be by July 22.

So, there will be Serological Sciences Capacity Building Centers. The goal is to expand the testing capacity and practice in the community, implementing standardization for serology development, and using these tests and scale up as necessary for testing, and to acquire convalescent sera from recovered patients who are seropositive, and to conduct surveillance trials, and to pursue focused serological science.

There will also be the Serological Sciences Centers of Excellence, and their goals are to understand the mechanisms driving serological, humoral, and cellular immune responses to SARS-CoV-2 viral infection, and to inform the development of novel serological tests, to determine the serological correlates with disease, pathogenesis, and protection against future infection, and improve population-based models of outbreak and susceptibility through serological focused studies. There will be a preference for cancer relevant components, and each center will have several projects and administrative core and the possibility of a technical core, and these will be U54 awards.

Serological sciences projects (RFA)



5-10 U01 awards (due July 22)

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

Goals

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

Budget set-aside for collaborative projects proposed post-award

Network Coordinating Center at Frederick National Lab

FNLCR Task Order

$750K total costs per year

Goals

- Provide program management, coordination and communication across the Serological Sciences Network for SARS-CoV-2
- Coordinate sharing of the data, reagent, sample, and assays
- Coordinate comparison of results among different centers and assays through inter-Center collaborative studies, leading to international serology standardization
- Coordinate partnerships with national and international associates such as the FDA, CDC, WHO, National Institute for Biological Standards and Control (NIBSC), and others
- Work in close collaboration with NCI program staff

The third component will be the serological sciences projects, and the goals will be to understand the mechanisms driving the serological, humoral, and cellular immune responses to infection, to inform the development of tests, determine the serological correlates, improve population-based models, and again, preference for cancer relevant component. These will be five to 10 U01

> We think that antibody titers are likely to become important, and we are in the process of developing quantitative assays, and I think in the near future that the FDA will also be evaluating quantitative assays.
>
> *– Douglas Lowy*

awards, and up to $500,000 cost per year and up to five years.

There will also be a Network Coordinating Center at the Frederick National Lab. It will be distinct from the dashboard that I mentioned, and the goals will be to provide program management, coordination and communication across the network.

Coordination for sharing of data, reagents, samples, assays and coordinate comparison of results among different centers and assays through inter-center collaborative studies leading to international serological standardization. And to coordinate the partnerships with national and international associates, such as FDA, CDC, World Health Organization, the National Institute for Biological Standards of Control, and others, and to work in collaboration with the program staff.

There was a request for information, an RFI, for strategy for the coronavirus testing and that was to seek input from the research community. It closed about three weeks ago and some of the responses are being incorporated into the scope of the network.

To summarize the hub-and-spoke notion of the Serological Sciences networks, and importantly, to acknowledge the many people who have been instrumental in putting this aspect together. Particularly, I'd like to acknowledge Dinah Singer, Crystal Wolfrey, and Sara Hook at NCI and at NIAID Carl Dieffenbach, Emily Erbelding, and Cristina Cassetti.

Collins: It's unknown whether COVID-19 antibody-positive test means protection against reinfection

By Alexandria Carolan

In March, as SARS-CoV-2 spread rapidly across the United States, cancer researchers scrambled to find clues about the virus and ways to mitigate its damage.

Earlier this week, at the annual meeting II of the American Society for Cancer Research, several of these SARS-CoV-2 researchers presented their findings about the immune system's response to the novel coronavirus.

Here are the highlights of their presentations:

- There may be crossover between immunity of SARS-CoV-2 and immunity to the seasonal coronavirus,
- Immune and clinical heterogeneity is high in COVID-19 hospitalized patients,
- High levels of inflammatory cytokines at diagnosis correlate with poor survival,
- In ICU patients with COVID-19, T cells appear to lose the ability to differentiate, and stay in the naive phenotype,
- The best predictor of severe COVID-19 is a rise in serum levels of calprotectin and early loss of non classical monocytes.

These presentations built on earlier results, presented at the AACR annual meeting I, which was held in April (*The Cancer Letter*, May 1, 2020).

Addressing the session on COVID-19, NIH Director Francis S. Collins warned that delayed breast and colorectal cancer diagnoses and treatment will result in higher mortality rates down the line (*The Cancer Letter*, June 19, 2020).

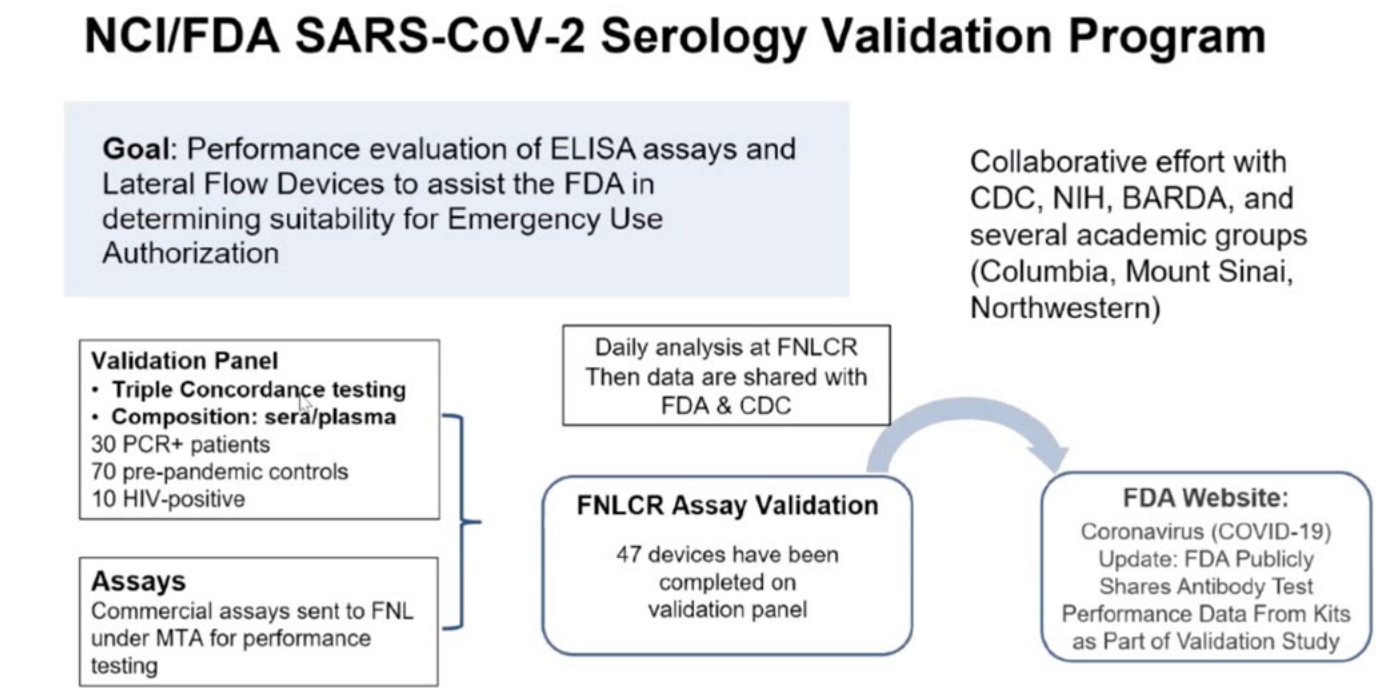
"That is deeply troubling. That is a consequence of what has happened because of this pandemic—these are not deaths that are going to be counted as directly due to the virus, but in a certain way—they are," Collins said. "We have to do everything that we possibly can now things are starting to open up, to catch up, and to make sure that those folks who have waited don't keep on waiting any longer."

Collins presented an overview of NCI's COVID-19 in Cancer Patients Study (NCCAPS), which aims to assess how COVID-19 has affected people with cancer who test positive for COVID-19.

"The idea is to try to study how this may disrupt cancer-directed therapy, what the long-term outcomes might be, and how this might guide future care for people who acquire this illness," Collins said.

Goals of the study are to:

- Enroll a large cohort of patients undergoing cancer therapy who test positive for SARS-CoV-2 to characterize factors associated with COVID-19 severity.
- Describe modifications to cancer treatment made due to COVID-19.



Source: Presented by Francis Collins at AACR virtual annual meeting II.

- Evaluate association of COVID-19 with cancer outcomes in clinico-pathologic subgroups,
- Assess anti-SARS-CoV-2 antibody development, cytokine abnormalities, genetic polymorphisms associated with severe COVID-19,
- Create bank of clinical data, research blood specimens, radiological images for future research.

"This is going to be a very important study to try to understand the interaction between a very common disease—cancer—and a very unexpected global pandemic of COVID-19."

From NIH

Over the past 9 weeks, Frederick National Lab received more than 130 commercial assays for validation—"most of the tests that they looked at weren't bad at all," Collins said.

"They were very well set up to be able to do validation of various commercial serology tests that were beginning to hit the market, and where FDA really needed some help assessing the performance of these," Collins said.

However, it's not known whether testing antibody-positive is associated with protection against reinfection, which antibody levels are associated with reinfection, or how long protection will last.

"In a few more months, we will know the answer to that, but let nobody try to tell you that 'OK, I have antibodies, so I'm now completely safe. I don't have to wear a mask. I don't have to worry about getting exposed again,'" Collins said. "We don't know that yet."

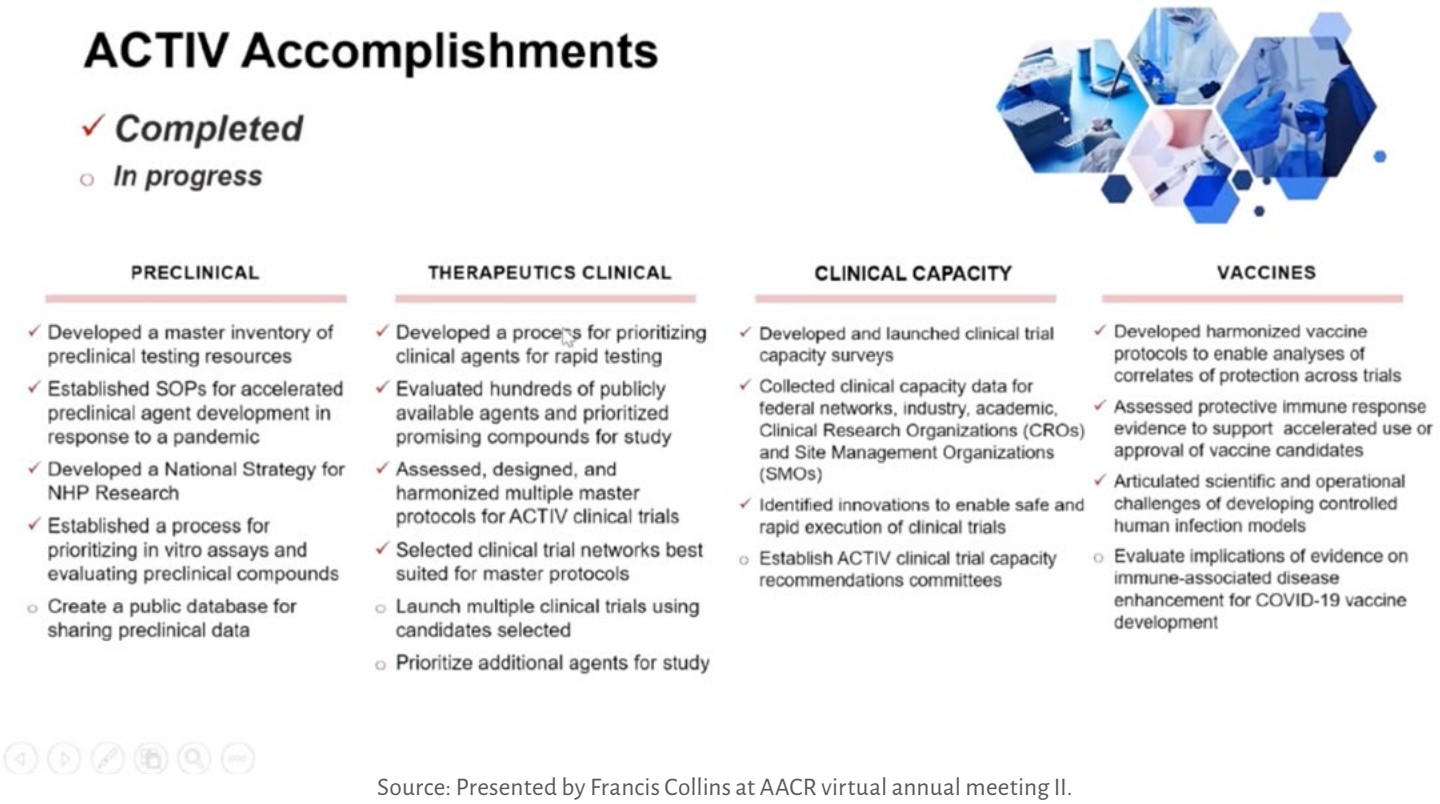
In addition to NCI's serology and NCAPPS efforts, NIH has been investigating COVID-19 on three fronts: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), a public-private collaboration, Warp Speed, which acts as oversight for ACTIV, and diagnostics research.

"What we try to do is bring the best and brightest scientists from all sectors around the same table, design what needs to be done, and then step forward, holding ourselves accountable to meet milestones," NIH Director Francis S. Collins said during the session.

ACTIV is made up of four working groups, each co-chaired by a member of industry and NIH:

- Preclinical
- Therapeutics clinical
- Clinical capacity
- Vaccines

ACTIV consists of leaders from FDA, CDC, Department of Defense, Veterans Administration, multiple institutes at NIH, Biomedical Advanced Research and Development Authority and 12 pharmaceutical companies.



Source: Presented by Francis Collins at AACR virtual annual meeting II.

> Even though this is a breathtaking time table, it might actually be achievable that we would have, by the fall, these kinds of new technologies that are usable, point-of-care, affordable, and give an answer in a big hurry.

Warp Speed, a government initiative, is overseeing ACTIV. Also, NIH has established the Rapid Acceleration of Diagnostics (RADx) Initiative to address the need for rapid diagnostic testing of COVID-19 in the U.S.

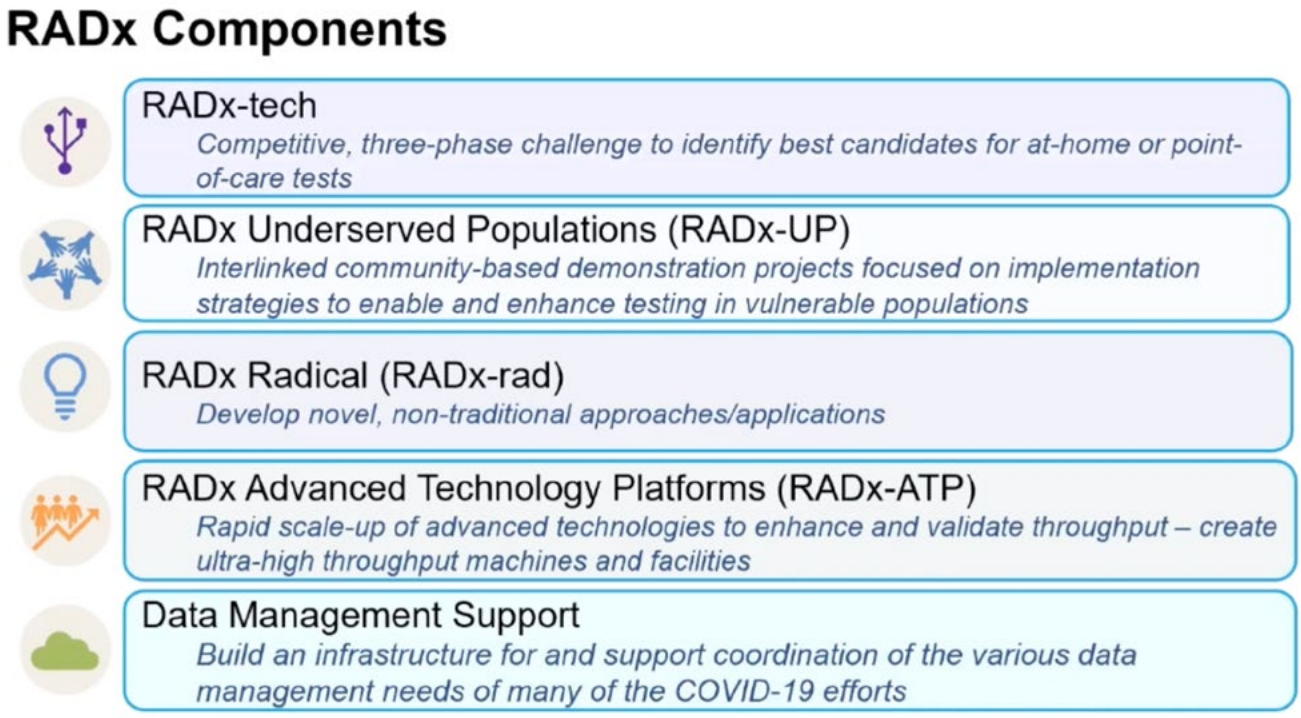
"The area where people are most urgently needing to see the expansion of diagnostics is the detection of the virus," Collins said. "About 500 applications have already come forward. Something over 10% of those have now gone into this phase 0 shark tank to see how they look. And some of those have now already graduated that into phase I, and phase II, where there's a real scale-up, is not far away."

Collins expects there to be widespread diagnostic, point-of-care testing by the fall.

"Even though this is a breathtaking time table, it might actually be achievable that we would have, by the fall, these kinds of new technologies that are usable, point-of-care, affordable, and give an answer in a big hurry," Collins said. "It is an engineer's dream to have this kind of innovative effort all thrown together to see what comes out of it."

Other aspects of RADx address diagnostics in underserved populations, novel applications, scale-up of technologies, an infrastructure building for data management of COVID-19 efforts.

"You can't look around right now and not be heartbroken when you see the way in which COVID-19 has particularly hit hard those same populations that have already been suffering from health disparities—individuals who are elderly but with chronic illnesses, and particularly those in lower socioeconomic status communities, African Americans, Hispanics—all of those individuals paying a much higher price for the serious illness part of this disease," Collins said. "One of those reasons is a lack of access to testing in those communities."



Source: Presented by Francis Collins at AACR virtual annual meeting II.

Research presented at the meeting

Distinguishing pre-existing and de novo antibody responses to SARS-CoV-2 is critical for serology, seroprevalence and vaccine studies, George Kassiotis, senior group leader and head of the laboratory of Retroviral Immunology at the Francis Crick Institute, London, said during the session.

Kassiotis, professor of retrovirology in the Department of Medicine, Imperial College London, sought to answer whether the introduction of SARS-CoV-2 in the human population, acquired in the absence of preexisting immunity, has an effect on symptoms of SARS-CoV-2.

Kassiotis presented data during his talk, titled "pre-existing and de novo humoral immunity to SARS-CoV-2 in humans," that suggest cross-reactive activity in SARS-CoV-2 and seasonal coronaviruses.

"The potential consequences of preexisting immunity for the course of SARS-CoV-2, or susceptibility to coronaviruses, are not yet fully known," he said.

The data show that:

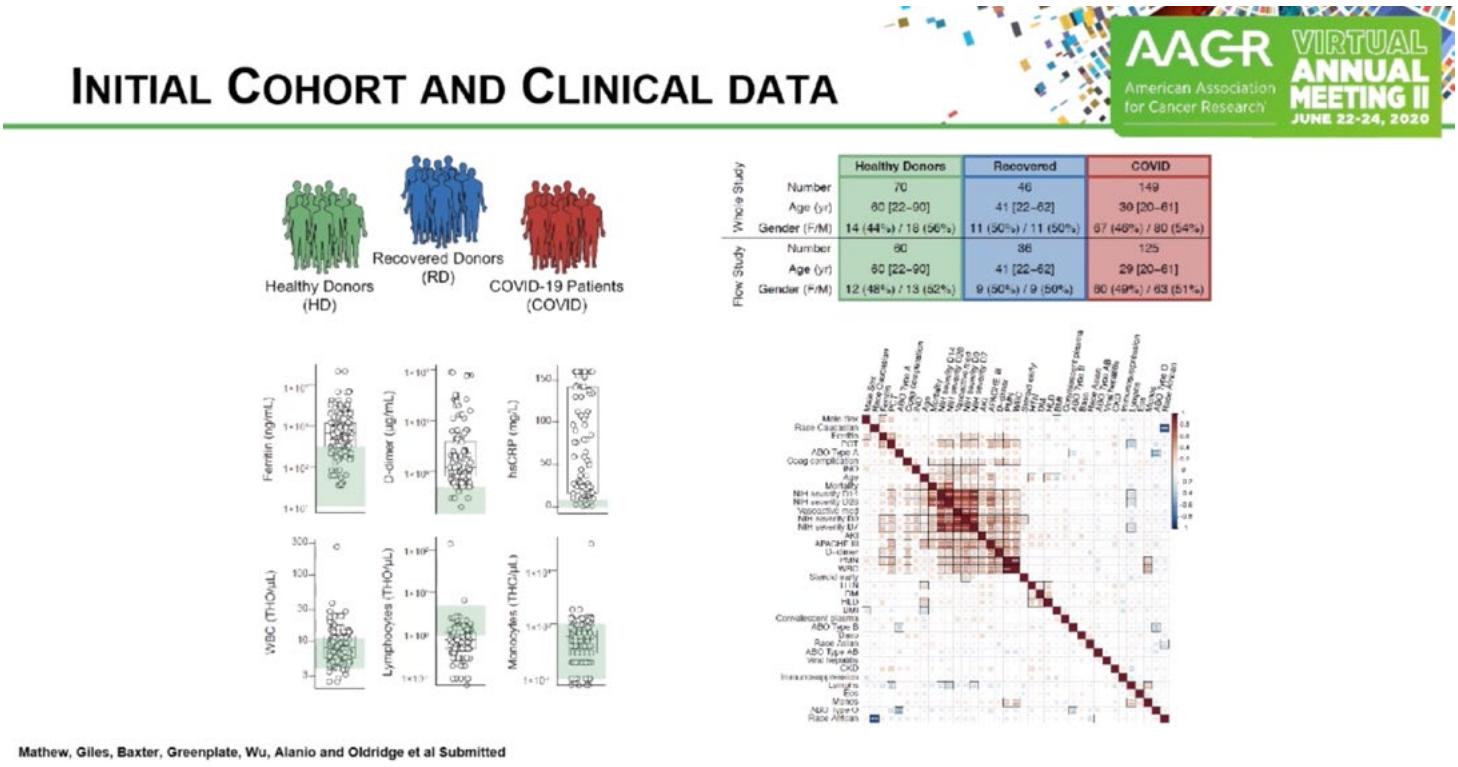
- SARS-CoV-2 cross-reactive bodies are detected in sera from uninfected individuals,
- Targeting predominantly of S2 might not interfere with S1 binding to the cellular receptor ACE2,
- S-2 binding neutralizing antibodies have been described,
- There may be alternative entry modes for SARS-CoV-2, such as the CD147 alternative receptor, or receptor independent entry.

"The public health measures intended to prevent the spread of SARS-CoV-2 will also prevent the spread—and consequently, maintain herd immunity to seasonal coronaviruses," Kassiotis said. "It is therefore imperative that any effects, positive or negative, of preexisting seasonal coronaviruses immunity on the measured course of SARS-CoV-2 infection is fully delineated."

Immune health profiling of COVID-19

Researchers at the University of Pennsylvania wanted to find out what a typical immune response in hospitalized COVID-19 patients looks like.

"What we wanted to do was try to understand the relationship of the immune response or the immune system to this respiratory viral infection," E. John Wherry, chair of the Department of Systems Pharmacology and Transla-



Source: Presented by George Kassiotis at AACR virtual annual meeting II.

tional Therapeutics, Richard and Barbara Schiffrin President's Distinguished Professor, and director, of the Institute for Immunology, University of Pennsylvania, said during the session.

To answer this, Penn researchers built a translational immunology profiling pipeline that allowed them to obtain samples from 140-150 hospitalized COVID-19 patients, 70 healthy controls, and 50 recovered patients. Pediatric and cancer cohorts are being developed.

The study sought to address three questions:

1. What type of immune response exists in COVID-19 patients?
2. Are there common pathways of immune activation or response?
3. How do immune responses relate to clinical failures of disease?

Here's what they found:

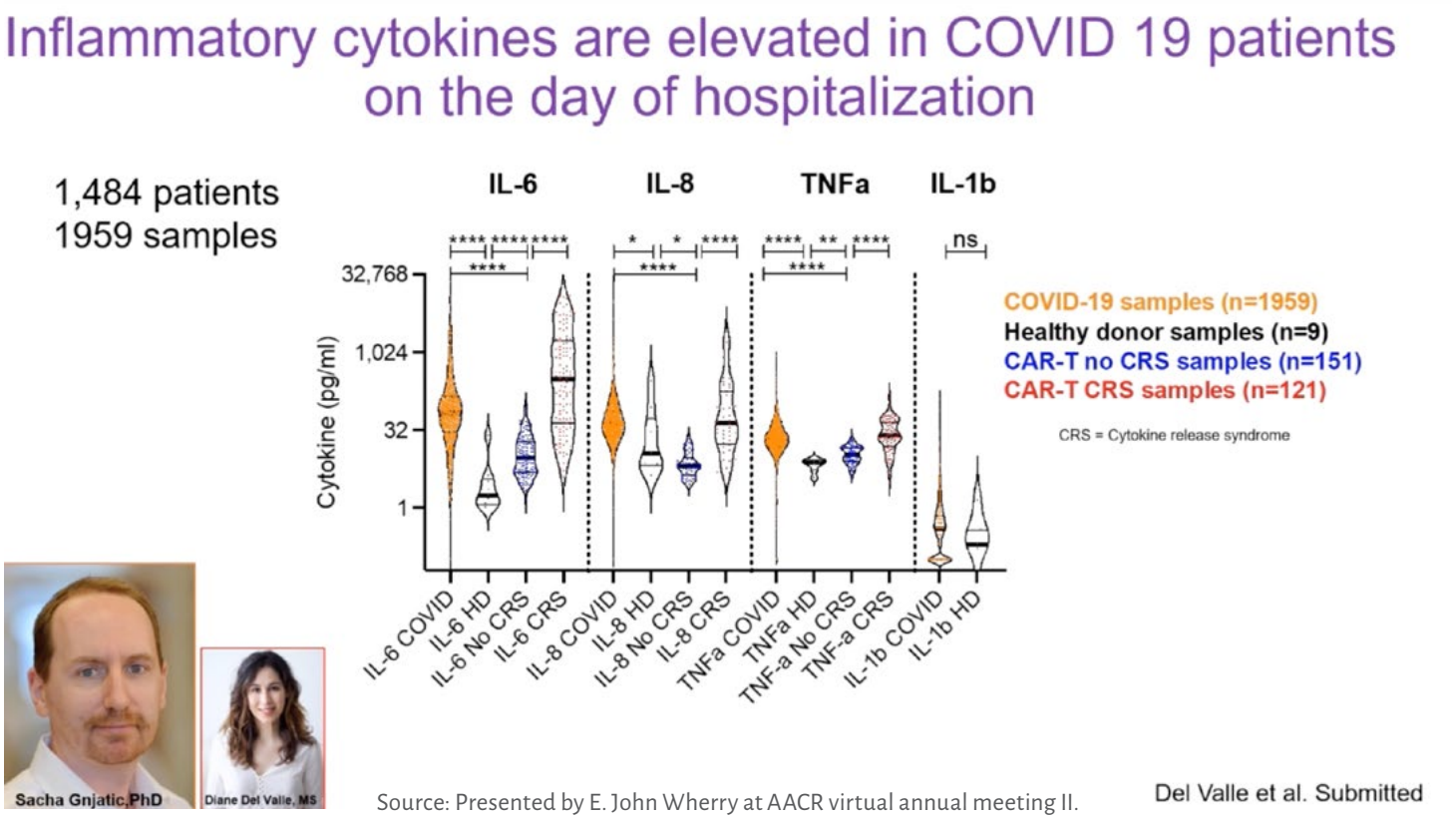
- Immune and clinical heterogeneity is high in COVID-19 hospitalized patients,
- There's a C8 biased lymphopenia that's somewhat unusual, and typical in severe viral infections,
- A massive plasmablast response rivals acute ebola and Dengue fever,
- A surprisingly stable T and PB responses over time,
- Three immunotypes defined by different immune features that are linked to clinical presentations—one of which is linked to high-levels of inflammation and inflammatory diseases,
- Links between immunotypes and clinical features might suggest ways to tailor different immune interventions to have the most effect on patients who have a certain type of immune response, such as suppressing versus activating the immune system.

Pathogenic inflammation in COVID-19 patients

New York was the epicenter of COVID-19 cases this spring, and accounted for one third of total cases in the U.S. Mount Sinai Health System in New York City had 6,936 patients with COVID-19 hospitalized there from Feb. 27-June 5.

Many COVID-19 deaths are associated with severe inflammation and embolic complications.

The focus of the Mount Sinai Immunology group has been to predict, prevent and treat pathogenic inflammation to reduce the COVID-19 death toll while waiting for curative and preventative therapies to become available, Miriam Merad, Mount Sinai Endowed professor in Cancer Immunology and the director of the Precision Immunology Institute at Mount Sinai School of Medicine, said in her talk.



Researchers at Mount Sinai, led by Merad, redeployed the hospital's Humane Immune Monitoring Center to serve the COVID-19 research effort with two goals in mind.

"The first was to a establish a rapid cytokine test to predict pathogenic inflammation, and also to build a longitudinal collection of COVID-19 biospecimens to identify immune correlates of disease severity and identify rationale-based immunotherapy strategies," Merad, who also co-leads the Cancer Immunology program at The Mount Sinai Tisch Cancer Institute and is the director of the Mount Sinai Human Immune Monitoring Center, said.

To assess pathogenic inflammation, researchers used a rapid cytokine test to evaluate 1,484 COVID-19 patients on their first day of hospitalization. They repeated tests on 218 patients and ended up with 1,959 samples.

Here's what they found:

- Inflammatory cytokines are elevated in COVID-19 patients on the day of hospitalization,
- High levels of inflammatory cytokines at diagnosis correlate with poor survival,
- High IL-6 and TNF-a levels are independent predictors of poor disease outcome that can help stratify patients and maximize response to immunomodulatory treatment,
- The cytokine combination blockade could benefit a subset of patients,
- Cytokine levels remain stable throughout the disease course.

The next component for the researchers was to establish a longitudinal biospecimen workflow.

"We had to build a research collection, which was not simple to do during a pandemic," Merad said.

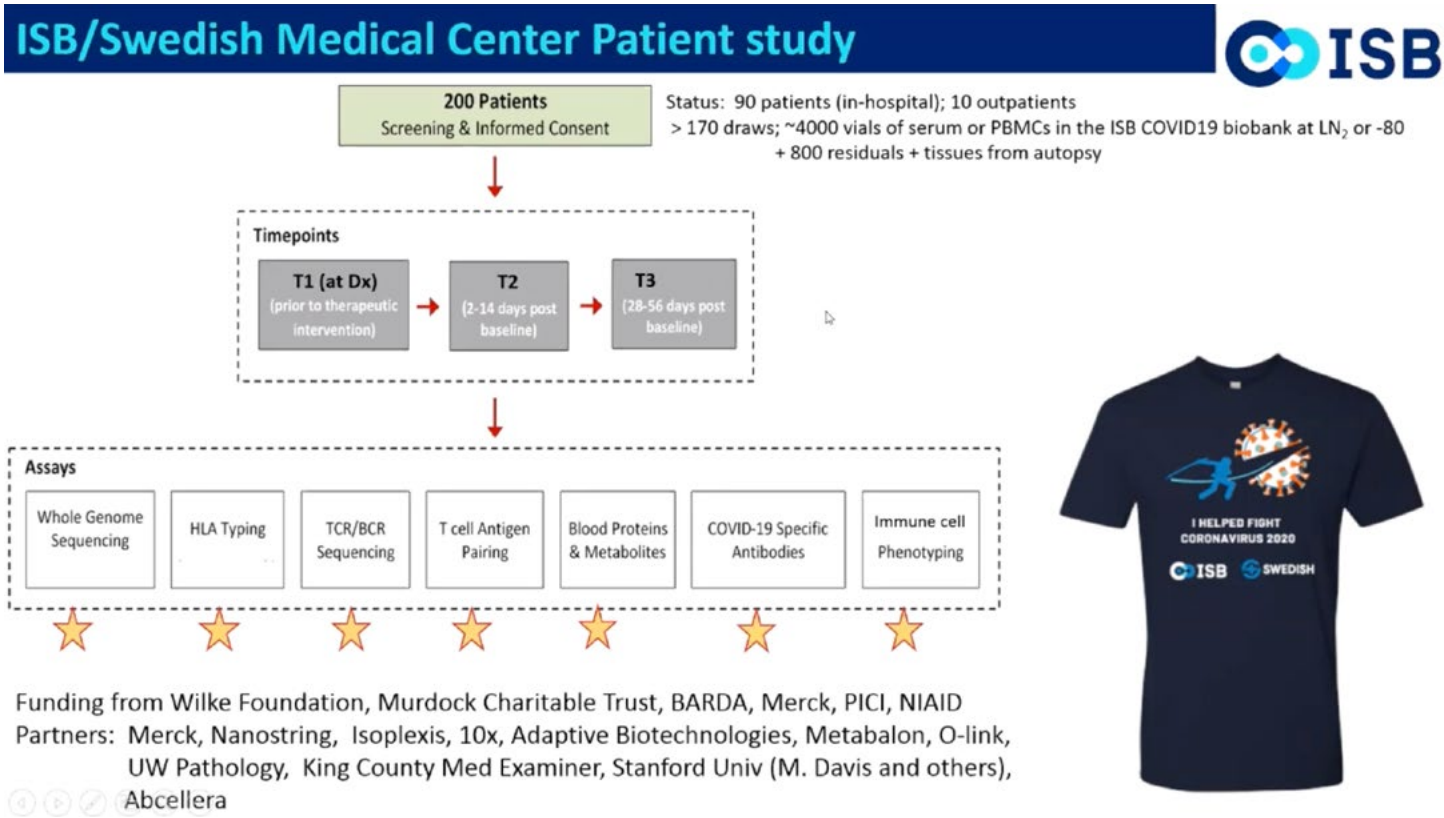
Researchers evaluated the following cohorts:

- Hospitalized patients (700),
- Clinical trials,
- Children,
- Convalescent (ongoing),
- Health care workers (ongoing, with a goal of 200).

In the hospitalized cohort, researchers collected more than 500 COVID-19 patients, and 200 who were hospitalized at the same time, unrelated to COVID-19.

Conclusions are:

- COVID-19 is a very heterogeneous disease, and large-scale cohorts can help inform disease pathogenesis,
- COVID-19 patients express different inflammation patterns,



Source: Presented by Miriam Merad at AACR virtual annual meeting II.

  - Patients with severe disease have high or low systemic inflammation,
  - Patients with moderate disease have a strong T cell priming signature and lack a tissue damage signature,
  - Inflammatory patterns are fixed during the disease course, suggesting distinct pathogenesis,
- It's important to continue to map deep molecular mapping of inflammatory patterns, unravel disease pathogenesis, stratify patients, and guide therapeutic strategy,
- It's important to measure the impact of inflammatory signatures on the quality and sustainability of the viral specific response, and potentially the susceptibility to reinfection.

T cell responses to COVID-19

A study by the Institutes for Systems Biology and Swedish Medical Center explores how T cells responses differ in COVID-19 patients. James R. Heath, president and professor at Institute for Systems Biology, presented the study.

The study includes 200 patients, who were enrolled beginning at the end of March. The study is evaluating 90 patients in the hospital and 10 outpatients. The researchers have collected 170 blood draws, with 4,000 vials of serum or PBMCs in the ISB COVID-19 biobank.

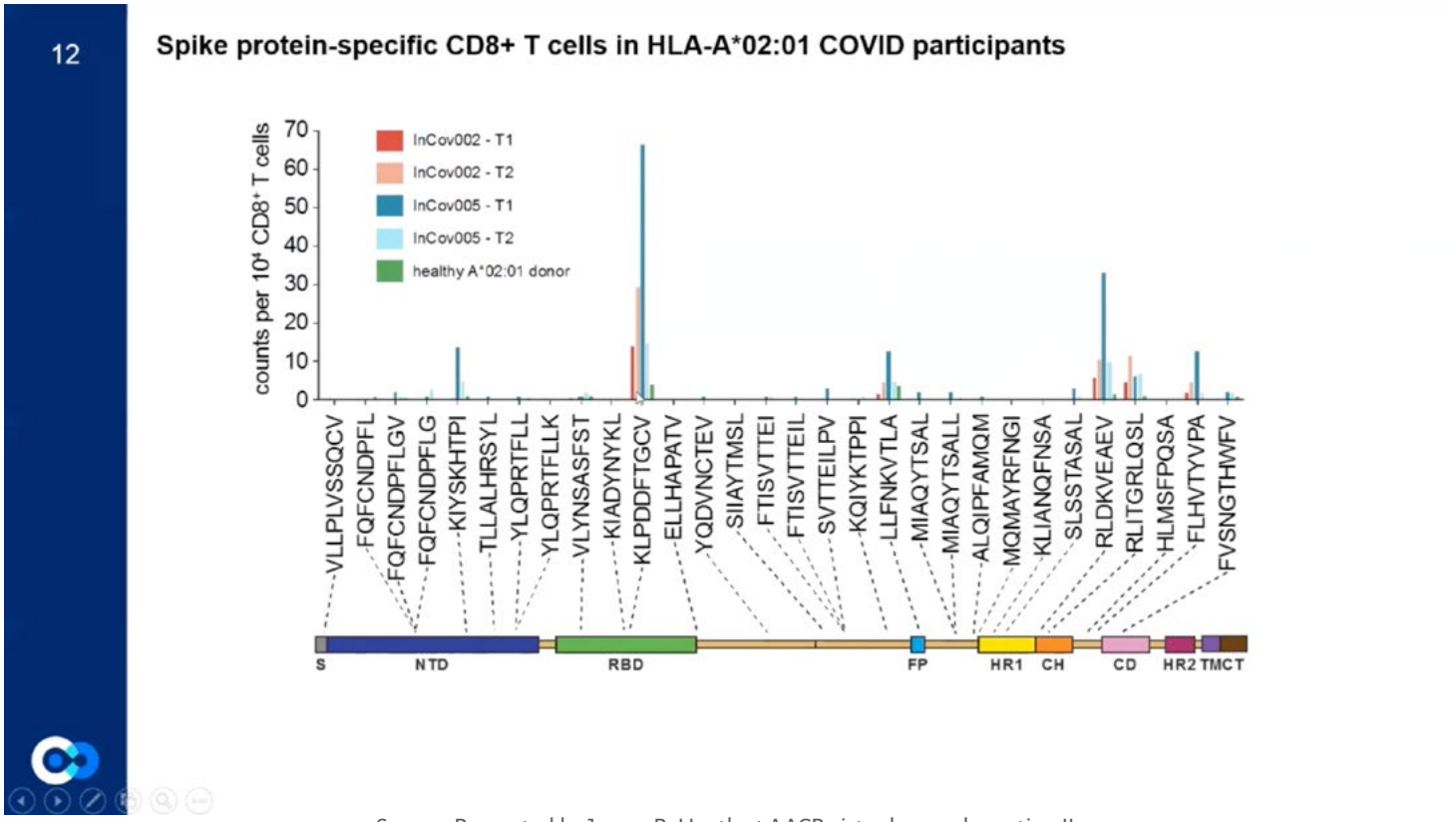
"If you compare a healthy patient cohort—these seven healthy patients we have here—you'll see a mixture of naive and effector T cells," Heath said. "For non ICU patients, you'd largely see effector T cells. The ICU patients—by and large the T cells appear to have largely lost the ability to differentiate, and they stay in the naive phenotype."

For patients who don't receive IL-6 inhibitors, there will be an increase of the effector phenotype over time, Heath said. For the IL-6 inhibitor patients, there will be an emergence of antigen-specific naive T cells that are of a protective memory phenotype.

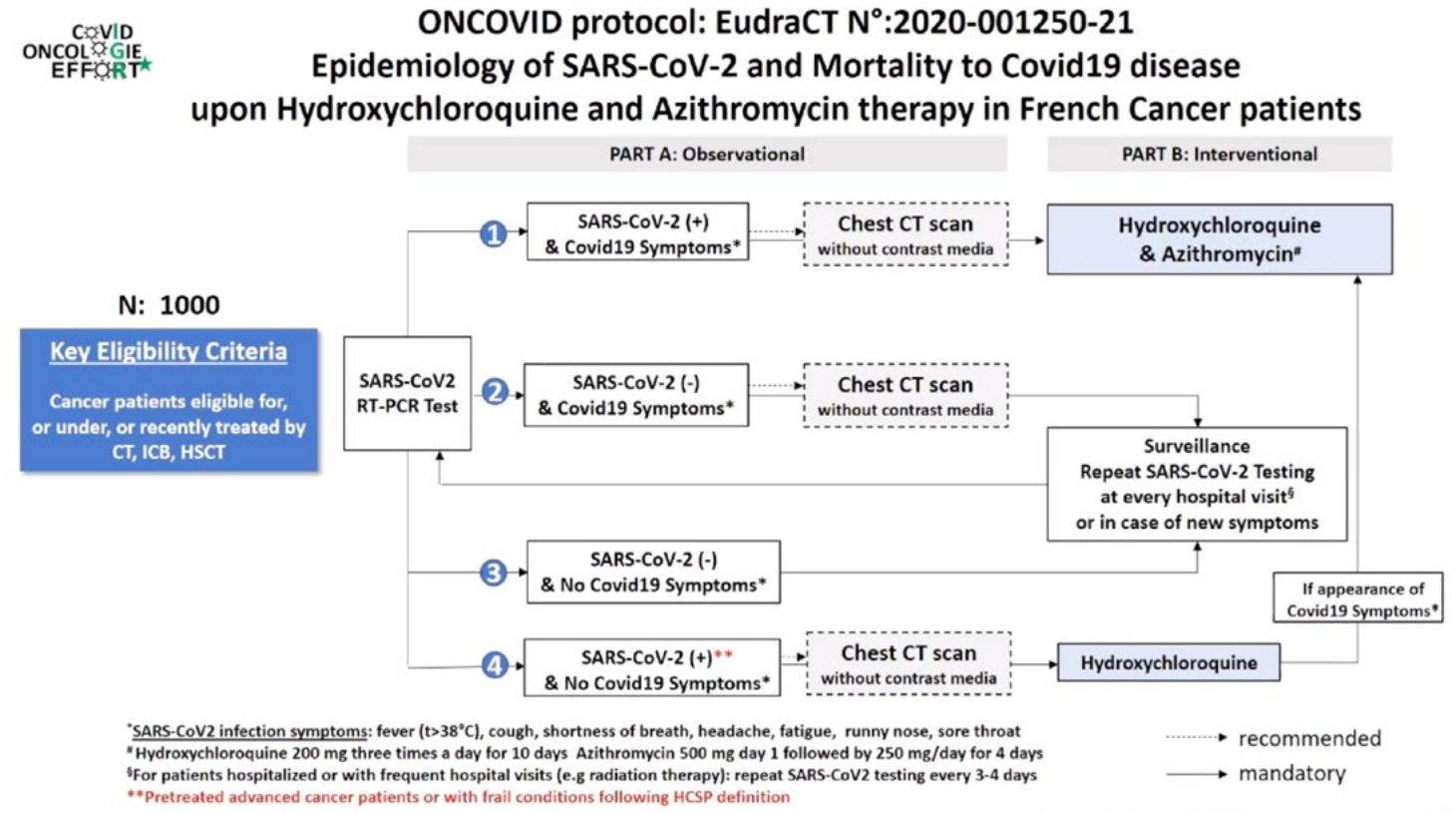
"The IL-6 inhibitor is more or less saying, at least from the point of view of these T cells, that the infection is over, but keep on the lookout for more virus when it comes," Heath said.

The takeaways?

"If one patient has antigens of T cells, generally the other patients will as well. These are truly immuno-dominant-type antigens," Heath said. "The time dependence of these populations—in this patient they all go up over time, but in [this] patient they're all decreasing all



Source: Presented by James R. Heath at AACR virtual annual meeting II.



Source: Presented by Laurence Zitvogel at AACR virtual annual meeting II.

the time—that also seems to be something that's consistently observed."

The most immuno-dominant antigen comes out of the receptor binding domain, Heath said.

"In the near future, we'll have some insights into how the different parts of the protein—not just generate different T cell populations—but how they can play a role in the immunoprotection of the patient against the virus," Heath said.

Elevated calprotein and abnormal myeloid cell subsets characterize severe COVID-19

The ONCOVID protocol at Institut Gustave Roussy aims to analyze the incidence, prevalence and severity of COVID 19 in 500 french individuals.

"At this stage, it's not clear whether cancer as such is an independent risk factor for severe COVID-19, or whether cancer-associated comorbidities will actually account for COVID outcomes in cancer patients," Laurence Zitvogel, head of the laboratory of pneumology and cancer immunotherapy at Institut Gustave Roussy, said in her talk.

There have been 178 cancer patients treated for COVID-19 at Gustave Roussy.

A total of 75% of cancer patients with COVID-19 were hospitalized, 26% clinically worsened, and 17% died. Increased risk of death was associated with aging, smoking, an ECOG Score higher than 2, metastatic disease, and use of cytotoxic therapies in the past 3 months. An ECOG Score higher than 2 was the strongest indicator of clinical worsening and death, Zitvogel said.

Researchers analyzed whether immune parameters could predict the switch from mild to severe COVID-19 in non-cancer patients.

The researchers concluded that immature neutrophils harboring an immunosuppressive fingerprint (NF-KB, ROS, NOS, IL-1R) secreting high levels of alarmins S100A8/A9 are associated with a switch from mild to severe COVID-19.

This poor prognosis is associated with an early loss of non-classical monocytes and a downregulation of DR and CD169 expressing classical monocytes, Zitvogel said.

> "The idea is to try to study how this may disrupt cancer-directed therapy, what the long-term outcomes might be, and how this might guide future care for people who acquire this illness."

"This conjecture was not observed in mild disease where type I interferon prevailed, and where circulating neutrophils and monocytes express SIGLEC1/CD169 and maintain the non-classical CD16high CD14 INT monocyte subset," Zitvogel said.

The best predictor of severe COVID-19 is a rise in serum levels of calprotectin and early loss of non-classical monocytes, she said.

THE CANCER LETTER | JUNE 26, 2020 | VOL 46 | ISSUE 26

GUEST EDITORIAL

To expedite progress against COVID-19, a public-private "accelerator" taps into real-world data

Jeff Allen, PhD
President, CEO,
Friends of Cancer Research

Susan C. Winckler, RPh, Esq.
CEO, Reagan-Udall Foundation for FDA

Real-world data is everywhere. During the COVID-19 global pandemic, we are literally generating, and collecting, real-world data every single day—from electronic health records, insurance claims, patient registries, and a myriad of other sources. But the question remains: how do we use this data to better understand, prevent, and treat this disease?

Data by itself does not tell us much. Real-world data comes from many different places in so many different formats that it can be like looking at a computerized image blown up so that all you see is pixels. But, if you scale that image and examine it from a different angle, a full picture begins to emerge. Real-world data needs that same refinement to illustrate the full picture of clinical and patient experience, creating real-world evidence that informs clinical practice and disease management.

The Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research, has launched the COVID-19 Evidence Accelerator specifically to move real-world data into real-world evidence. Working closely with FDA, the Evidence Accelerator brings together top experts in healthcare data and analytics to share insights, compare results, and answer key questions to inform the nation's COVID-19 response.

Through the Therapeutics Evidence Accelerator, which launched in May, and the Diagnostics Evidence Accelerator announced last week, the project supports the research community in not only addressing specific questions about preventing, testing and treating COVID-19, but also in understanding the natural history of the disease.

Participants include experts from FDA, major data organizations, patient advocacy, healthcare and hospital systems, clinical laboratories, insurers, academic research institutions as well as drug and device manufacturers and technology companies. The Evidence Accelerator is comprised of three main workstreams:

- **Therapeutics Evidence Accelerator Collaborative** provides a venue for scientists across the country to discuss data generated from quick turnaround queries and share results with peers and experts from FDA, major data organizations, academic research institutions, professional societies, and health systems to help accelerate, and potentially confirm, findings from different data sources and leverage existing expertise.

“Real-world data needs that same refinement to illustrate the full picture of clinical and patient experience, creating real-world evidence that informs clinical practice and disease management.”

- **Therapeutics Evidence Accelerator Parallel Analysis Workgroup** invites multiple teams to simultaneously address key research questions developed with FDA. The Workgroup pools participant expertise to determine how data elements are being extracted and how they are being defined to be operationalized. Initial activities include (1) rapidly revising a list of core data elements; (2) identifying those elements critical to answering the primary question; and (3) establishing uniform collection parameters. Repeating analyses in parallel through collaborators using different analytical techniques and data sources helps strengthen findings and learnings.
- **Diagnostics Evidence Accelerator**, a hybrid of the Therapeutics Collaborative and Parallel Analysis approaches, addresses the diagnostic and serological study space. The goal is to present and discuss information on recent analyses of real-world data related to diagnostic test performance, contemporaneous symptoms and presentation, surveillance trends and immunity.

Just as the best art often takes a combination of creativity and discipline, so does crafting real-world evidence now and in the future. The Evidence Accelerator is building a platform to answer current questions around COVID-19 that can also be used post-pandemic.

The public-private partnerships being built and the methodologies being employed help structure how real-world research activities could be conducted in the future, thus validating the role of real-world data as a tool for rapidly learning about patient characteristics, treatment patterns, and outcomes.

For more information please visit: www.evidenceaccelerator.org

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OPPORTUNITIES TO OPTIMIZE CANCER DRUG POLICIES

THE INTERVENTIONAL PHARMACOECONOMIC TOOLBOX

FOCUS ON OPTIMAL DOSING OF IBRUTINIB

WELCOME ADDRESS

Allen Lichter
Value in Cancer Care Consortium

KEYNOTE SPEAKER

Cliff Hudis
American Society of Clinical Oncology

Web Conference Organizers

Daniel Goldstein, MD – Davidoff Center, Rabin Medical Center, Israel
Mark J Ratain, MD – The University of Chicago

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IN BRIEF

Kids v Cancer urges Congress to permanently reauthorize pediatric voucher program

Kids v Cancer is urging Congress to pass the Creating Hope Reauthorization Act (S. 4010), which would permanently reauthorize the pediatric voucher program.

The pediatric priority review voucher program encourages the development of new drugs for seriously ill children, including children with cancer, by providing a voucher to pharmaceutical companies which develop such drugs. Vouchers can be used to expedite FDA approval for any other future drug, which allows those future drugs to reach markets faster.

The pediatric voucher program will sunset if Congress does not approve the act by September 30, "ending a critical incentive program for the development of drugs for kids with life threatening illnesses," Nancy Goodman, executive director of Kids v Cancer, said in a statement.

Bob Casey (D-PA) and Susan Collins (R-ME) introduced the bill to the Senate. G.K. Butterfield and Michael McCaul introduced the Creating Hope Reauthorization Act in the House in September 2019 (H.R. 4439).

The rare pediatric priority review voucher program has resulted in 22 novel therapies for seriously ill children, and in over one billion dollars of incentives for companies to develop rare pediatric disease drugs with no cost to consumers or taxpayers, Goodman said.

"The Children's Oncology Group is highly supportive of the impact that the Creating Hope Reauthorization Act brings to the care of children with cancer," Doug Hawkins, chair of the Children's Oncology Group, said in a statement. "There remains a significant need to focus effort on making better medicines more available for all children and the pediatric voucher program plays an instrumental role in this effort."

UAMS Winthrop P. Rockefeller Cancer Institute joins Kiyatec clinical study

Winthrop P. Rockefeller Cancer Institute at the University of Arkansas for Medical Sciences has joined the 3D-PREDICT clinical study, by Kiyatec Inc., to validate the company's test as a patient-specific predictor of response to recommended drug therapies for patients with ovarian cancer.

"We developed our investigational ovarian cancer drug response profile to help optimize therapeutic decision-making over the course of the disease," Matthew Gevaert, CEO of Kiyatec, said in a statement.

3D-PREDICT is a prospective, open-label, non-interventional study to validate Kiyatec's ovarian cancer drug response profile, which leverages the company's ex vivo 3D cell culture technology platform to assess pre-treatment, patient-specific response to a panel of 11 drugs most commonly used to treat patients with newly diagnosed or recurrent ovarian cancer.

Kiyatec uses its ex vivo 3D cell culture technology platforms to accurately model and predict response to approved and investigational cancer drugs targeting a spectrum of solid tumors.

AACR BRIEFS

AACR
American Association for Cancer Research

David A. Tuveson elected AACR president-elect for 2020-2021

David A. Tuveson, was elected president-elect of the American Association for Cancer Research for 2021-22 by the members of the AACR.

He became president-elect on April 29, 2020, during the AACR's Business Meeting of Members and will assume the presidency in April 2021 at the AACR annual meeting in Washington, D.C.

Tuveson is director of the Cold Spring Harbor Laboratory Cancer Center, where he is also the Roy J. Zuckerberg Professor of Cancer Research. He is chief scientist for the Lustgarten Foundation, the largest pancreatic cancer research philanthropy.

Tuveson is a medical staff affiliate at Memorial Sloan Kettering Cancer Center, and also works closely with the Cancer Institute at Northwell Health. He serves on the Board of Scientific Advisors of the NCI. His basic and translational research focuses on increasing our understanding of the biology of pancreatic cancer and on identifying and testing in preclinical and clinical settings new approaches for diagnosing and treating the disease.

James R. Downing receives inaugural AACR-St. Baldrick's Foundation award for pediatric cancer research

James R. Downing, CEO of St. Jude Children's Research Hospital, received the inaugural award of the American Association for Cancer Research-St. Baldrick's Foundation for outstanding achievement in pediatric cancer research.

Downing also holds the Donald Pinkel Chair of Childhood Cancer Treatment and is the director of the Molecular Pathology Laboratory at St. Jude Children's Research Hospital.

The AACR-St. Baldrick's Foundation Award for Outstanding Achievement in Pediatric Cancer Research was established in 2019 to recognize major research discoveries in pediatric cancer research and to honor an individual who has significantly contributed to any area of pediatric cancer research, resulting in the fundamental improvement of the understanding and/or treatment of pediatric cancer.

The award recipient receives the opportunity to nominate junior faculty at the assistant professor level or equivalent, who are affiliated with an academic institution involved in cancer research, cancer medicine, or cancer-related sciences, to be considered to receive a one-year, $75,000 AACR-St. Baldrick's Foundation Pediatric Cancer Research Fellowship.

Downing's group published one of the earliest gene expression studies classifying pediatric cancer and demonstrating that subsets of acute lymphoblastic leukemia can be defined by unique gene expression profiles. These findings drove the formation of the St. Jude-Washington University Pediatric Cancer Genome Project. This effort led to the genomic sequencing of nearly 2,000 pediatric cancer patients, resulting in the identification of genetic driver mutations not previously linked to cancer onset and progression.

TCGA founding members and project team receive AACR 2020 Team Science Awards

The founding members and the current project team associated with The Cancer Genome Atlas Project received the 2020 AACR Team Science Awards.

TCGA founders and project team received the award during the AACR Virtual annual meeting II.

AACR is honoring the contributions of Anna D. Barker, chief strategy officer at the Ellison Institute for Transformative Medicine, University of Southern California, and former NCI principal deputy director, and Francis S. Collins, director of NIH, who were directly responsible for the project's inception and establishment.

Also recognized with this award are past NCI Directors Andrew C. von Eschenbach, and John E. Niederhuber, whose leadership throughout the years of the TCGA pilot project helped with the financial stability of the project. Eric S. Lander, and Leland H. Hartwell, are recognized for their efforts associated with the establishment of the initial TCGA pilot project, specifically their contributions as co-chairs of the National Cancer Advisory Board's Working Group on Biomedical Technology.

Also being recognized with this award are 34 other individuals who contributed to the success of TCGA, including those who were, and some of whom continue to be, involved with various facets of the TCGA network including the TCGA Project Management Team, TCGA Advisory Committee, Cancer Genome Characterization Centers, Genome Sequencing Centers, Biospecimen Core Resource Center, and the Data Coordinating Center.

Click here for the full listing of recipients of the first 2020 AACR Team Science Award.

The second 2020 AACR Team Science Award is being presented to Jean Claude Zenklusen, and the 129 additional members of the current TCGA project team for their recent and ongoing efforts to functionalize the data generated by the project. Zenklusen has served as director of TCGA in the NCI Center for Cancer Genomics since August 2013 and continues to lead the evolution of the program.

The Cancer Genome Atlas Project began in 2006 as a joint effort between NCI and the National Human Genome Research Institute, bringing together researchers from diverse disciplines and institutions to create a detailed catalog of genomic changes associated with specific types of cancer.

The AACR Team Science Award was established by the AACR and Eli Lilly and Co. in 2007 to acknowledge how interdisciplinary teams enhance the understanding of cancer and/or the translation of research discoveries into clinical cancer applications.

Jedd D. Wolchok receives AACR-Joseph H. Burchenal Award for clinical cancer research

Jedd D. Wolchok received the 2020 AACR-Joseph Burchenal Award for Outstanding Achievement in Clinical Cancer Research.

Wolchok is the Lloyd J. Old/Virginia and Daniel K. Ludwig Chair in Clinical Investigation and chief of Immuno-Oncology Service at Memorial Sloan Kettering Cancer Center. He also serves as director of the Parker Institute for Cancer Immunotherapy at MSK, associate director of the Ludwig Center for Cancer Immunotherapy, and professor of medicine at Weill Medical College of Cornell University.

Wolchok is recognized for his leadership in the groundbreaking clinical development of CTLA-4 antibody therapy for melanoma and for his pivotal role in ushering in the field of checkpoint inhibitor therapies for cancer.

The AACR and Bristol-Myers Squibb established this award in 1996 to recognize outstanding achievements in clinical cancer research. The award honors Dr. Joseph H. Burchenal, honorary member and Past President of the AACR, and a major figure in clinical cancer research.

Wolchok played a seminal role in developing ipilimumab (Yervoy), an anti-CTLA-4 monoclonal antibody that promotes the release of cancer-fighting T cells in the body. Wolchok led the pivotal phase III clinical trial demonstrating that treatment with ipilimumab and the chemotherapeutic dacarbazine yields superior overall survival in patients with metastatic melanoma compared with dacarbazine treatment alone.

Through his work with ipilimumab, Wolchok discovered differences in the kinetics of clinical tumor responses to immunotherapy and chemotherapy, which prompted him and his team to develop new criteria for evaluating treatment responses to immunotherapy. These criteria are now standard practice for immunotherapy trials.

After determining that ipilimumab is capable of promoting tumor regression in 20% of melanoma patients, Wolchok began designing and conducting clinical trials testing immunotherapy combinations, including the combination of ipilimumab and the PD-1 monoclonal antibody nivolumab (Opdivo), which was subsequently approved by the U.S. Food and Drug Administration as a treatment for advanced melanoma in 2015.

In 2011, Wolchok founded the Immunotherapeutics Clinical Core at MSK, a program focused on novel immunotherapy phase I-II clinical trials expanding beyond melanoma.

Cigall Kadoch receives AACR Award for basic cancer research

Cigall Kadoch received the 2020 AACR Award for Outstanding Achievement in Basic Cancer Research.

Kadoch is assistant professor of pediatric oncology at Dana-Farber Cancer Institute, assistant professor of pediatrics at Harvard Medical School, and an Institute Member at the Broad Institute of MIT and Harvard.

She is being recognized for her pioneering biochemical and functional characterization of normal and aberrant SWI/SNF chromatin remodeling complexes and her elucidation of the mechanisms by which the disruption of these complexes contributes to over one-fifth of human cancers.

The AACR Award for Outstanding Achievement in Basic Cancer Research was established by the AACR to recognize an early-career investigator for meritorious achievements in basic cancer research. The award is intended to recognize an individual who has not yet reached 46 years of age at the time of their award presentation.

Kadoch is known for her work involving the biology of ATP-dependent chromatin remodeling complexes, which are groups of proteins that influence how DNA is packaged, thereby controlling when and how strongly genes are expressed.

In a landmark study early in her career, Kadoch discovered that more than 20% of cancers have mutations in genes encoding proteins that are part of mammalian SWI/SNF chromatin remodeling complexes. Since then, the focus of her research has been on characterizing the role of each of the 29 potential subunits of the SWI/SNF chromatin remodeling complexes in normal tissue development and defining how mutated forms of these subunits contribute to cancer development.

Lisa A. Newman receives AACR-Minorities in Cancer Research Jane Cooke Wright Lectureship

Lisa A. Newman received the AACR-Minorities in Cancer Research Jane Cooke Wright Lectureship from AACR.

Newman is chief of the Section of Breast Surgery at New York-Presbyterian/Weill Cornell Medical Center and Weill Cornell Medicine, and leader of the multidisciplinary breast oncology programs at the New York-Presbyterian David H. Koch Center.

Newman is receiving this award in recognition of her significant contributions to the identification of biomarkers for triple-negative breast cancer in African American and African women, and her dedication to mentoring students and trainees from groups traditionally underrepresented in medicine and research.

The AACR-Minorities in Cancer Research Jane Cooke Wright Lectureship was first presented in 2006. The lectureship is intended to recognize an outstanding scientist who has made meritorious contributions to the field of cancer research and who has, through leadership or by example, furthered the advancement of minority investigators in cancer research.

Patricia S. Steeg receives 2020 AACR-Women in Cancer Research Charlotte Friend Lectureship

Patricia S. Steeg received the 2020 AACR-Women in Cancer Research Charlotte Friend Memorial Lectureship.

Steeg, co-director of the Office of Translational Resources and associate director of the Center for Cancer Research at NCI, is being recognized for her groundbreaking research on breast cancer metastasis, including the discovery of the first metastasis suppressor gene and development of a clinical-translational program dedicated to investigating brain metastases of breast cancer.

The AACR-Women in Cancer Research Charlotte Friend Lectureship was established in 1998 in honor of renowned virologist and discoverer of the Friend virus, Charlotte Friend, PhD, for her pioneering research on viruses, cell differentiation, and cancer. This lectureship recognizes an outstanding female or male scientist who has made meritorious contributions to the field of cancer research and who has, through leadership or by example, furthered the advancement of women in science.

Steeg is best known for research on breast cancer metastasis. In 1988, she discovered the first metastasis suppressor gene, nm23 (NME). Her work demonstrated that the previously unknown NME gene is commonly downregulated in cells with increased metastatic potential.

Steeg later cloned the NME family of genes and further characterized the biological and enzymatic activities of NME by conducting experiments in which she reintroduced NME into metastatic tumor cells. This innovative research has since helped to establish an entire field devoted to understanding the structure and function of metastasis suppressor genes.

Her research lab is working to study the composition and function of the blood-tumor barrier in tumor metastasis, while also identifying signaling pathways and molecular targets that exhibit the capability to mediate brain metastasis.

Benjamin F. Cravatt receives 2020 AACR Award for chemistry in cancer research

Benjamin F. Cravatt has received the 2020 AACR Award for Outstanding Achievement in Chemistry in Cancer Research.

Cravatt, professor at the Skaggs Institute for Chemical Biology and the Gilula Chair of Chemical Biology for the Department of Chemistry at The Scripps Research Institute in La Jolla, California, is being recognized for major technical advances in activity-based protein profiling.

His methods exploit the power of chemistry to generate new tools and assays for the global analysis of protein activities. He has applied these tools to the identification of new targets and drug candidates for cancer treatment.

The AACR Award for Outstanding Achievement in Chemistry in Cancer Research was established by the AACR and its Chemistry in Cancer Research Working Group in 2007, through the initial support of GlaxoSmithKline, to recognize the importance of chemistry to advancements in cancer research. The award is intended to recognize outstanding, novel, and significant chemistry research that has led to important contributions in basic cancer research, translational cancer research, cancer diagnosis, the prevention of cancer, or the treatment of patients with cancer.

Christopher I. Amos receives 2020 AACR-American Cancer Society Award for research in cancer epidemiology and prevention

Christopher I. Amos has received the 2020 AACR-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention.

Amos, the Selzman Endowed Professor, director of the Institute for Clinical and Translational Research, and associate director of Quantitative Science at Baylor College of Medicine, is being recognized for his unique blend of expertise in biostatistics and bioinformatics, genetics, and cancer epidemiology.

Amos has leveraged these skills to expand upon emerging genomic technologies, making seminal contributions to the understanding of how genetic and environmental factors can cause complex diseases such as cancer.

The 2020 AACR-American Cancer Society Award for Research Excellence in Cancer Epidemiology and Prevention was established by the AACR and the American Cancer Society in 1992 to recognize outstanding research accomplishments in the fields of cancer epidemiology, biomarkers, and prevention.

Amos helped develop novel and robust methods for the analysis of quantitative traits using variance components and strong linkage approaches for understanding the etiological basis of complex diseases such as cancer. The methods that Amos has developed are now widely applied and highly regarded, in part because they do not require genetic models to be specified.

He was the first author of a landmark paper in *Nature Genetics* that identified a region of robust linkage disequilibrium within 15q25 as a lung cancer susceptibility gene locus. This region encompasses the nicotinic acetylcholine receptor subunit genes CHRNA3 and CHRNA5, which have a defined role in nicotine dependence and a hypothesized direct role in downstream signaling pathways that promote carcinogenesis.

Michael Karin receives 2020 AACR-G.H.A. Clowes Award for basic cancer research

Michael Karin, fellow of the AACR Academy, received the 2020 AACR-G.H.A. Clowes Award for Outstanding Basic Cancer Research.

Karin, distinguished professor of pharmacology and pathology at the University of California San Diego School of Medicine, is being recognized for unraveling the role of metabolic stress, inflammation, and immunosuppression in cancer by establishing the tumorigenic function of NF-κB in cancer

progenitors and myeloid cells, and for explaining how inflammation and cancer are linked, laying down the basis for use of anti-cytokine and anti-inflammatory drugs in cancer prevention and treatment.

The AACR-G.H.A. Clowes Award for Outstanding Basic Cancer Research was established by the AACR and Eli Lilly and Co. in 1961 to honor Dr. G.H.A. Clowes, who was a founding member of the AACR and a research director at Eli Lilly. The award is intended to recognize an individual who has made outstanding recent accomplishments in basic cancer research.

Karin's research establishes the relationship between chronic inflammation and cancer, particularly colorectal cancer. He discovered that members of the IL-6 family of cytokines are capable of activating oncogenic transcription factors such as STAT3, resulting in colorectal and liver cancer onset.

Michelle M. Le Beau receives AACR-Margaret Foti Award for leadership and achievements in cancer research

Michelle M. Le Beau has received the 2020 AACR-Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research.

Le Beau is director of the Cancer Cytogenetics Laboratory and Arthur and Marian Edelstein Professor of Medicine at the University of Chicago, and director of the University of Chicago Medicine Comprehensive Cancer Center, a position she has held since 2004.

She is receiving the award in recognition of her leadership, direction, and strategic vision at University of Chicago Medicine.

Le Beau is an expert on the molecular analysis of recurring chromosomal abnormalities in human leukemias and lymphomas, the correlation of specific abnormalities with morphological and clinical features, and the development of risk-adapted therapy.

Through her work, she has been instrumental in deepening the understanding of the onset and progression of numerous hematological malignancies, including implicating deletions on chromosomes 5 and 7 as oncogenic drivers of therapy-related myeloid leukemias. Her current work focuses on the analysis of the genes on chromosome 5 that are involved in therapy-related AML; the development and characterization of mouse models harboring AML driver mutations; the identification of secondary mutations and genetic pathways essential to leukemogenesis; and the application of mouse models for preclinical testing of potential therapeutics.

The Margaret Foti Award for Leadership and Extraordinary Achievements in Cancer Research was established in 2007 to recognize a champion of cancer research whose leadership and extraordinary achievements in cancer research have had a major impact on the field.

Barbara J. Wold receives AACR-Irving Weinstein Foundation lectureship

Barbara J. Wold received the AACR-Irving Weinstein Foundation Distinguished Lectureship.

Wold was recently appointed as the director of the Merkin Institute for Translational Research at the California Institute of Technology (Caltech). She is also the Bren Professor of Molecular Biology and the principal investigator of the Functional Genomics Resource Center at the Beckman Institute at Caltech. Wold was previously the Beckman Institute director from 2001 to 2011.

Wold has used next-generation sequencing techniques to study RNA expression in mice. Wold was among the first to use deep NGS profiling, noting the expres-

sion of both known and not-yet-annotated genes and splice isoforms.

Wold helped found the L. K. Whittier Gene Expression Center and the Special Center for Biological Circuit Design at Caltech. In 2012, she founded the National Cancer Institute's Center for Cancer Genomics.

The AACR-Irving Weinstein Foundation Distinguished Lectureship was established in 2004 to acknowledge an individual whose outstanding scientific innovation and thought leadership has inspired creative thinking and new directions in cancer research. The recipient of this award is selected annually by the AACR President. Wold was chosen by Elaine R. Mardis, AACR president for the 2019-2020 term.

Luis A. Diaz receives AACR-Waun Ki Hong Award

Luis A. Diaz has received the AACR-Waun Ki Hong Award for Outstanding Achievement in Translational and Clinical Cancer Research.

Diaz is head of the Division of Solid Tumor Oncology, Grayer Family Chair, and director of the Precision Intervention and Prevention Program at Memorial Sloan Kettering Cancer Center.

Diaz also serves as an attending physician at Memorial Hospital for Cancer and Allied Diseases in New York.

Diaz is being recognized for pioneering novel applications of cancer genomics and circulating tumor DNA for early cancer detection as well as prognosis and recurrence prediction, and for his groundbreaking work involving immune checkpoint blockade in DNA mismatch repair-deficient tumors.

Diaz has focused his career on developing novel genomic approaches to the diagnosis and treatment of cancer. In landmark studies, he demonstrated the potential clinical utility of analyzing ctDNA to detect tumor mutations in the blood, showing that ctDNA could be used to not only track the emergence of mutations conferring therapeutic resistance in patients receiving targeted therapy, but also predict tumor recurrence after surgery.

He has also applied his expertise to expand the use of immunotherapeutics such as immune checkpoint inhibitors in the treatment of patients with cancer. FDA approval of pembrolizumab for advanced MMR-deficient cancers arising in any location in the body was a direct result of Diaz's research, which showed curative responses in the majority of metastatic patients with MMR-deficient cancers. Diaz is working to harness his cancer genetics knowledge to develop a "molecular Pap test" for the early detection of ovarian and endometrial cancers.

Tyler Jacks receives AACR Princess Takamatsu Memorial Lectureship

Tyler Jacks, fellow of the AACR Academy, received the the 2020 AACR Princess Takamatsu Memorial Lectureship.

Jacks is director of the David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology, co-director of the Ludwig Center at MIT, and a Howard Hughes Medical Institute Investigator.

He is being recognized for transforming cancer research and the development of therapeutic treatments through his advancement of genetically engineered mouse models and for his seminal discoveries related to oncogenes, tumor suppressor genes, cell death, and immune system regulation of tumor progression.

He and researchers in his laboratory have engineered mice to carry mutations in many genes known to be involved in human cancer, including tumor suppressor genes such as Rb; oncogenes such as K-Ras; and genes involved in oxidative stress, DNA damage and repair, and epigenetic control of gene expression.

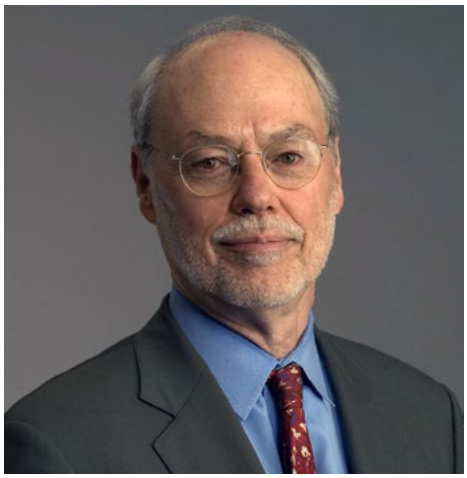
The AACR Princess Takamatsu Memorial Lectureship is awarded to a scientist whose novel and significant fundamental scientific work has had or may have a far-reaching impact on the detection, diagnosis, treatment, or prevention of cancer, and who embodies the dedication of the princess to outstanding cancer research and advances that emanate from multinational collaborations.

Phillip A. Sharp receives award for lifetime achievement in cancer research

Phillip A. Sharp, fellow of the AACR Academy and Nobel Laureate, received the 17th AACR Award for Lifetime Achievement in Cancer Research.

Sharp, an institute professor at Massachusetts Institute of Technology's David

H. Koch Institute for Integrative Cancer Research, is being honored for his body of groundbreaking and high-impact basic research, including his seminal co-discovery of RNA splicing.



For this discovery, Sharp was awarded the 1993 Nobel Prize in Physiology or Medicine, along with Sir Richard J. Roberts. This body of research fundamentally changed scientists' understanding of the structure of genes, shaping our understanding of RNA biology and our knowledge of the genetic causes of cancer and other diseases.

After first describing the phenomenon of RNA splicing, Sharp's work focused on elucidating the biochemical mechanisms of RNA splicing and mammalian transcription. Today, his research continues to enhance our understanding of RNA structure and function and has been particularly focused on defining the biology of small RNAs and other types of noncoding RNAs. Additionally, his research has led the emerging field of convergence science for many years, resulting in the generation of the first CAS9 mouse model, which has proven vital to in vivo screening experiments dedicated to identifying genes involved in metastasis. To date, Sharp's career publications in peer-reviewed journals total more than 440.

Sharp's scientific influence extends far beyond his research accomplishments and has informed public policies and funding decisions at the nation's highest level. Additionally, he has been an inspiration and mentor to more than 90 postdoctoral fellows and almost 40 graduate students, many of whom are now preeminent scientists in their respective areas of expertise.

Sharp, an AACR member since 1986, was elected to the inaugural class of the Fellows of the AACR Academy in 2013 and has been Chair of the Stand Up To Cancer (SU2C) Scientific Advisory Committee for more than a decade, leading the selection of 26 "Dream Teams" of top researchers and other SU2C research groups. The AACR is the Scientific Partner of SU2C. Further he served as program chair of the AACR's Inaugural Special Conference in 1988. That conference, "Gene Regulation and Oncogenes," has been characterized as a watershed meeting that stimulated novel, transformative thinking about the molecular biology of cancer.

Sharp co-founded Biogen and Alnylam, both of which have developed therapeutics including rituximab and obinutuzumab for lymphoma, natalizumab and peginterferon for multiple sclerosis, and the first small interfering RNA-based therapy for transthyretin-mediated amyloidosis.

The AACR Award for Lifetime Achievement in Cancer Research was established in 2004 to honor individuals who have made significant fundamental contributions to cancer research, either through a single scientific discovery or a collective body of work. These contributions, whether they have been in research, leadership, or mentorship, must have had a lasting impact on the cancer field and must have demonstrated a lifetime commitment to progress against cancer.

Herbst, Lowy, Majima, Spears, receive AACR distinguished public service award

Roy S. Herbst, Douglas R. Lowy, Yoshiyuki Majima, and Patricia Spears, received the AACR Distinguished Public Service Awards.

The awards recognize their groundbreaking, innovative work in the cancer research community that reflect a wide range of contributions. This year's award recipients are honored for their work in clinical research, scientific leadership, and cancer policy and advocacy, respectively.

Roy S. Herbst received the 2020 AACR Distinguished Public Service Award in recognition of his sustained, outstanding leadership in cancer science policy for the AACR. This includes his stewardship as chair of the AACR Tobacco Products and Cancer Subcommittee, a position that he has held since the subcommittee's inception in 2009.

Herbst is a member AACR's Science Policy and Government Affairs Committee and its Regulatory Science and Policy Subcommittee, and represents the AACR in joint initiatives with FDA and NCI.

Herbst is Ensign Professor of Medicine, chief of Medical Oncology, and associate cancer center director for Translational Research at the Yale Cancer Center. Herbst's research on the effects of tobacco has driven the Tobacco Products and Cancer Subcommittee to educate policymakers, scientists, physicians, and members of the public about the harms caused by tobacco products and addiction.

Herbst advocates for strong tobacco control policies and regulations and embodies the AACR's goal to advance research to eliminate cancer incidence and mortality due to tobacco use. Herbst's tobacco policy sessions at AACR Annual Meetings and participation in AACR congressional briefings play a crucial role in driving national tobacco policy changes.

Herbst was recently elected to serve as a member of the Board of Directors for the 2020-2023 term. He has served as chair (2016–2017) and vice chair (2012–2015), Science Policy and Government Affairs Committee; cochair, AACR-IASLC Joint Conference on Molecular Origins of Lung Cancer: Biology, Therapy, and Personalized Medicine (2012); senior editor, Clinical Cancer Research (2009–2015); and cochair, AACR Annual Meeting Program Committee (2008–2009).

Douglas R. Lowy received the 2020 AACR Distinguished Public Service Award in recognition of his leadership of the NCI during his tenure as the acting director. Lowy is the principal deputy director and chief of the Laboratory of Cellular Oncology within the Center for Cancer Research at the NCI.

As acting director of the NCI from April 2015 to October 2017, Lowy provided national leadership to advance the National Cancer Moonshot Initiative. He served a second term as acting NCI director from January 2019 to November 2019. In his current role as principal deputy director, Lowy continues to help lead the NCI's key scientific initiatives.

Lowy is best known for helping to develop the technology underlying most human papillomavirus vaccines. For his work on HPV vaccines, Lowy and his collaborator John T. Schiller, received the Lasker-DeBakey Clinical Medical Research Award in 2017.

Lowy was elected as a Fellow of the AACR Academy in 2015. He received the Dorothy P. Landon-AACR Prize for Translational Cancer Research in 2009. He served on the AACR Research Grant Review Committee in 2009-2010.

Yoshiyuki Majima received the 2020 AACR Distinguished Public Service Award in recognition of his outstanding leadership in patient advocacy, education, and support through the Pancreatic Cancer Action Network Japan (PanCAN Japan).

Majima founded PanCAN Japan in 2006 after his sister's death from pancreatic cancer. The organization has since grown to become the largest support organization for pancreatic cancer patients in Japan. Under Majima's exceptional guidance, PanCAN Japan has set an ambitious mission to advance research, create clinical trial awareness, stimulate faster drug approvals, support patients, and offer hope to patients through service and advocacy.

One of Majima's most notable achievements has been his effort to address the "drug lag" for first-line pancreatic cancer drugs imported to Japan. Under his leadership, more than 100,000 signatures were submitted to the Japanese Ministry of Health, Labor, and Welfare. As a direct result of this action, the ministry reduced the approval time for imported drugs from six years to two years.

In addition, Majima, a graduate of the AACR's Scientist↔Survivor Program has been instrumental in launching and promoting a similar educational program in Japan, building bridges and unity among leaders of the scientific, survivor, and advocacy communities. The program has been so successful in Japan, it was presented at the Annual Meeting of the Japanese Cancer Association.

Patricia Spears, BS, will receive the 2020 AACR Distinguished Public Service Award in recognition of her longstanding advocacy for cancer patients and their loved ones and caregivers.

Spears has devoted her time and visionary leadership to more than a dozen initiatives, committees, and workshops with organizations such as the AACR, NCI, FDA, and others. These include

the AACR Conflict of Interest Working Group, AACR Scientist↔Survivor Program, 2018-2019 AACR Annual Meeting Program Committee, the Translational Breast Cancer Research Consortium, the NCI Breast Cancer Steering Committee, Alliance for Clinical Trials in Oncology, NCI Core Correlative Science Committee, the FDA-AACR-ASTRO Clinical Development of Drug Radiotherapy Combinations Workshop, the FDA-ASCO Innovations in Breast Cancer Drug Development – Neoadjuvant Breast Cancer Workshop, the Patient-Centered Outcomes Research Institute, the Duke Cancer Institute cancer protocol committee, the ASCO Young Investigator Award Program, the University of North Carolina Lineberger Patient Research Advocacy Group, and the UNC Breast Cancer SPORE Advocates.

As a breast cancer survivor, Spears inspires clinicians and researchers by reminding them of the critical importance of the patient voice in treatment, communicating science and clinical research to the public, and facilitating the engagement of patients with basic and clinical researchers. Spears also urges patients to participate in clinical trials and has advocated for the incorporation of patient-reported outcomes into those trials.

AACR names fellows of the AACR Academy class of 2020

AACR has named its newly elected class of Fellows of the AACR Academy.

The mission of the AACR Academy is to recognize and honor distinguished scientists whose scientific contributions have propelled significant innovation and progress against cancer. fellows of the AACR Academy serve as a global brain trust in the cancer field, helping to advance the mission of the AACR to prevent and cure all cancers through research, education, communication, collaboration, science policy and advocacy, and funding for cancer research.

All fellows are nominated and elected through an annual peer review process conducted by existing Fellows of the AACR Academy and ratified by the AACR Academy Steering Committee and AACR Executive Committee. This process involves a rigorous assessment of each candidate's scientific accomplishments in cancer research and cancer-related sciences. Only individuals whose work has had a significant and enduring impact on cancer research are considered for election and induction into the AACR Academy.

The members of the 2020 class of Fellows of the AACR Academy are:

Myles A. Brown, Emil Frei III professor of medicine; director, Center for Functional Cancer Epigenetics, Dana-Farber Cancer Institute

For elucidating the role of steroid hormones and their receptors in promoting the onset and progression of various hormone-dependent malignancies and for the discovery of regulatory complex components such as the p160 class of transcriptional co-activators that facilitate the epigenetic regulation of steroid receptor activity.

Judith Campisi, professor, Buck Institute for Research on Aging, senior scientist, Lawrence Berkeley National Laboratory

For contributions to the understanding of the links between aging and cancer and for her research related to identifying the molecular mechanisms associated with cellular senescence, aging, and tumorigenesis that has defined the role of DNA damage and repair in genomic instability and premature aging.

Arul Chinnaiyan, director, Michigan Center for Translational Pathology; S.P. Hicks Endowed Professor of Pathology; professor of urology, American Cancer Society Research Professor, University of Michigan, Ann Arbor

For demonstrating the presence of chromosomal rearrangements in solid tumors including the identification of the TMPRSS2-ETS family of gene fusions and for harnessing such discoveries to define novel underlying pathologies in prostate cancer as well as other epithelial cancers.

Alan D. D'Andrea, director, Susan F. Smith Center for Women's Cancers; director of the Center for DNA Damage and Repair, Dana-Farber Cancer Institute, Alvan T. and Viola D. Fuller American Cancer Society Professor of Radiation Oncology, Harvard Medical School

For pivotal contributions to the field of DNA damage and repair that have defined the specific defects responsible for the development of Fanconi anemia and for elucidating the role of nuclear protein complexes on chromatin remodeling, cell cycle checkpoints, and DNA repair.

Mark M. Davis, director, Stanford Institute for Immunity, Transplantation and Infection, The Burt and Marion Avery Family Professor of Immunology, Stanford University School of Medicine

For identifying the first T cell receptor genes responsible for the detection of foreign antigens, contributing to the characterization of T cell receptor variable regions and for developing imaging techniques capable of capturing interactions that occur at immunological synapses.

Gregory J. Hannon, director and senior group leader, Cancer Research UK Cambridge Institute, professor of oncology,

University of Cambridge, Cambridge, United Kingdom

For fundamental contributions to characterizing the role of cyclin-dependent kinases and small RNAs including microRNAs, piwi-interacting, and short-hairpin RNAs in cell cycle regulation, carcinogenesis, and drug development.

Rakesh K. Jain, A. W. Cook Professor of Radiation Oncology (Tumor Biology), director, E.L. Steele Laboratories, Department of Radiation Oncology, Harvard Medical School and Massachusetts General Hospital

For landmark studies describing and highlighting the relationship between the tumor microenvironment and surrounding vasculature and for his investigations involving antiangiogenic therapy to induce tumor vascular normalization that have resulted in improved survival rates for a number of solid tumors.

Maria Jasin, laboratory head, Memorial Sloan Kettering Cancer Center

For illuminating the role of homologous recombination in maintaining genetic stability, demonstrating the crucial role of BRCA1 and BRCA2 in facilitating such genetic events and for proving that BRCA2 loss, coupled with aberrant p53 activity in breast cells, can result in replication stress and subsequent tumorigenesis.

Robert S. Langer, David H. Koch Institute Professor, Massachusetts Institute of Technology

For contributions in the field of drug delivery systems and for spearheading the fields of tissue engineering and regenerative medicine, generating synthetic polymer systems capable of facilitating controlled drug release as well as serving as platforms for the engineering of blood vessels, cartilage, and skin.

Bert W. O'Malley, Thomas C. Thompson Chair in Molecular and Cellular Biology, chancellor, Baylor College of Medicine, and associate director of basic research, Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine

For pioneering research focused on the understanding of molecular endocrinology, gene regulation, and steroid receptor biology that has revealed how intracellular hormones and cofactors function at the DNA level to regulate protein production, affect cellular function, and modulate cancer cell metastasis.

Drew M. Pardoll, professor of oncology, director of Bloomberg~Kimmel Institute for Cancer Immunotherapy; director of Cancer Immunology, The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University

For enriching the understanding of tumor immunology and immunotherapy through his discovery of gamma-delta T cells and interferon-producing killer dendritic cells and for his contributions to developing GVAX and Listeria monocytogenes-based cancer vaccines.

Kornelia Polyak, professor of medicine, Harvard Medical School, Dana-Farber Cancer Institute

For dissecting the role of intratumor heterogeneity in breast cancer and metastatic disease to develop risk assessment and personalized cancer therapy models and for extensively characterizing the metastatic potential of polyclonal tumors compared to monoclonal tumors.

Peter J. Ratcliffe, Nuffield Professor of Clinical Medicine, director, Target Discovery Institute, Nuffield Department of Medicine, University of Oxford, director of Clinical Research, Francis Crick Institute

For his landmark, Nobel Prize-winning contributions to the understanding of the molecular responses to oxygen depletion, specifically the identification of oxygen sensing and signaling pathways that link hypoxia-inducible factor 1 to the availability of oxygen, which has proven to be critically important to the understanding of tumor initiation and progression.

Antoni Ribas, professor of medicine, surgery and molecular and medical pharmacology, University of California Los Angeles Medical Center

For his seminal clinical research contributions that have led to the development of pembrolizumab as the first-in-class approved anti-PD-1 immunotherapy for the treatment of melanoma, for his characterization of BRAF, CTLA-4, and MEK in cancer, and for deciphering the molecular mechanisms responsible for immunotherapeutic resistance, which have since fueled additional efforts to understand the relationship between the immune system and cancer.

Gregg L. Semenza, director, Vascular Program, Institute for Cell Engineering, C. Michael Armstrong Professor of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore

For his revolutionary, Nobel Prize-winning contributions to uncovering the molecular mechanisms of oxygen regulation within cells and for discovering hypoxia-inducible factor 1, critical for cellular adaptation to changing oxygen levels, which has had far-reaching implications for the treatment of numerous diseases characterized by low oxygen levels, including diabetes, heart disease, and cancer.

Charles Swanton, group leader, The Francis Crick Institute and University

College London Cancer Institute, Thoracic Oncologist University College London Hospitals

For his innovative research focused on identifying molecular mechanisms of cancer evolution and its impact on drug resistance and patient stratification and for demonstrating the crucial biological connection between intratumor heterogeneity and clinical cancer biomarker efficacy.

David A. Tuveson, Roy J. Zuckerberg Professor of Cancer Research, director, Cold Spring Harbor Laboratory Cancer Center

For his trailblazing contributions to establishing human pancreatic cancer mouse models, for developing preclinical and clinical therapeutic strategies for the disease, and for characterizing many of the barriers to successful pancreatic cancer treatment, including poor drug delivery and the presence of survival factors in the microenvironment.

Michael Wigler, Russell and Janet Doubleday Professor of Cancer Research, Cold Spring Harbor Laboratory

For his renowned contributions to cancer genetics and the establishment of genetically engineered animal cells and for first describing a role for the RAS gene family in human cancer and describing how point mutations are capable of activating the oncogenic potential of select genes.

Sir Gregory P. Winter, Master, Trinity College, professor emeritus, Medical Research Council Laboratory of Molecular Biology, Cambridge

For Nobel Prize-winning scientific breakthroughs including the development of the first humanized antibodies, for establishment of refined phage display technology that has led to the development of adalimumab, the first marketed fully human antibody approved by the FDA, and for collective contributions to the generation of therapeutic antibodies for the treatment of various cancers and autoimmune diseases.

Charles L. Sawyers named AACR Academy president-elect

Charles L. Sawyers, chair of the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering Cancer Center, was elected president-elect by the fellows of the American Association for Cancer Research for 2020-2021.

Sawyers will assume the presidency during the 2021 AACR annual meeting.

As the AACR Academy president-elect, Sawyers will work with the other members of AACR Academy's Steering Committee and other elected fellows of the AACR Academy to provide advice and counsel to the AACR leadership.

Sawyers investigates the signaling pathways that drive the growth and drug resistance of cancer cells. He played a critical role in developing the molecularly targeted cancer drug imatinib (Gleevec) for the treatment of chronic myeloid leukemia.

Sawyers' research into treatments for cancer that becomes resistant to established therapies led to the development of dasatinib (Sprycel) for patients with imatinib-resistant chronic myeloid leukemia and enzalutamide (Xtandi) for metastatic prostate cancer that has become resistant to docetaxel.

In addition to serving as chair of HOPP at MSK, Sawyers holds the Marie-Josée and Henry R. Kravis Chair in Human Oncology and Pathogenesis and is an internist and hematologic oncologist.

Sawyers, an AACR member since 1997, was elected as a fellow of the AACR Academy in 2014. He served as the president of the AACR from 2013-2014 and as a member of the board of directors from 2003-2006.

Sawyers conceptualized AACR Project GENIE and has served as chair of the AACR Project GENIE Steering Committee since its inception in 2015. He received the AACR-Princess Takamatsu Memorial Lectureship (2019); the AACR Team Science Award (2015); the Dorothy Landon-AACR Prize for Translational Medicine (2009); and the AACR-Richard and Hinda Rosenthal Award (2005).

Sawyers was associate editor for the AACR scientific journals *Cancer Research* (2000-2004) and *Clinical Cancer Research* (2002-2006). Sawyers served as scientific editor for the AACR's journal *Cancer Discovery*.

Steven A. Rosenberg receives AACR-CRI Lloyd J. Old Award in cancer immunology

Steven A. Rosenberg, fellow of the AACR Academy, has received the 2020 AACR-CRI Lloyd J. Old Award in Cancer Immunology.

The AACR-Cancer Research Institute Lloyd J. Old Award in Cancer Immunology recognizes an active scientist whose outstanding and innovative research has had a major impact on the cancer field and has the potential to stimulate new directions in cancer immunology.

Rosenberg is a senior investigator at the Center for Cancer Research, NCI, chief, Surgery Branch at the NCI, and professor of surgery at the George Washington University School of Medicine and Health Sciences.

Rosenberg is being recognized for his discoveries that led to the first effective cancer immunotherapy, interleukin-2 (IL-2), and the first adoptive cell transfer immunotherapies for both solid and blood cancers, including genetically modified T cells.

Rosenberg's research established IL-2 as a growth factor for antitumor T cells in mice and humans, both in vitro and in vivo, and demonstrated that treating patients with metastatic melanoma with high doses of IL-2 could induce long-term tumor regression. These landmark discoveries led to IL-2 becoming the first cancer immunotherapy approved by the U.S. Food and Drug Administration (FDA), and it has been used to treat patients with metastatic renal cell carcinoma and metastatic melanoma since the 1990s.

Building on this work, Rosenberg pioneered adoptive cell immunotherapies by leveraging IL-2 activity to stimulate the growth of tumor-infiltrating lymphocytes (TILs) isolated from the tumors of melanoma patients. Reintroduction of these expanded TIL cell populations back into patients subsequently led to long-term tumor regression in many cases. Rosenberg and his team have since extended this approach and generated similar promising clinical results for breast, colorectal, and liver cancer patients. They also discovered that T cells are able to be genetically modified to express chimeric antigen receptors (CARs), and that these CAR-expressing T cells are able to target molecules expressed by tumor cells such as CD19 and may therefore be used to specifically target and treat chemorefractory CD19-expressing B-cell lymphomas. CD19-targeting CAR T cells have since been FDA-approved for this use and for the treatment of children with acute lymphocytic leukemia.

John E. Dick receives 2020 Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research

John E. Dick, fellow of the AACR Academy, has received the the Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research.

Dick is being honored for discovering and characterizing the mechanisms by which stem cells contribute to normal and leukemic hematopoiesis. He is recognized for his discovery of leukemic stem cells and for developing the first hematopoietic xenograft assay using human hematopoietic cells transplanted into immune-compromised mice, a technique capable of giving rise to distinct blood lineages.

Using this assay, Dick has developed xenograft models of human acute lymphoid leukemia, acute myeloid leukemia, and chronic myeloid leukemia that have provided crucial insights into the onset and progression of such diseases.

Dick's findings uncovered a gene signature of leukemia stemness that can be used to predict survival rates and response to treatment. In addition, this gene signature has provided actionable targets for drug development, led to the identification of preleukemic mutations in normal hematopoietic cells, and laid the groundwork for three drugs currently being tested in clinical trials.

The Pezcoller Foundation-AACR International Award for Extraordinary Achievement in Cancer Research was established in 1997 to annually recognize a scientist who has made a major scientific discovery in basic or translational cancer research. The awardee must be active in cancer research, have a record of recent noteworthy publications, and be conducting ongoing work that holds promise for continued substantive contributions to progress in the field of cancer.

Dick is the Canada Research Chair in Stem Cell Biology, a senior scientist at the Princess Margaret Cancer Centre, and an investigator at the McEwen Stem Cell Institute at the University Health Network in Toronto.

He is a professor of molecular genetics at the University of Toronto, and co-leader of the Acute Leukemia Translational Research Initiative for the Ontario Institute for Cancer Research. Dick has also served as a senior scientist in the Department of Genetics at the Research Institute of the Hospital for Sick Children.

THE CLINICAL CANCER LETTER

CLINICAL ROUNDUP

FDA pilot program to communicate patient reported outcomes from cancer clinical trials

FDA has launched Project Patient Voice, an initiative of the FDA's Oncology Center of Excellence that aims to communicate patient-reported outcomes from cancer clinical trials, making them more accessible to the public.

Through a new website, Project Patient Voice creates a consistent source of publicly available information describing patient-reported symptoms from cancer trials for marketed treatments. While this patient-reported data has historically been analyzed by FDA during the drug approval process, it is rarely included in product labeling and, therefore, is largely inaccessible to the public.

"Project Patient Voice has been initiated by the Oncology Center of Excellence to give patients and healthcare professionals unique information on symptomatic side effects to better inform their treatment choices," FDA Principal Deputy Commissioner Amy Abernethy, said in a statement. "The Project Patient Voice pilot is a significant step in advancing a patient-centered approach to oncology drug development. Where patient-reported symptom information is collected rigorously, this information should be readily available to patients."

Patient-reported data can provide additional, complementary information for healthcare professionals to discuss with patients, specifically when discussing the potential side effects of a particular cancer treatment. In contrast to the clinician-reported safety data in product labeling, the data in Project Patient Voice is obtained directly from patients and can show symptoms before treatment starts and at multiple time points while receiving cancer treatment.

The Project Patient Voice website will include a list of cancer clinical trials that have available patient-reported symptom data. Each trial will include a table of the patient-reported symptoms collected. Each patient-reported symptom can be selected to display a series of bar and pie charts describing the patient-reported symptom at baseline (before treatment starts) and over the first 6 months of treatment. This information provides insights into side effects not currently available in standard FDA safety tables, including existing symptoms before the start of treatment, symptoms over time, and the subset of patients who did not have a particular symptom prior to starting treatment.

In the first phase of this pilot website, only one trial will be included while the FDA seeks public feedback on how the information is presented. The FDA will use this feedback to consider improvements to the website in order to make the information as user-friendly as possible.

The visualizations and data included on the website are voluntarily provided by the drug companies that conducted the clinical trials. AstraZeneca is the first company to provide patient-reported outcome data for one of their FDA-approved drugs and has collaborated with the FDA to identify methods to display the information in a way that is informative to healthcare professionals and patients.

"There have long been calls to provide information to patients about how they may feel and function when receiving a cancer treatment. By initiating Project Patient Voice, we are moving towards standardized methods to display these outcomes, starting with patient-reported symptomatic adverse events," Paul Kluetz, deputy director of the FDA's OCE, said in a statement. "We encourage sponsors to collect this data systematically and look forward to welcoming additional sponsor collaboration as we work to help further serve the patient community."

Project Patient Voice is not meant to replace the clinician-reported safety information that is available as part of a drug's labeling. Data from Project Patient Voice should not substitute for advice from a health care professional. Rather, Project Patient Voice serves as a complement to FDA patient labeling and patient information, not a sole

source of information on which to make decisions about medical care.

FDA will seek public feedback regarding the Project Patient Voice pilot effort at a virtual public workshop co-sponsored with the American Society of Clinical Oncology on July 17. The "Clinical Outcome Assessments in Cancer Clinical Trials" workshop will include healthcare providers, patients, health outcomes researchers, industry, advocacy groups and other stakeholders interested in rigorous measurement of symptom and functional outcomes. In addition to discussing trial design considerations to obtain patient-reported symptomatic side effects, the FDA will obtain feedback on the presentation of PRO symptomatic side effect data on the Project Patient Voice website to further ensure that the information is clear and meaningful to healthcare professionals and patients.

Black cancer patients better represented in publicly-funded clinical trials

Black patients are better represented in taxpayer-funded clinical trials testing new cancer treatments compared to trials run by pharmaceutical companies, according to a study conducted by SWOG Cancer Research Network, a member of NCI's National Clinical Trials Network.

The study also found that black patients are not fully represented in cancer clinical trials.

The results are published in *JNCI Cancer Spectrum*, and were presented as a poster in the 2020 American Association for Cancer Research virtual annual meeting II.

A companion network to NCTN, the NCI Community Oncology Research Program runs prevention and cancer care delivery trials, and includes community and rural hospitals in its network, including sites with significant minority and underserved patient populations.

About 25% of all NCORP trial volunteers are racial and ethnic minorities. Both NCTN and NCORP trials are designed by doctors, paid for with public funds from the NIH through the NCI, and powered by patient volunteers.

The study compared black enrollment in NCI-sponsored trials and industry-sponsored trials.

"Everyone can get cancer, so everyone should have the same access to investigational cancer treatments," Joseph Unger, a SWOG biostatistician and health services researcher based at Fred Hutchinson Cancer Research Center, who specializes in cancer disparities research with a focus on the impacts of insurance status, race and ethnicity, and income on health outcomes, said in a statement. "In addition, it's very important from a scientific standpoint to evaluate new treatments in patients who reflect the demographics of the general cancer population."

To conduct the study, Unger and his team used three databases. One was the SWOG trials database, used as a proxy to estimate the rate of participation among NCI trials. Unger's colleagues, led by Kanwal P.S. Raghav, of MD Anderson Cancer Center and Jonathan M. Loree, of BC Cancer, created a database of pharmaceutical company-sponsored trials that supported new drug applications and included data on trial participation by race.

The team also used data from the NCI's Surveillance, Epidemiology and End Results program, as well as data compiled by the U.S. Census Bureau, to estimate the expected rate of black participation in the cancers they studied.

Unger and his team analyzed data from a total of 358 trials—85 industry trials and 273 SWOG trials—that enrolled 93,825 patients being treated for 15 different cancer types. Enrollments spanned the years 2003-2018. In those 15 cancers, the rate of black enrollment in industry trials was 3% compared to 9% in SWOG trials, and 12% in the corresponding U.S. cancer population/.

"This study confirmed that black cancer patients are severely underrepresented in pharmaceutical company sponsored trials, with fewer than one in four of the expected number enrolled," Unger said. "Black representation in industry trials was also far below that of NCTN trials, with only one black patient enrolled for every three enrolled in NCTN trials."

FDA and AACR are examining how to improve representation of black patients in FDA registration trials. Registration trials are specially designed studies conducted with the expectation that the data they produce will be used to apply to the FDA for new drug approval, or to expand the uses of a currently approved cancer drug. Unger serves on this FDA and AACR task force.

"NCI sponsored trials have a broader mandate," Unger said. "They reach beyond just the major cancer centers to serve patients in a more diverse community-based clinical setting. This could serve as a model for pharma trials aiming to increase representativeness of all patients."

Unger's study was funded by the NIH through NCI grant award CA189974 and CA189873 and in part by The Hope Foundation for Cancer Research and the Michael Smith Health Professional Investigator program.

Unger's research team included Dawn Hershman, of Columbia University; Raymond U. Osarogiagbon, of Baptist Cancer Center; Anirudh Gothwal, of Baylor University; Seerat Anand, of MD

Anderson Cancer Center; Arvind Dasari, of MD Anderson Cancer Center; Michael Overman, of MD Anderson Cancer Center; Jonathan M. Loree, of BC Cancer; and Kanwal Raghav, of MD Anderson Cancer Center.

AI dual-stain approach improved accuracy, efficiency of cervical cancer screening in NCI study

A computer algorithm improved the accuracy and efficiency of cervical cancer screening compared with cytology, the current standard for follow-up of women who test positive with primary human papillomavirus screening.

The new approach uses artificial intelligence to automate dual-stain evaluation and has clear implications for clinical care.

Findings from the study were published in the *Journal of the National Cancer Institute*. The algorithm was developed and the study conducted by investigators at NCI, in collaboration with researchers from several other institutions.

"Based on our results, [a fully automated approach] could increase the efficiency of cervical cancer screening by finding more precancers and reducing false positives, which has the potential to eliminate a substantial number of unnecessary procedures among HPV-positive women," lead-author Nicolas Wentzensen, of NCI's Division of Cancer Epidemiology and Genetics, said in a statement. "Women who test negative for HPV are at low risk for cervical cancer for the following decade, and even most cervical HPV infections—which cause positive HPV tests—will not result in precancer. The challenge is to identify which women with positive HPV test results are most likely to have precancerous changes in their cervical cells and should, therefore, have a colposcopy to examine the cervix and take samples for biopsy, or who need immediate treatment."

Currently, women with positive HPV tests may have additional HPV tests or Pap cytology tests to assess the need for colposcopy, biopsy, or treatment.

Dual-stain testing has emerged as a way to more accurately predict the chance that a woman with a positive HPV test has precancerous cervical changes. The test measures the presence of two proteins, p16 and Ki-67, in cervical samples.

In two previous studies, Wentzensen and his colleagues found that women who had a negative result on a dual-stain test had a low risk of developing cervical precancer in the following five years and that fewer women test positive for dual-stain compared to Pap cytology. In March 2020, the manual dual-stain cytology test was approved by FDA for women who have received a positive result on a primary HPV screening.

The manual dual-stain test has a subjective component, in that a cytotechnologist must look at the slide to determine the results. In the new study, the investigators wanted to see if a fully automated dual-stain test could match or exceed the performance of the manual approach.

In collaboration with Niels Grabe and Bernd Lahrmann, of the Steinbeis Transfer Center for Medical Systems Biology, which is associated with the University of Heidelberg, they developed a whole-slide imaging platform that, after being trained with deep learning, could determine if any cervical cells were stained for both p16 and Ki-67. They compared this method with both conventional Pap cytology and manual dual-stain testing in samples from a total of 4,253 people participating in one of three epidemiological studies of HPV-positive cervical and anal precancers at Kaiser Permanente Northern California and the University of Oklahoma.

The researchers found that the AI-based dual-stain test had a lower rate of positive tests than both Pap cytology and manual dual-stain, with better sensitivity (the ability to correctly identify precancers) and substantially higher specificity (the ability to correctly identify those without precancers) than Pap cytology. AI-based dual-stain reduced referral to colposcopy by about a third compared with Pap (approximately 42% vs. 60%). The testing method was also robust, showing comparable performance in anal cytology.

The automated test surpassed the performance of the current standard, Pap cytology, reducing the number of false positive results and substantially reducing referral to unnecessary colposcopy procedures. The results also support further evaluation of the test as an option for anal cancer screening.

The researchers note that their approach has clear clinical application, and through cloud-based implementation, it would be globally accessible. Other applications of the platform include assisted evaluation, second opinion, and quality control.

Because the manual dual-stain test has only recently received FDA approval for screening of women who have HPV-positive test results, its use is just getting started. Additional regulatory approval will be needed to allow using a fully automated dual-stain test for screening of HPV-positive women.

IPATential150 study meets rPFS primary endpoint in mCRPC

The phase III IPATential150 study met its co-primary endpoint of radiographic progression-free survival in patients

with metastatic castration-resistant prostate cancer, and whose tumors had PTEN loss.

In this patient group, ipatasertib in combination with abiraterone and prednisone/prednisolone provided a statistically significant reduction in the risk of disease worsening or death, compared to current standard of care (abiraterone and prednisone/prednisolone) plus placebo. The other co-primary endpoint of rPFS in the overall study population (intention-to-treat) was not met.

The trial is funded by Genentech, a member of the Roche Group.The safety profile for the combination of ipatasertib and abiraterone was consistent with previous analyses and known risks.

Overall survival benefit and additional secondary endpoints are not yet mature. The trial will continue until the next planned analysis and data will be shared with health authorities.

Ipatasertib is an oral, highly specific, investigational medicine designed to target and bind to all three isoforms of AKT, which blocks the PI3K/AKT signaling pathway—a key driver of cancer cell growth and proliferation in prostate cancer. The PI3K/AKT pathway has also been implicated in resistance to anti-androgen therapy as androgen receptor inhibition is associated with an increase in AKT pathway activation.

Functional loss of the tumor suppressor protein PTEN within the tumor, seen in approximately 40-60% of mCRPC patients, results in hyperactivation of the PI3K/AKT pathway and is associated with adverse outcomes such as increased tumor grade and stage, earlier biochemical recurrence after radical prostatectomy, metastasis, prostate-cancer-specific death, and androgen-independent progression.

Genentech's clinical development program for ipatasertib focuses on tumors that are frequently found to have activation of the PI3K/AKT pathway. In addition to prostate cancer, ipatasertib is being studied in certain types of breast cancer including triple-negative breast cancer (TNBC) and hormone-receptor positive (HR+), HER2- negative breast cancer. Results are anticipated later in 2020.

City of Hope, TGen study shows T cells can predict how patients respond to immunotherapy

Scientists at City of Hope, working in collaboration with researchers at Translational Genomics Research Institute and other colleagues have found that the actions of circulating immune cells at the start of immunotherapy treatment for cancer can inform how a patient will respond to the therapy.

The team's findings were published in the *Proceedings of the National Academy of Sciences of the United States of America*.

"We used an ecological population model to understand the interactions between circulating white blood cell abundance and tumor response to immunotherapy," senior author Andrea Bild, professor in the Division of Molecular Pharmacology within the Department of Medical Oncology and Therapeutics Research at City of Hope, said in a statement.

In an effort to find ways of identifying who is more likely to respond to immunotherapy at the start of treatment, or possibly even before it starts, researchers used a mathematical model developed by Bild and colleagues.

The team used the model to analyze data from the results of patients with advanced colorectal or other gastrointestinal cancers who were enrolled in a clinical trial led by Sunil Sharma, deputy director of Clinical Services at TGen, an affiliate of City of Hope. The trial involved a chemotherapy regimen followed by a combination of chemotherapy and immunotherapy. It measured the strength of patients' tumor-immune cell interactions, which was then related to different immune cells categorized by their behavior.

The findings highlight, for the first time, an important predator-prey relationship between circulating immune cell dynamics and a tumor's response to immunotherapy. In particular, predator T cells showed increased differentiation and activity of interferon, a protein that exerts anti-tumor effects, during immunotherapy treatment in patients that respond to treatment, said Bild. This relationship was not found in patients during chemotherapy, nor was it seen in those who were non-responsive to immunotherapy.

"The study shows that subsets of immune cells in the blood indicate how each cancer patient responded to this combination of chemotherapy and immunotherapy," Sharma, who also is director of TGen's Applied Cancer Research and Drug Discovery Division and one of the study's senior authors, said in a statement. "We found, using this combination drug approach, that the body's own immune response and its activation correlated with a higher response to the therapy among cancer patients," said Sharma.

Next steps include further testing the ability of circulating immune cells to reflect tumor response to therapy in a clinical trial at City of Hope in collaboration with TGen.

The study, titled "Circulating immune cell phenotype dynamics reflect the strength of tumor-immune cell 2 interactions in patients during immunotherapy," features additional City of Hope authors and researchers from University of Utah, University of Minnesota, University of Texas Health Science Center at Houston and University of California Los Angeles.

Portions of the work were supported by a research grant from Merck Pharmaceuticals, NCI (P30CA042014, U54CA2099780), and the Cancer Prevention Research Institute of Texas Core Facility Support Award (RP170668).

Liquid biopsies using urine and plasma help detect NSCLC

University of Illinois College of Medicine researchers have developed an epigenetic-based approach that helps detect non-small cell lung cancer through liquid biopsies using urine and plasma.

In recent years, scientists have been using new techniques such as methylation-specific PCR – one of the most commonly used methods for epigenetic studies which assesses the changes in DNA expression without altering its sequence.

In a paper published in the *Clinical Cancer Research*, lead author Alicia Hulbert, assistant professor of surgery, suggests that liquid biopsy biomarkers based on methylation detection from plasma and urine could be used as an aid to computed tomography screening to help guide the decision to proceed with further invasive procedures.

"Urine samples have the potential to be easily implemented in a primary care practice," Hulbert, who is also a member of the University of Illinois Cancer Center's Translational Oncology Program, said in a statement. "Plasma and urine yield low false positive rates and the methylation of these genes is associated with a high risk of lung cancer independent of age, race or how much a person smokes."

The strategy detects epigenetic changes in circulating DNA in blood and urine using a specific set of genes for lung cancer.

The National Lung Screening Trial, sponsored by NCI, was conducted to determine whether screening with low-dose helical computed tomography could reduce mortality from lung cancer. However, CT screening has a false discovery rate of nearly 96%.

"Biomarkers from liquid biopsy assays hold promise for enhancing the diagnostic accuracy of early stage lung cancer screening in conjunction with CT imaging," Hulbert said. "In this regard, epigenetic molecular markers for early detection of lung cancer have been studied and developed for years."

However, those methods had a significantly lower yield of detecting DNA in circulating liquid biopsies. Hulbert developed an improved DNA extraction method that allows for methylation detection from liquid biopsies with a process optimized and reduced to just six hours, along with the use of highly prevalent cancer specific methylation targets.

The study was funded by the University of Illinois Cancer Center, the NCI Early Detection Research Network, and U.S. Department Of Defense.

Online program significantly improves insomnia in adolescent and young adult cancer survivors

Dana-Farber Cancer Institute researchers found that an online program developed specifically for adolescent and young adult cancer survivors can significantly alleviate insomnia and improve overall quality of life.

Adolescents and young adults who have survived cancer often continue to suffer from insomnia long after treatment ends, interfering with a range of daily activities.

The study, published in *Pediatric Blood and Cancer*, shows that an online program developed specifically for AYA cancer survivors can significantly alleviate insomnia and improve overall quality of life.

The insomnia intervention tested in the study is known as SHUTi (Sleep Healthy Using the Internet) was developed by researchers at the University of Virginia and adapted for AYA cancer survivors by Zhou and Recklitis. The interactive program uses text, images, and video to explain how insomnia develops and how it can be overcome. In adapting the program, Dana-Farber researchers replaced vignettes—brief stories of individuals struggling with insomnia—from the original version with ones more relatable to young people.

The program discusses how sleep behaviors that helped patients weather cancer treatment can become maladaptive when they return to normal life.

In the study, 22 AYA cancer survivors--mean age 20.4 years--with insomnia enrolled to use the specially adapted SHUTi. As part of the program, participants kept a sleep diary, tracking when they slept, and entered the information into SHUTi, which adjusted its sleep recommendations accordingly.

At eight and 16 weeks after starting to use SHUTi, participants reported a significant lessening in insomnia severity, daytime sleepiness, and fatigue, and an overall improvement in quality of life.

The program, which consists of six, 20-30 minute sessions, shows how sleep habits that may have helped patients cope with their intensive cancer treatments can become obstacles to healthy sleep as survivors move beyond treatment. Its automated format makes it particularly well-suited to the moment, as telehealth and online programs that are

already adopted by many hospitals and clinics, are becoming even more widely used as a result of the COVID-19 crisis.

"Cognitive-behavioral therapy for insomnia, which helps patients understand the behavioral and thought patterns that lead to long-term troubles with falling or staying asleep, has been shown to be very effective in adult cancer survivors. However, it has not been widely tested in the AYA survivor group, Eric Zhou who conducted the study, said in a statement. "We wanted to explore whether a CBT-I program, specifically tailored to AYA survivors and available online, could be helpful in this population."

Zhou conducted the study with Dana-Farber's Christopher Recklitis.

"Our results demonstrate that an internet-delivered CBT-I program targeting AYA cancer survivors reduced their insomnia and improved their quality of life," Recklitis said in a statement. "Notably, our participants' insomnia severity continued to get better after the intervention had ended, suggesting that the continued to make sleep-related decisions that helped their sleep even after they had finished using the program."

Support for the study was provided by a Psychosocial Launch Grant from Alex's Lemonade Stand Foundation.

Study: LifeTracDx blood test shows positive results in detection of early stage cancer in solid tumors

LifeTracDx, a blood test for the universal screening of early stage cancer, identified invasive cancer with 87% accuracy in a new study.

LifeTracdX is sponsored by Creatv MicroTech, a privately-held biotechnology company.

The results are from a training set of 10 cancer types, Cha-Mei Tang, chief executive officer of Creatv, said in a statement.

"The data shows that we obtained 85% sensitivity for all cancers (from 79% of patients in stage I and increasing to 95% of patients in stage IV), and also shows 100% specificity when tested against healthy normal controls," Tang said. "This represents a significant step towards pan cancer screening by a routine blood draw with high sensitivity and specificity."

The test analyzed the patient's immune response to the presence of cancer by isolating stromal cells originating from cancer sites that have migrated into the bloodstream. Creatv has shown that a particular subtype of circulating stromal cell, Cancer Associated Macrophage-Like cells, can be used to identify patients with cancer but are absent in healthy persons.

CAMLs are phagocytic myeloid cells derived from the patient's immunological response to active malignancy that have engorged cancer cells, thereby containing cancer protein markers and cancer DNA.

In a large multi-institutional study, 7.5mL of peripheral blood was taken from 308 cancer patients after a diagnosis of invasive malignancy, [stage I (n=76), stage II (n=73), stage III (n=72), stage IV (n=65) and unstaged non-metastatic (n=22)]. Patients were recruited with lung, pancreas, breast, prostate, esophageal, renal cell, hepatocellular, neuroblastoma, melanoma, and others. To compare specificity of the test, blood was also taken from 39 patients with untreated non-malignant conditions (i.e. benign breast masses, lupus, liver cirrhosis, etc.), and from 76 healthy volunteers. CAMLs were 87% accurate at identifying cancer patients when compared to healthy controls or from patients with non-malignant conditions.

These initial findings were granted funding from NCI/, Department of Defense and NCI/NIH for validation studies in the screening of 1,000 breast patients, 1,000 lung patients and 300 prostate patients.

DRUGS & TARGETS

FDA approves Keytruda for cutaneous squamous cell carcinoma

Keytruda was approved by FDA for patients with recurrent or metastatic cutaneous squamous cell carcinoma that is not curable by surgery or radiation.

Keytruda is sponsored by Merck.

Efficacy was investigated in KEYNOTE-629 (NCT03284424), a multicenter, multi-cohort, non-randomized, open-label trial. The trial excluded patients who had previously received therapy with an anti-PD-1, anti-PD-L1, or anti-CTLA-4 antibody and those with autoimmune disease or a medical condition that required immunosuppression. Patients received pembrolizumab 200 mg intravenously every 3 weeks until disease progression, unacceptable toxicity, or a maximum of 24 months. Assessment of tumor status was performed

every 6 weeks during the first year and every 9 weeks during the second year.

The major efficacy outcome measures were objective response rate and response duration as assessed by blinded independent central review according to RECIST 1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The ORR was 34% (95% CI: 24, 44) and median response duration was not reached (range: 2.7, 13.1+ months)

Selinexor receives FDA approval for relapsed/refractory diffuse large B-cell lymphoma

Selinexor (Xpovio) was granted accelerated approval from FDA for adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified, including DLBCL arising from follicular lymphoma, after at least two lines of systemic therapy.

Xpovio is sponsored by Karyopharm Therapeutics.

Approval was based on SADAL (KCP-330-009; NCT02227251), a multicenter, single-arm, open-label trial in patients with DLBCL after two to five systemic regimens. Patients received selinexor 60 mg orally on days one and three of each week.

Efficacy was based on overall response rate and response duration, as assessed by an independent review committee using Lugano 2014 criteria. In 134 patients, the ORR was 29% (95% CI: 22, 38), with complete response in 13%. Of the 39 patients who achieved a partial or complete response, 38% had response durations of at least 6 months and 15% had response durations of at least 12 months.

Oral relugolix NDA accepted for Priority Review by FDA

Myovant Sciences' New Drug Application for once-daily, oral relugolix (120 mg) for the treatment of men with advanced prostate cancer has been accepted for Priority Review by FDA.

"As recently published in the New England Journal of Medicine, relugolix demonstrated superior efficacy and a 54% lower risk of major adverse cardiovascular events compared to the current standard of care, leuprolide acetate injections, in the Phase 3 HERO study," Lynn Seely, chief executive officer of Myovant Sciences, said in a statement.

FDA has set a target action date of December 20, 2020 under the Prescription Drug User Fee Act. In its acceptance letter, the FDA also stated that it is currently not planning to hold an advisory committee meeting for this application. If approved, relugolix would be the first and only oral gonadotropin-releasing hormone receptor antagonist treatment for men with advanced prostate cancer.

Keytruda approved in China for second-line treatment of locally advanced or metastatic ESCC indication

Keytruda was approved by the National Medical Products Administration in China as monotherapy for the treatment of patients with locally advanced or metastatic esophageal squamous cell carcinoma whose tumors express PD-L1 (Combined Positive Score [CPS] ≥10) as determined by a fully validated test, following failure of one prior line of systemic therapy.

This new indication was granted full approval based on the overall survival findings from the global phase 3 KEYNOTE-181 trial, including data from an extension of the global study in Chinese patients. With this new approval,

Keytruda is sponsored by Merck.

Keytruda is now approved for five indications across three cancer types in China, including as a first-line treatment for appropriate patients with advanced non-small cell lung cancer (monotherapy and in combination with chemotherapy) and as a second-line treatment for advanced melanoma. The FDA approval in July 2019 was based upon the global KEYNOTE-181 trial.

"In China, more than 90% of esophageal cancers are squamous cell carcinomas, and patients with advanced types of this disease face a poor prognosis and have few treatment options," Shen Lin, vice president of Clinical Oncology at Beijing Cancer Hospital and Peking University and deputy director of Beijing Institute for Cancer Research, said in a statement.

In the KEYNOTE-181 trial, an improvement in OS was observed in patients who were treated with Keytruda monotherapy compared with chemotherapy in previously treated patients with recurrent or metastatic ESCC whose tumors expressed PD-L1 (CPS ≥10) (HR=0.64 [95% CI, 0.46-0.90]). The median OS was 10.3 months for Keytruda compared with 6.7 months for chemotherapy.

In the extension of the KEYNOTE-181 study in Chinese patients, consistent with the KEYNOTE-181 global study, there was an improvement in OS for patients who were treated with Keytruda monotherapy compared with chemotherapy in previously treated patients with recurrent or metastatic ESCC whose tumors expressed PD-L1 (CPS ≥10) (HR=0.38 [95% CI, 0.19-0.77]). The median OS was 12.0 months for KEYTRUDA compared with 5.4 months for chemotherapy.