

# THE CANCER LETTER

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## Moonshot May Play Role in \$400 Million Annual Contract for NCI's Frederick Lab

*By Matthew Bin Han Ong*

The contract for operations and technical support at the Frederick National Laboratory for Cancer Research could be accepting proposals as early as next month—but NCI advisors said they are hoping to slow the recompetition process to reform the laboratory's mission.

Moreover, NCI should consider how the laboratory could contribute to Vice President Joe Biden's National Cancer Moonshot Initiative, members of

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## U.S. Preventive Services Task Force Adds Tests to Colon Screening Guideline

*By Paul Goldberg*

The final version of guidelines for colorectal cancer screening by the U.S. Preventive Services Task Force differ substantively from the group's draft version published last October.

The final version—unlike the draft—lists CT colonography and FIT-DNA as screening methods that are equal to others.

It's unclear whether political pressure had any role in prompting the panel to broaden its list of detection strategies from three to seven in the past six months.

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### In Brief

## Obama Names Six Appointees to NCAB

**PRESIDENT BARACK OBAMA** named six appointees to the **National Cancer Advisory Board**. They are:

- **Francis Ali-Osman**, professor of surgery and pathology and the Margaret Harris & David Silverman Professor of Neuro-Oncology Research at Duke University School of Medicine. Ali-Osman served as associate director

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# Moonshot May Play Role in Frederick Lab Recompetition

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the Frederick National Laboratory Advisory Committee said at a recent meeting.

The lab, located on a 68-acre campus in Frederick, Md., and at the Advanced Technology Research Facility, a 330,000-square-foot complex with a biopharmaceutical development wing, is one of 42 Federally Funded Research and Development Centers.

The Frederick lab is the only FFRDC dedicated to biomedical research, specifically in the areas of cancer and other diseases. FFRDCs receive 70 percent or more of their financial support from the federal government. By statute, these centers are designed to be operated by contractors.

Since it's run through a contract, the Frederick lab has greater flexibility than NCI's intramural program in funding projects. This means that the laboratory has more independence to initiate and conduct research that complement NCI's. When all works well, this allows researchers at Frederick to pursue innovative ideas expeditiously.

However, the flow of funds at FNLCR hasn't always been clear or transparent. Since funding is project-specific, even NCI leadership and members of the laboratory's advisory committee may not always know exactly how federal dollars are being used at the laboratory.

The Frederick lab is currently operated by Leidos Biomedical Research Inc.—formerly known as SAIC-Frederick—the same contractor that has ran the lab

CONTRACTOR NAME	PERIOD OF PERFORMANCE
LITTON BIONETICS, INC.	1972 – 1977
LITTON BIONETICS, INC.	1977 – 1982
PROGRAM RESOURCES, INC.	1982 – 1987
DYNACORP, INC.	1987 – 1995
SAIC, INC.	1995 – 2001
SAIC-FREDERICK, INC.	2001 – 2008
LEIDOS BIOMEDICAL RESEARCH, INC. (FORMERLY SAIC-FREDERICK, INC.)	2008 – 2018

since 1995.

The current contract, which was awarded in 2008, is scheduled to end in September 2018. Leidos received \$400.2 million to run the lab in fiscal 2014. According to a recent job posting, Leidos said it employs about 1,900 staff and manages a \$450 million annual operating budget. It is not publicly known how much NCI is budgeting for the 2018 contract.

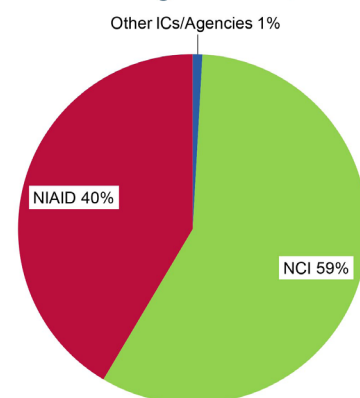
“There is no established budget at this time,” NCI officials said to The Cancer Letter. “Any previous references to the estimated ceiling for contract award do not represent an annual budget and are subject to change.”

Leidos manages a subcontract for the NCI Genomic Data Commons, a portal that consolidates NCI's diverse datasets. The \$20 million project, funded through President Barack Obama's Precision Medicine Initiative, was recently designated by Biden as the foundation for the moonshot's data-sharing goals (The Cancer Letter, [June 10](#)).

As the institute prepares to re-compete FNLCR's contract, NCI officials see the process as an opportunity to:

- Assess the FNLCR's potential for contributing to big-picture goals in oncology, including the goals set out in the moonshot,
- Review how federal funds are used at the laboratory,
- Select a contractor that can best meet NCI's most “urgent needs”—including fostering collaboration between FNLCR and the extramural academic

**FNLCR FY15 Obligations**  
All Federal Agencies: \$579.5M



**Editor & Publisher:** Paul Goldberg

**Associate Editor:** Conor Hale and  
Matthew Bin Han Ong

**Intern:** Laura Brawley and Katie McKinney

Editorial, Subscriptions and Customer Service:

202-362-1809 Fax: 202-379-1787

PO Box 9905, Washington DC 20016

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- Population health-related discoveries with risk and prevention implications for cervical cancer



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community, and

- Focus FNLCR resources towards conducting research that would be difficult to perform elsewhere.

### NCI to Set Research Agenda

How much independence should FNLCR have when deciding which funds should be spent and which projects should be pursued?

NCI officials say recompetition, which comes up once a decade, is the time for redrawing the lines of command.

At a recent meeting of FNLCR's advisory committee, NCI Acting Director Doug Lowy opened the discussion with a request for suggestions on how FNLCR's mission should be redefined.

"We were interested in your talking about the capabilities of the Frederick National Lab and particularly thinking about the future," Lowy said. "We're really interested in hearing about your perspective on this in terms of where you see the potential for the FNLCR going, now that we have the model of various kinds of initiatives, etc.

"What is your perspective on how we should thinking about positioning the FNLCR for the future?"

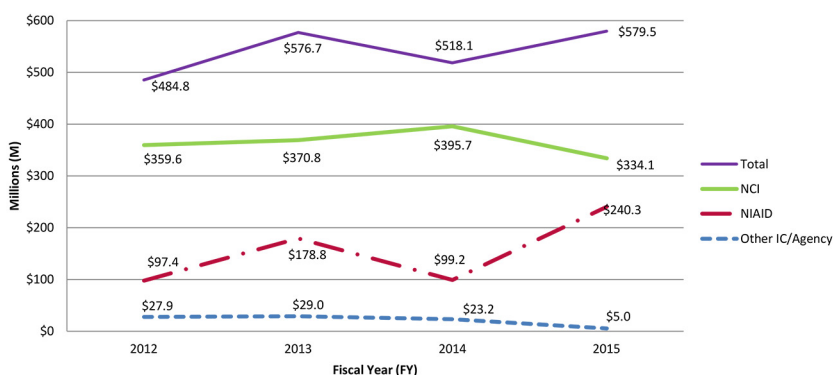
Operating the national laboratory via a contractor gives NCI the flexibility to fund programs and hire staff without having to use government mechanisms—giving the institute the ability to shift projects and move dollars with greater ease.

In the past, NCI directors have sheltered their pet projects from peer review by funding them as subcontracts of the SAIC contract. Under previous directors, the institute has been known to use the contract as a place for "parking" funds left over at the end of the fiscal year, thereby preserving these funds for the following year's budget, sources said.

The Frederick National Lab evolved from a little-understood outpost of the NCI into a national laboratory in February 2012, two years after Harold Varmus was appointed NCI director.

To align the contractor with the institute, Varmus created the Frederick National Laboratory Advisory Committee to guide its programs and, in his words, to "reuse resources in a

FNLCR Obligations from FY12 through FY15  
All Federal Agencies



sort of very sensible way to foster the best use of NCI's money." (The Cancer Letter, [Feb. 28, 2014](#)).

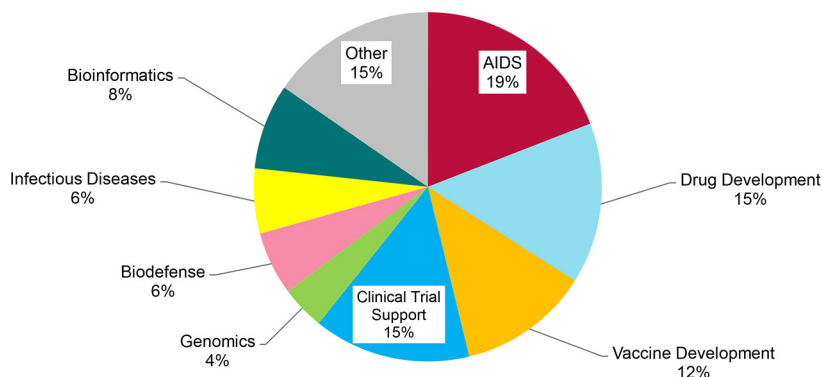
Varmus was succeeded by Lowy on April 1, 2015 (The Cancer Letter, [April 17, 2015](#)).

FNLCR staff should be able to propose research ideas, but the final decision needs to be made by NCI, said Joe Gray, chair of the Frederick National Laboratory Advisory Committee.

"It seems to me that a reasonable model that one could aspire to for Frederick is where the NCI actually defines, with reasonable granularity, areas of interest, and Frederick has the opportunity to propose to address topics in those work areas of interest," Gray said at the May 11 meeting of FNLCR's advisory committee. "This would be done in collaboration with the community: they would develop within Frederick a proposal to address a particular NCI need.

"NCI would then say, 'Yes, we like it,' or 'No, we don't.' If the answer is no, then you're back to the drawing board, but it seems to me that this would give the Frederick lab the opportunity to engage the community and to have initiative on their own. That would be quite the workable model."

FNLCR FY15 Obligations by Research Type Estimates  
All Federal Agencies: \$579.5M



Other committee members expressed support for an NCI-driven research agenda.

“First of all, I don’t think Frederick should be independent from the NCI, I think that’s not correct, but I’m open to other people’s views. That’s my initial response, pretty strongly,” said committee member Cheryl Willman, director and CEO of the University of New Mexico Comprehensive Cancer Center. “Is Frederick its own independent, idea-generating laboratory in which it pursues projects? Is it more of a highly-advanced technology, almost like a shared resource where the NCI intramural program and other entities are bringing projects that aren’t easily reproduced at other centers, because of technologic demands?”

“That’s the direction I think we’ve been moving in over the last few years, which I think is pretty satisfying,” said Willman, the Maurice & Marguerite Liberman Distinguished Endowed Chair in Cancer Research and professor of pathology at the UNM School of Medicine. “Or is Frederick also—and none of these are necessarily mutually exclusive—a convening function for high performance computing problems applied to cancer where there is science going on here and collaboration with DOE, but also could involve the extramural community?”

“All of those are possible, but I think the mission has to be tightly linked to NCI’s mission.”

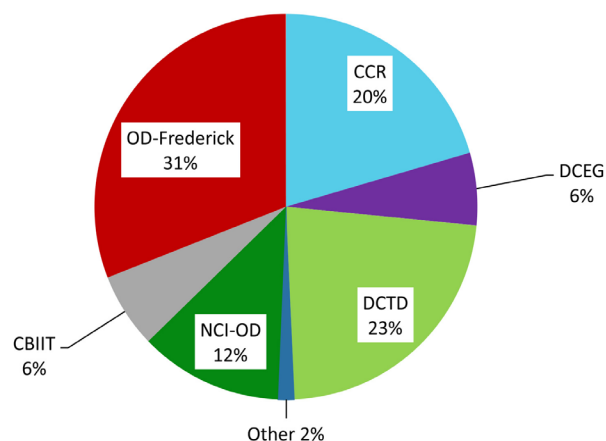
The process by which FNLCR identifies promising research projects is unclear—an issue that the recompetition needs to address, said Kenneth Pienta, advisory committee member and director of the urology research laboratories at Johns Hopkins Hospital.

“The root question we need to ask moving forward is, ‘How does Frederick elevate us as a scientific community in decreasing the morbidity and mortality from cancer?’” said Pienta, professor of oncology, pharmacology and molecular sciences at Hopkins. “I think what’s really cool is that over the last three years, we’ve seen two examples of that in this community, very clearly, that started with the RAS project and get around a problem and attack it in a way that nobody else is and how it’s going to give us downstream output.”

[The RAS Initiative](#) was established in 2013 to explore innovative approaches for attacking the proteins encoded by mutant forms of RAS genes and to ultimately create effective, new therapies for RAS-related cancers. All 180 RAS pathway genes are now available.

“The question is, what’s the process that Frederick sets up to identify that type of science, and do we, or do we not, involve the extramural community in those

FNLCR FY15  
NCI Obligations: \$334.1M



decisions? Is it purely NCI-driven intramural, is it NCI-driven around this table?” Pienta said at the advisory committee meeting. “But I think the whole idea around how to define that process is key, because I think we’ve seen a glimmer of, ‘Wow, this can be really great!’”

“I think that we are going to have to do it with awareness of the moonshot, that’s going to affect this somehow. I don’t know how, but we’re going to have to be aware of that.”

### NCI: Delay, Wait for Moonshot

Committee members should consider delaying the process and create a plan for how FNLCR’s resources can be used for the moonshot, Gray said.

“This competition comes at an interesting time in history, that is to say right in the middle of the moonshot,” Gray said at the meeting May 11. “It’s not clear to me what role Frederick is going to play in this moonshot project, but it is a fast track enterprise. One of the things that you are running the risk of is changing management right in the middle of the time when Frederick would be really well positioned to play an important role in moonshot activities.

“I will just not ask for an answer on this question, but at least ask that you think about whether or not this is the right time to be competing this contract considering the timeliness of moonshot activities.”

The timeframe is urgent, but compromise should be possible, said committee member Robert Grossman, director of the Center for Data Intensive Science and professor at the University of Chicago.

“This is a unique time in terms of some of the large-scale initiatives going on with the moonshot and related things that are going to have an impact for a long time,” Grossman said. “The Frederick National Lab has a very important, I think, role to play in that.”

“One thing that this committee might want to discuss is part of the challenge right now is there’s a certain level of distraction as you prepare for a recompetition, at the same time, there has to be a certain level of focus to prepare for these larger changes related to the moonshot.

“I know money is very tight, but one thing that could be done is to consider providing some mechanism or funding so that you could protect and provide focus for the current lab to engage in some long term planning at the same this other distracting activity is taking place.

“It’s a compromise, but you almost need a little bit of protection so they can think of the long term, no matter what that looks like.”

NCI has the authority to move FNLCR funds for the moonshot, said NCI Acting Director Lowy.

“I think just that as we can modify the amount of funds at the Frederick national lab down, we can also modify them up,” Lowy said. “But there needs to be really strong justification for doing it.

“Let’s just take a hypothetical example that something that comes out of the Blue Ribbon Panel that people feel the Frederick national lab would be an excellent place to do this, because it has certain characteristics that aren’t met by the usual extramural activities etc.

“The funds for doing that could be added.”

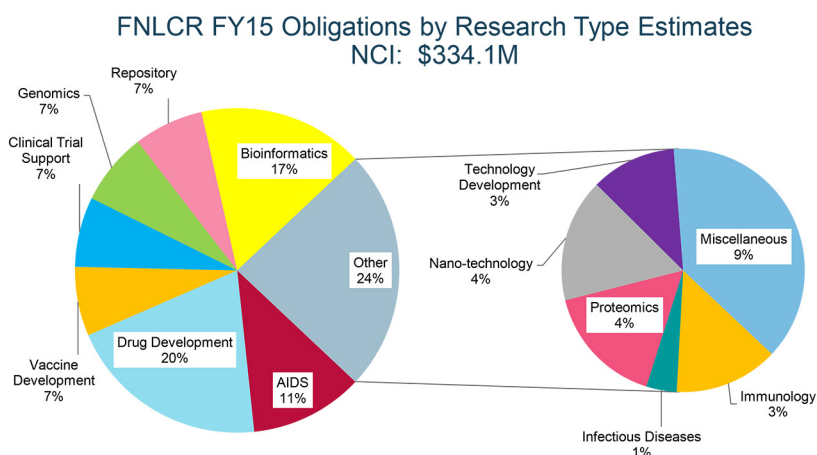
A detailed breakdown of FNLCR’s current flow of funds would be necessary to inform NCI’s decisions going forward, Gray said.

“Maybe some document that goes along with all of this that in essence describes the current Frederick National Laboratory operation, that would be very helpful,” Gray said.

Several FNLCR staff members objected, saying that research projects might be disrupted if the recompetition does not adhere to a strict timeline and the process is not completed by September.

Nevertheless, NCI should consider how FNLCR can contribute to the moonshot, Gray said.

“I can see expressions of angst, but let’s just say we put it on the table as something that the NCI should



at least think about in the context of the moonshot,” Gray said.

Responding to numerous, tense moments of awkward silence, Gray said:

“OK, I’m going to look around the room at my fellow advisory committee members here and make the following statement:

“This is probably the single most important contribution that we could’ve made in the last five years, is to help get this recompetition right.

“It’s going to have a major impact on the way that Frederick is run in the future and if now is not the right time to be making comments that would be helpful, there certainly is an opportunity to make comments publicly about this to give some pretty deep thought to this.

“I think we’ve got a really good thing going here. If we’re going to change things, let’s make sure that we help them do the best that we possibly can in terms of making it greater.”

### **Gray: Struggle to Understand Frederick**

Some members of the advisory committee expressed frustration at how difficult it was for them to understand FNLCR’s complex flow of funds and research activities.

NCI and the laboratory will work on making those details more transparent, Gray said.

“All of us on this committee have gone through the same struggle to try to understand how Frederick actually works, and obviously, we have not succeeded in making this perfectly transparent to people who are new to the enterprise,” Gray said. “I think we also haven’t made it particularly transparent to people who may be thinking about competing for the operating contract, and I think that’s a really important thing for people who are going to try to put proposals together to know in some detail.

"I think we do need to aspire as the Frederick National Lab to have information out there readily consumable about what they actually do as we go forward to help the community understand how to engage it."

Gray provided a critique of the FNLCR's draft of the request for proposal for the recompetition, saying that it isn't sufficiently informative.

"My take on this is the statement of work was sufficiently general as to not actually convey a lot of the information that we just spent the last two hours discussing," Gray said. "For example, how Frederick actually operates, how it interacts with NCI, what the actual funds flow are—the real money, there were sort of ballpark numbers given, but I didn't actually find the details that we've seen posted today."

"To me, the RFP was sufficiently high level, but it didn't give me a sense of how to actually operate it or what the NCI would consider to be a good proposal."

Other committee members agreed, saying that the proposal needs to re-envision its statement of work.

"The way this is written, it seems almost that it's encouraging business as usual, and I'm just slightly rewording what people say," Grossman said. "There's going to be a lot of effort put into this by a lot of people, and it would be good just to sort of frame it with the vision of encouraging this and presenting this as more of an opportunity to create even better pipes of technology development and translation."

"I just didn't get that sense of possibility from this document."

Frederick should be an "interface" for NCI to establish greater collaboration with other scientific communities, they said.

"I've always looked at the Frederick opportunity as one that's, in part, the innovation driver for the NCI's program," Willman said. "But I also think it's become almost the advanced technology component, when you think about bioengineering, computing, about the science that many of the national labs are engaged in."

"What's the most important question we could address now using this structure here at Frederick and who would need to be engaged in that, is, 'How can the Frederick lab be NCI's interface to those communities that you need to pull together?'"

"So that's why I still think there really needs to be mission alignment between the NCI's national agenda or the national agenda for cancer research and sorting out

## Schedule of Acquisition

- Draft RFP Released: Apr 15, 2016
- Planned RFP Release: 4<sup>th</sup> Quarter FY16 (Jul 2016)
- Proposals Due: 1<sup>st</sup> Quarter FY17 (Oct 2016 - Dec 2016)
- Peer Review: 2<sup>nd</sup> Quarter FY17 (Jan 2017 - Mar 2017)
- Negotiations: 3<sup>rd</sup> Quarter FY17 (Apr 2017- May 2017)
- Award: 3<sup>rd</sup> Quarter FY17 (Jun 2017)

the unique role Frederick can play with its innovative funding model and its ability to convene great science."

Gray set out a number of questions he said should be answered in the RFP:

"What are the things that the NCI is really hoping to accomplish through this recompetition that in the eyes of the NCI would make it better? Is there a role for an academic collaborator and if so, what? How much flexibility does the potential competitor have to actually change the business model?"

"You could imagine that people would bring in a lot of new creative ideas about how to run Frederick national laboratory. Those were some of the things that came to my mind as I read it," Gray said. "To me, it was just too high level."

"It would be useful to have some set of rather quantitative criteria by which the proposals would be judged so that people could understand where to put the emphasis on the development of the proposal."

Gray, who has served as chair of the advisory committee since 2016, will be succeeded by Lawrence Marnett, associate vice chancellor for research and senior associate dean for biomedical sciences, the Mary Geddes Stahlman Professor of Cancer Research, and professor of biochemistry, chemistry and pharmacology at Vanderbilt University School of Medicine.

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## USPSTF Adds Tests to Colon Cancer Screening Guideline

(Continued from page 1)

In its final recommendation statement, USPSTF notes that clinical outcomes are affected by many “moving parts,” of which the most important is the patient’s willingness to undergo screening with a test that has been deemed acceptable. It’s also clear that the task force had been relying on computerized modeling and lower-level evidence to draw comparison between screening modalities.

Experts in screening say it remains to be seen how the task force decides what is acceptable, and therefore subject to “shared decision-making.” The change could signal that the task force would not be guided by the sometimes-small differences in modeling, but would instead consider real-world issues, including quality and adherence.

In the recommendation statement, USPSTF notes that clinical outcomes are affected by many “moving parts” of which the most important is the patient’s willingness to undergo screening with a test that has been deemed acceptable. It’s also clear that USPSTF was relying on computerized modeling and lower-level evidence to draw comparison between screening modalities.

A conversation with Douglas Owens, a former USPSTF member who was involved in developing the colorectal cancer screening guideline appears here. It remains to be seen whether USPSTF has just sent out a smoke signal indicating that it is vulnerable to political pressure.

USPSTF recommends screening for colorectal cancer starting at age 50 and continuing until age 75 (an “A” recommendation). The decision to screen for colorectal cancer in adults aged 76 to 85 years should be an individual one, taking into account the patient’s overall health and prior screening history (a “C” recommendation).

The stakes are high: the Affordable Care Act requires private insurers to fully cover, with no co-pay, screening exams that earn A or B grades from the task force. Medicare makes its own determination.

“Mandatory insurance coverage of CT colonography and the other USPSTF-recognized exams is a major step forward in the battle against colorectal cancer,” Judy Yee, chair of the American College of Radiology Colon Cancer Committee, said in a statement. “Medicare coverage for CT colonography would remove a financial barrier to this screening and

enable more seniors to be screened. This would help prevent many cancers, find more cancers before they progress and save thousands of people who might otherwise die from a disease that is often preventable. Medicare needs to follow through on this USPSTF ‘A’ grading for the USPSTF-recognized exams.”

The sponsor of Cologuard, a FIT-DNA test, applauded the change of position by USPSTF. “We believe the final recommendations provide an important level of clarity to patients, physicians and insurers and that Cologuard should receive the benefits given to A-rated preventive services under the Affordable Care Act,” Kevin Conroy, chairman and CEO Of Exact Sciences, said in a statement. “We thank the Task Force for carefully reviewing the body of scientific evidence supporting Cologuard and for providing this clear guidance.”

USPSTF said it has reconsidered [its draft recommendations](#) in response to public comment received since publication.

[The final recommendation](#) offers this explanation for the task force’s rethinking of the draft recommendation:

“A draft version of this recommendation statement was posted for public comment on the USPSTF website from Oct. 6 to Nov. 2, 2015. Many comments expressed concern that the terms ‘recommended’ and ‘alternative’ to describe the testing strategies lacked clarity and were confusing to interpret.

“In response, the USPSTF removed these terms from the final recommendation to better communicate the primary message of importance: there is convincing evidence that screening for colorectal cancer provides substantial benefit for adults aged 50 to 75 years, and a sizable proportion of the eligible U.S. population is not taking advantage of this effective preventive health strategy. With this recommendation, the USPSTF acknowledges that there is no ‘one size fits all’ approach to colorectal cancer screening and seeks to provide clinicians and patients with the best possible evidence about the various screening methods to enable informed, individual decision making.

“Accordingly, both the [Table](#) and [Figure 3](#) were updated to provide more detailed information about the available evidence on the effectiveness of each method, as well as the strengths, limitations, and unique considerations for the various screening tests.”

In [a commentary published by JAMA](#) with the USPSTF recommendation, John Inadomi, of the Division of Gastroenterology of the University of Washington School of Medicine and the Department



Table. Characteristics of Colorectal Cancer Screening Strategies<sup>a</sup>

Screening Method	Frequency <sup>b</sup>	Evidence of Efficacy	Other Considerations
<b>Stool-Based Tests</b>			
gFOBT	Every year	RCTs with mortality end points: High-sensitivity versions (eg, Hemoccult SENSa) have superior test performance characteristics than older tests (eg, Hemoccult II)	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT <sup>c</sup>	Every year	Test characteristic studies: Improved accuracy compared with gFOBT Can be done with a single specimen	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every 1 or 3 y <sup>d</sup>	Test characteristic studies: Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test	There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test
<b>Direct Visualization Tests</b>			
Colonoscopy <sup>c</sup>	Every 10 y	Prospective cohort study with mortality end point	Requires less frequent screening Screening and diagnostic follow-up of positive findings can be performed during the same examination
CT colonography <sup>e</sup>	Every 5 y	Test characteristic studies	There is insufficient evidence about the potential harms of associated extracolonic findings, which are common
Flexible sigmoidoscopy	Every 5 y	RCTs with mortality end points: Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies	Test availability has declined in the United States
Flexible sigmoidoscopy with FIT <sup>c</sup>	Flexible sigmoidoscopy every 10 y plus FIT every year	RCT with mortality end point (subgroup analysis)	Test availability has declined in the United States Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

Abbreviations: FIT, fecal immunochemical test; FIT-DNA, multitargeted stool DNA test; gFOBT, guaiac-based fecal occult blood test; RCT, randomized clinical trial.

<sup>a</sup> Although a serology test to detect methylated *SEPT9* DNA was included in the systematic evidence review, this screening method currently has limited evidence evaluating its use (a single published test characteristic study met inclusion criteria, which found it had a sensitivity to detect colorectal cancer of <50%).<sup>1</sup> It is therefore not included in this table.

<sup>b</sup> Applies to persons with negative findings (including hyperplastic polyps) and is not intended for persons in surveillance programs. Evidence of efficacy is not informative of screening frequency, with the exception of gFOBT and flexible sigmoidoscopy alone.

<sup>c</sup> Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling.<sup>2</sup>

<sup>d</sup> Suggested by manufacturer.

<sup>e</sup> Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling when lifetime number of colonoscopies is used as the proxy measure for the burden of screening, but not if lifetime number of cathartic bowel preparations is used as the proxy measure.<sup>2</sup>

of Health Services at the University of Washington School of Public Health, wrote that the absence of the USPSTF recommendation for any specific strategy leaves clinicians with a dilemma:

“The highest-quality data exist for gFOBT, which has been replaced by FIT, and sigmoidoscopy, which is largely unavailable. Colonoscopy is the most often used screening test, and observational studies report reductions in cancer incidence and mortality, yet validation from randomized clinical trials is lacking. The FIT-DNA should be at least as good as FIT, but there are no data to demonstrate greater reductions in cancer mortality beyond FIT. Radiographic and blood-based screening likewise have a paucity of clinical outcome data. It is in this context that the USPSTF has chosen to forgo specific test recommendations and instead highlight the advantages and disadvantages of the strategies presented in their statement. Perhaps the absence of data should not indicate the absence of

benefit, and these recommendations should be viewed as a living document that is expected to change as more information become available.”

The recommendation doesn’t specifically include serology tests. It states only that earlier this year FDA approved a blood test to detect circulating methylated *SEPT9* DNA (Epi proColon; Epigenomics).

“A single test characteristic study met the inclusion criteria for the systematic evidence review supporting this recommendation statement; it found the *SEPT9* DNA test to have low sensitivity (48%) for detecting colorectal cancer,” the USPSTF recommendations state.

The *SEPT9* test isn’t included in the tables. However, its sponsor, Epigenomics AG, said in a press release that USPSTF “has included Epi proColon in its new recommendation statement for colorectal cancer screening, published in [JAMA]. USPSTF is the first U.S. guideline body to recognize this novel colorectal

cancer screening test after its recent FDA approval.”

The test received FDA approval based on sensitivity and specificity. Its impact on disease-specific mortality wasn’t measured.

In [a JAMA editorial](#) published earlier this week, Ravi Parikh, of the Department of Medicine, Brigham and Women’s Hospital in Boston, and Vinay Prasad, of the Knight Cancer Institute Division of Hematology and Medical Oncology and the Department of Public Health and Preventive Medicine, wrote that SEPT9 isn’t ready for clinical use.

“First, the adequacy of the end point for approval should be questioned. In cancer screening, proof that a test can detect cancer is not the same as proof that the test can reduce disease-specific mortality,” Parikh and Prasad wrote. “For instance, ovarian cancer screening with transvaginal ultrasound and a CA-125 measurement clearly increases cancer detection; however, there is no good evidence that acting on these findings improves disease-specific mortality, with at least two randomized trials failing to find such a benefit in the primary analysis. In contrast with imaging-based screening, the blood-based screening test for colon cancer was accepted without demonstrating an improvement in survival for colorectal cancer.

“Why does disease-specific mortality matter? Not all colon cancer is biologically similar and amenable to mortality reduction through early detection. For instance, there is persistent debate as to whether colonoscopy improves disease-specific mortality beyond the benefits from sigmoidoscopy, even though only colonoscopy is able to screen the right-sided colon. Multiple observational studies suggest that the benefit of colonoscopy is limited to a reduction in death from left-sided but not right-sided colon cancer. One putative biological explanation for this is that right-sided cancers have more aggressive early genetic events and are more difficult to detect and resect with endoscopy.”

Though the test is not included in the table summarizing the testing strategies, the company has interpreted its inclusion in the USPSTF report as an endorsement by the task force.

“We are excited about the inclusion of Epi proColon in the new USPSTF recommendation, which recognizes the potential role of our novel blood-based test in colorectal cancer screening, especially in driving patient compliance in individuals who are reluctant to collect stool samples or undergo colonoscopy” Thomas Taapken, CEO and CFO of Epigenomics AG, said [in a press release](#). “This recommendation emphasizes the

need for additional screening options and will help to drive medical adoption and support reimbursement coverage of Epi proColon in U.S. market.”

A footnote to the table in which USPSTF summarizes the screening strategies states that the SEPT9 test was evaluated, but not included—because its sensitivity was below 50 percent, and because no evidence on the test is available.

Peter Vogt, vice president of corporate communications and investor relations at Epigenomics, stood by his company’s interpretation of the USPSTF guideline. “We wouldn’t have issued a press release if we weren’t sure about this,” he said.

“USPSTF has changed its approach to cancer screening,” Vogt said. “They say the important thing is that people get screened. They are not choosing a method.” Vogt said he is aware of the task force’s statement that data on SEPT9 aren’t ready for evaluation and that a peer-reviewed study points to low sensitivity.

“Why are we not there? Because they don’t have the use of the test. They recognize that our test may play a role. This is up to the future experience with the test. For us, the glass is more than full. This is a major acknowledgment of our test.”

Owens, one of the authors of the USPSTF report, said SEPT9 DNA isn’t among strategies the task force considers appropriate for screening.

“The table has in it the strategies that we considered as options,” Owens said to The Cancer Letter. “And the footnote about SEPT9 DNA, as I indicated, suggested the evidence we had for that was really quite limited...The strategies that we are considering for adoption are the ones that are in the paper itself.”

Epigenomics stock is traded on Frankfurt Prime Standard under the symbol ECX and in the U.S. under the symbol EPGNY.

In [another JAMA editorial](#), David Ransohoff, of the University of North Carolina Lineberger Comprehensive Cancer Center and Departments of Medicine and Epidemiology, and Harold Sox, of the Patient-Centered Outcomes Research Institute and the Geisel School of Medicine at Dartmouth, note that USPSTF isn’t being as specific as it has been in the past.

“The USPSTF appears to be saying that some tests are better than others, but then does not specify a preference,” Ransohoff and Sox write. “How can tests differ and yet be the same in the eyes of the task force? In the Recommendation Statement, the task force states

a principle that may explain this paradox: ‘the best screening test is the one that gets performed.’ A test can rank low when tested on a representative population but still be better aligned with an individual patient’s preferences and, therefore, be most likely to get done.”

USPSTF has been in a war over its recommendations on breast cancer screening (The Cancer Letter, [April 24](#)). Its recommendations for breast cancer screening have been, in effect, nullified, and disaffected constituencies have called for the task force’s dissolution.

An amendment to the ACA, called the Women’s Preventive Health Amendment in effect invalidates the unimpressive “C” that USPSTF gave to mammography screening for women between ages 40 and 49.

Nonetheless, [the final guideline on breast cancer screening](#) once again gave a “C” to mammography in younger women.

*Laura Brawley contributed to this story.*

## ***Conversation with The Cancer Letter*** **Guideline Edits Rooted in Science,** **Former USPSTF Member Says**

“I don’t see this recommendation as differing in any substantial way from some others that we’ve made, where we suggested that patients talk with their clinicians, and the important messages here is that colorectal cancer screening works, that colorectal cancer screening reduces deaths from colorectal cancer,” said Douglas Owens, a who has rotated off the U.S. Preventive Services Task Force, and was involved in developing the colorectal cancer screening guideline published earlier this week.

“The draft guideline, as you know, was a recommendation for screening for colorectal cancer, and we got comments from a broad variety of people,” Owens said. “What we saw from the comments that in our original draft, the distinction between recommended and alternative tests was confusing to both clinicians and patients.

“In reviewing those comments, we decided that that language was confusing people, so we decided to eliminate it.”

Owens is the Henry J. Kaiser, Jr. Professor and director of the Center for Health Policy in the Freeman Spogli Institute for International Studies and of the Center for Primary Care and Outcomes Research in the Department of Medicine and School of Medicine at Stanford University. He is a general internist and

associate director of the Center for Innovation to Implementation, a health services research center of excellence, at the VA Palo Alto Health Care System. Owens is a professor of medicine and, by courtesy, professor of health research and policy, and a professor of management science and engineering at Stanford University.

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

**Paul Goldberg:** *I’ve been covering USPSTF for years, and I don’t think I’ve ever seen a final guideline differ that much from the draft. What happened? How is this one different?*

**Douglas Owens:** As I’m sure you know, Paul, our process is to post the draft guideline, and then there is a public comment period in which we get comments, and we often get comments.

We review those very carefully and then go back to the guideline. Sometimes those comments talk about additional evidence. Often they ask for points of clarification, and then, based on our review of the comments, we decide whether or not we need to make any modifications of the guidelines.

**PG:** *But what happened here that made it so different? Usually they’re fairly close.*

**DO:** The draft guideline, as you know, was a recommendation for screening for colorectal cancer, and we got comments from a broad variety of people. What we saw from the comments was that, in our original draft, the distinction between recommended and alternative tests was confusing to both clinicians and patients.

In reviewing those comments, we decided that that language was confusing people, so we decided to eliminate it.

**PG:** *It went from three to seven strategies as a result.*

**DO:** The strategies were all in the draft. And the draft had this language about recommended versus alternative care, so that was really the thing we changed primarily in the final guideline.

**PG:** *Does this set a precedent? I’m wondering whether USPSTF is saying that informed decision making has perhaps a greater role to play, as opposed to looking for a marginal improvement, or, say, modeling, or clinical trials.*

**DO:** I don’t see this recommendation as differing in any substantial way from some others that we’ve made, where we suggested that patients talk with their clinicians, and the important messages here is



that colorectal cancer screening works, that colorectal cancer screening reduces deaths from colorectal cancer.

We also know that a third of people who should be screened from ages 50 to 75 are not being screened. So our important message is that what matters is getting screened, and there are several accepted strategies to do that, and we suggest that patients discuss with their clinicians the different options that have different strengths and limitations—and that patients pick one that works for them, and then follow through with the screening.

The important message is that people should be screened, and there are options they can use, and we hope that people avail themselves of at least one of those strategies.

**PG:** *Was there any political pressure?*

**DO:** You know our role is to focus on the science, and that's what we do. Our role is to evaluate the harms and benefits of different preventive interventions and inform the public and clinicians about that, and really that's, that's what we focus on.

**PG:** *So you were able to block it out, if there was any, or were protected from it?*

**DO:** Yes, our focus was really on the evidence, and about benefits and harms of different strategies and the science behind screening for colorectal cancer.

**PG:** *Is SEPT9 DNA on the list of strategies?*

**DO:** No. There is a footnote in the table about it. There was very limited information for us to review about SEPT9. There was a study that was included in our review, and that's why we suggested that SEPT9 had a sensitivity to detect colorectal cancer that was less than fifty percent, which is quite low. So we think that's an important area for further research, but at the time of our review, there was limited published data about SEPT9.

**PG:** *Right. I'm asking because I saw a press release from the company that sponsors this, and they are saying that they are on the list of recommended strategies. Are they wrong?*

**DO:** Let me just grab the—

**PG:** *It's in [the footnote to the table](#).*

**DO:** The table has in it the strategies that we considered as options. And the footnote about SEPT9 DNA, as I indicated, suggested the evidence we had for that was really quite limited.

**PG:** *So they're mistaken?*

**DO:** The strategies that we are considering for adoption are the ones that are in the paper itself.

**PG:** *Well, that's very helpful. Is there anything we've missed? Anything you'd like to add?*

**DO:** I think the main message we're hoping to get out to people is that colorectal screening reduces deaths from colorectal cancer, so the important thing is that people get screened, and they can have a conversation with their clinicians about which of the options that are available would work best from them.

### *In Brief*

## **Obama Names Six Members to National Cancer Advisory Board**

(Continued from page 1)

of translational research at the Duke University Cancer Center from 2003 to 2010.

- **Lawrence Gostin**, faculty director of the O'Neill Institute for National and Global Health Law and the Founding O'Neill Chair in Global Health Law at Georgetown Law School. Gostin is also director of the World Health Organization Collaborating Center on Public Health Law and Human Rights, a professor of public health at The Johns Hopkins University, and a professor of medicine at Georgetown University.

- **Scott Hiebert**, the Hortense B. Ingram Chair in Cancer Research, a professor of biochemistry, and an associate professor of medicine at Vanderbilt University School of Medicine. He has served as a professor at Vanderbilt since 1997.

- **Electra Paskett**, the Marion N. Rowley Professor of Cancer Research at The Ohio State University, director of the Division of Cancer Prevention and Control in the College of Medicine, a professor in the Division of Epidemiology in the College of Public Health, and associate director for population sciences and leader of the center's Cancer Control Program.

- **Nancy Raab-Traub**, a professor at the Lineberger Comprehensive Cancer Center at the University of North Carolina. Her laboratory research focuses on the role of the Epstein-Barr virus in the etiology of human disease, including Burkitt's lymphoma, Hodgkin's lymphoma and nasopharyngeal carcinoma.

- **Margaret Spitz**, a professor at the Baylor College of Medicine Dan L. Duncan Comprehensive Cancer Center. Previously, Spitz served on the faculty at MD Anderson Cancer Center for 27 years, was the founding chair of the Epidemiology Department, and held the Olga Keith Wiess Distinguished Chair for Cancer Research. She has served as co-chair of the NCI Lung Cancer Progress Review Group.

"I am confident that these experienced and

hardworking individuals will help us tackle the important challenges facing America, and I am grateful for their service,” Obama said in a statement. “I look forward to working with them.”

They will replace the following members, who are ending their six-year terms on the board: **Kevin Cullen**, director of the Marlene and Stewart Greenebaum Cancer Center and professor of medicine at the University of Maryland; **Marcia Cruz-Correa**, associate professor of medicine and biochemistry at the University of Puerto Rico; **Olufunmilayo Olopade**, professor of medicine and human genetics and director of the Center for Clinical Cancer Genetics at the University of Chicago Pritzker School of Medicine; **Jonathan Samet**, professor and chair of the Department of Preventive Medicine at the University of Southern California; **William Sellers**, vice president and global head of oncology at Novartis Institutes for BioMedical Research; and **Tyler Jacks**, current chair of the NCAB, and director of the Koch Institute for Integrative Cancer Research and professor of biology at the Massachusetts Institute of Technology.

**STAND UP TO CANCER** will host its fifth-biennial televised fundraising special on Sept. 9.

The telecast will broadcast live from The Music Center’s Walt Disney Concert Hall in Los Angeles. ABC, CBS, FOX, and NBC, along with American Forces Network, ASPIRE, AUDIENCE Network, Bloomberg TV, Bravo, Comedy Central, Discovery Life, EPIX, ESPNEWS, FM, FS2, FXM, Great American Country, HBO, HBO Latino, HLN, ION Television, LMN, Logo, MLB Network, National Geographic, Pivot, RLTV, SHOWTIME, Smithsonian Channel, STARZ, STARZ ENCORE, STARZ ENCORE ESPAÑOL, TBS, Tr3s, VH1, and WGN America are donating one hour of simultaneous commercial-free primetime for the telecast. In addition, the show will stream live on Yahoo Canada and will be available on shomi and Telus.

Stand Up To Cancer Canada will simultaneously broadcast the Canadian-inclusive telecast across all four major English-language Canadian broadcasters: CBC, City,CTV, and Global. Additionally, Canadian services AMI, Bloomberg TV Canada, CHCH, CHEK, Fight Network, Hollywood Suite, Joytv, NTV and TLN will also air the telecast.

Academy Award-nominated actor Bradley Cooper will serve as executive producer along with producers Done + Dusted. Additional stars and performers will be announced in the coming weeks.

“No one is ever fully prepared to deal with the overwhelming and complex journey that comes with a cancer diagnosis,” said Bradley Cooper, who lost his father, Charles Cooper, to lung cancer in 2011. “SU2C’s mission, to ensure that all cancer patients become cancer survivors, is one that is very close to my heart. I am proud to join forces to make this vision a reality and to be part of this movement that is dedicated to getting lifesaving treatments to cancer patients faster.” He founded the Charles J Cooper Patient Support Fund.

**KETY DURON** joins **City of Hope** as chief human resources and diversity officer

Kety Duron joined City of Hope as chief human resources and diversity officer. Duron will provide executive and strategic oversight for all of City of Hope’s human resources initiatives.

Duron was vice president of human resources at Stanford Health Care. Before that, she served in a variety of human resources leadership roles at UCLA Health for more than 25 years.

At City of Hope, Duron will be responsible for all areas of human resources, including compensation, benefits, employee/labor relations, organizational design, development and effectiveness, succession planning and leadership development, training and development, talent acquisition and selection, workforce planning, performance management and diversity.

**MIAMI CANCER INSTITUTE at Baptist Health South Florida** received a 220-ton proton therapy cyclotron. The institute offers the only proton therapy center in South Florida, and plans to offer treatment beginning in 2017.

“The arrival of the cyclotron signifies the beginning of the most sophisticated cancer treatment technology in the history of our organization,” said Brian Keeley, president and CEO of Baptist Health South Florida. “This historic milestone is not just one for Baptist Health to celebrate, but one for our entire community as we come together in the fight against cancer.”

The cyclotron began its 4,700-mile transatlantic journey from Louvain-la-Neuve, Belgium, approximately two weeks ago. After arriving at Port Everglades in Fort Lauderdale, Fla., the cyclotron was loaded onto a flatbed truck operated by two drivers who made the overnight drive to Miami. Then, a 140-ton gantry crane lifted the cyclotron into its permanent

home at the Miami Cancer Institute. The \$430 million facility, situated on the campus of Baptist Hospital of Miami, is scheduled to open this year.

**TAKEDA Pharmaceutical Company Ltd.** and **M2Gen** plan to collaborate with **ORIEN** to generate broad genomic data from cancer patients.

Under the agreement, Takeda will help build M2Gen's Oncology Research Information Exchange Network Avatar Research Program based on the Total Cancer Care Protocol, a prospective observational study enrolling patients with various cancers, and access information generated under this program.

The genomic data will accompany clinical information such as stage of disease, demographics and treatment history, further enhancing translational medicine efforts.

Takeda will have access to patient de-identified information generated through the ORIEN Avatar Program, representing ORIEN's growing network of participating cancer centers. These 12 institutions, all leaders in cancer care, treat diverse populations of patients, who can elect to join the Total Cancer Care Protocol to potentially gain access to therapies and clinical trials. Patients who consent to participate in the protocol agree to be followed throughout their lifetime.

Takeda and M2Gen previously partnered in 2014 to identify patients for several phase II studies in gastric and pancreatic cancer.

**MAYO CLINIC** will collaborate with **Kiyatec Inc.** on technology platforms for ovarian cancer care.

Mayo Clinic is enrolling patients in a study that uses patient-derived xenografts to generate living tumor samples specific to each enrolled ovarian cancer patient. The study assesses whether those samples can help determine which chemotherapy is most effective to treat that individual ovarian cancer patient should they become platinum resistant. Kiyatec uses a 3D cell culture platform to generate patient-specific drug response prediction data in seven days, as opposed to months with traditional PDX models.

**ST. JUDE'S Department of Pathology** received accreditation to the ISO15189 standard under an accreditation program through the **College of American Pathologists**. St. Jude is the first children's hospital in the nation to be accredited under this program.

The accreditation is based on the standard for laboratories' technical competence, management, and

improvement. It focuses on improved patient safety and risk reduction, outlining standards for quality, and competence particular to medical laboratories. The CAP is a Centers for Medicare and Medicaid Services-approved accreditation authority.

CAP 15189 is a voluntary, non-regulatory accreditation to the ISO 15189:2012 Standard. The program does not replace the CAP's Clinical Laboratory Improvement Amendments-based Laboratory Accreditation Program.

## *Drugs and Targets* **Canadian Review Agency Delivers Positive Opinion for Opdivo**

**The Canadian Agency for Drugs and Technologies in Health made a positive recommendation for Opdivo (nivolumab)** for the treatment of non-small cell lung cancer. The CADTH evaluation of Opdivo was made under the pan-Canadian Oncology Drug Review process.

In just over eight months, Opdivo has received Health Canada approval as a treatment for three distinct tumor types, including metastatic NSCLC, metastatic melanoma and advanced or metastatic renal cell carcinoma.

The Health Canada submissions received priority reviews, and the Opdivo lung and melanoma phase III studies were stopped early for demonstrating superior overall survival versus standard of care, according to Bristol-Myers Squibb Canada, the drug's sponsor.

**Genomic Health Inc. launched Oncotype SEQ Liquid Select**, the first of several non-invasive liquid biopsy tests that the company plans to deliver through its Oncotype IQ Genomic Intelligence Platform.

Oncotype SEQ is a blood-based test that identifies and assesses actionable genomic alterations in a panel of 17 select genes to inform the treatment of stage IV solid tumors, including lung, breast, colon, melanoma, ovarian and gastrointestinal stromal tumors, according to Genomic Health.

The test is designed to provide information focused on genomic markers that have either been included in National Comprehensive Cancer Network guidelines or associated with sensitivity or resistance to relevant FDA-approved therapies. The test can also match eligible patients with actively enrolling phase II-IV clinical trials specific to their tumor type.