THE CANCER LETTER

Nov. 6, 2015 • www.cancerletter.com • Vol. 41 No. 41

Vince DeVita's going-away portrait as NCI director. It hangs on the 13th floor at NCI. (Credit: Mike Mitchell, cancer.gov.)

DeVita: 50 Years of Stories On Cancer Wars and Skirmishes

Vincent T. DeVita Jr. has seen the cancer field as a confident young doc eager to challenge the system, as a general in the War on Cancer, as an academic oncologist and, most recently, as a patient.

"I've been in a unique position. Partly, the War on Cancer happened because of what we were doing. I watched it grow, and then I ran it at the NCI. And then I came out of the NCI and I watched it from a private cancer

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Book Review

DeVita's History of Oncology Told with Candor and Optimism

By Otis W. Brawley

"The Emperor of All Maladies" was a history of oncology, and a good one. "The Death of Cancer" is a memoir of one of the greats of medical oncology. It is a history from someone who was there, making history.

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Judge Rebukes Brigham for Placing Morcellation Critic Under Guard While His Wife Underwent Surgery

By Matthew Bin Han Ong

A Boston judge ruled Nov. 3 that Brigham & Women's Hospital had violated the First Amendment rights of a couple who led an aggressive national campaign to stop power morcellation, a surgical procedure routinely used by gynecologists.

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DeVita: 50 Years of Stories On Cancer Wars and Skirmishes

(Continued from page 1)

center and a university cancer center," said DeVita, co-author, with his daughter, Elizabeth DeVita-Raeburn, of The Death of Cancer: After Fifty Years on the Front Lines of Medicine, a Pioneering Oncologist Reveals Why the War on Cancer Is Winnable—and How We Can Get There, a just-published memoir.

"There are very few people who have been in that position. But I felt I owed it to the field to give a description of how I saw it, from the beginning to watching it from the outside—watching the field go through some very exciting times."

DeVita, 80, served as director of the NCI from 1980 to 1988. Currently, he is the Amy and Joseph Perella Professor of Medicine and a professor of epidemiology and public health at the Yale School of Medicine.

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

Paul Goldberg: *Here at The Cancer Letter we don't usually cover books, probably because so many of our readers write them, but this book is special. It's a robust history of early triumphs at NCI and the beginning of the War on Cancer. I think everybody should read it. How long have you been working on it?*

Vincent T. DeVita: I've been talking about it for at least 20 years. But the actual writing was relatively short, over about a two-year period. My daughter and I used to sit and talk about the stories, and which ones were good and which ones were not. We've been doing that on and off for a very long time.

But then we signed a contract with Farrar, Straus and Giroux, and we started to write. Then we slowed down for a while, but about two years ago we kicked into high gear and finished it. The actual writing itself did not take long.

The editing is a different story: I had a written something like 320,000 words; that would be an almost 900-page book that no one would read. So my daughter had the job of cutting it down to size, and smoothing it out. She did a really great job.

PG: *Were you writing in real time at all, back in the 70s? Did you keep diaries, archives? Are you a pack rat?*

VTD: Most of it I did from memory, but I can qualify that. Years ago, when I was director of the DCT [NCI Division of Cancer Treatment], my college contacted me and asked me to submit my papers. They said I was a distinguished graduate and asked if they could collect my papers. And I said to them, what's important is the War on Cancer, and could I submit the papers for the War on Cancer? They said that would be fine.

So it turns out there were files—a few on the drug development program, that were to be discarded, but I resurrected them and sent them down to the College of William and Mary.

PG: *So your records and archives are at William and Mary?*

VTD: Right. And I kept doing that. As [NCI] director [from 1980 to 1988], I kept moving correspondence down there. And I have a big collection of stuff here. So over the years, I put a lot into it, so I knew it. And all I had to do when we wrote the book was to pull it out and verify it.

So yes, when I typed, I didn't type from a memo or from something like that, I typed it from memory, but I already had collected all this material over time.

PG: *Some of these stories are so vivid. Like the story of Jay Freireich, mixing martinis, and Tom Frei walking drunkenly on his hands, and I'm quoting here, "his long legs in the air," that's just a hoot. And then there's this other bit: the Society of Jabbering of Idiots, that's really priceless.*

VTD: The Society of Jabbering Idiots—it was a quote by George Canellos [a colleague at NCI]—was a room where everyone tried to talk at once. But it was a very exciting meeting.

I tell people here, I don't think I've ever attended a more exciting meeting than that—or a meeting that turned out to be more productive--because we were able to take things that we decided on in that room and put out a protocol the next day. You can't do that sort of thing anymore.

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Editorial, Subscriptions and Customer Service:
202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
General Information: www.cancerletter.com

Subscription $405 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.

The gang of five at the Medicine Branch in 1973. From left to right: George Canellos, Bruce Chabner, Philip Schein, DeVita, and Robert Young.

And then [NCI childhood leukemia researchers] Frei and Freireich, and I wrote a note to Jay—because he comes out as a hero in the book—telling him that he might be uncomfortable with these stories, but what it shows is that they were so intense, you know, they worked very hard, and they played very hard.

It was a revelation to watch them. They really were very intense individuals. I'm very fond of Jay Freireich. I owe him a lot. He was a good role model for me.

PG: *This is an epistemological question: Did you realize in real time that you were making medical history?*

VTD: There had been a paper that came out—I think it was in The Lancet, or British Medical Journal—by two radiotherapists who used the word "cure" in the title, referring to the cure of Hodgkin's disease.

And there was a big stir, because people were afraid to use the word "cure." And we were looking at the leukemia work that was going on, and so we designed the MOMP program and the MOPP program to be cures. And that was unusual, and at the time we knew that if we succeeded it would be unusual.

It was a bit cheeky, I think, for two young guys [DeVita and John Moxley] to do that. We weren't sure we would succeed, but we certainly wanted to try. And the thing about the NIH in those days was that you could do that sort of thing. You had the resources to do it. You could bring patients in from all over the country, and keep them there, and be self-limited by what was going on between your ears.

So we had a sense of that. I keep in touch with Jack Moxley, and he feels the same way. We were two cocky guys who thought we were pretty smart, so I look back on those days very fondly with Jack.

PG: *It's interesting because it's the only book that—and I think I've pretty much read everything there is on this subject—and the only material that's close in terms of its detail is the interview that Jay Freireich gave John Laszlo in a book about childhood leukemia, and Laszlo basically kept the tape recorder running. And it's just basically a transcript. It's been mined and mined and mined by many people, including me.*

VTD: We interviewed Jay when Elizabeth and I went to ASCO [annual meeting] and we interviewed Jay for something like four hours. So we have very similar transcripts.

But also I remember Jay as a very vivid character, and I remember him very well. I trained 93 medical oncologists when we were at the NCI, and sometimes when I meet with them, they say to me, "Dr. DeVita," because they still try to call me Dr. DeVita, "Do you remember when we were standing by the bed for Mrs. Jones, and you told me the following, and I've never forgotten it." And I look at him and I say, "Sure," but I don't remember a thing about it. Because when you're training people you say things, and it makes an impact

George Canellos, DeVita, and Robert Young, left-to-right, circa 1971. By this time, Canellos and DeVita were working on combination chemotherapy for breast cancer. Young was in charge of chemotherapy for early-stage Hodgkin's disease and the ovarian cancer program. *(Credit: Joel Carl Freid.)*

on them and sometimes the impact just stays with you.

Jay had those kinds of impacts on me.

I think there's one thing in the book that Jay doesn't agree with in terms of our meeting, but I remember it very vividly. I think those are the kind of things that maybe Jay wouldn't give in an interview, because there was no impact on him, the impact was on somebody else.

But he had a laugh about me standing there with me pointing at the label of Polymyxin bottles saying don't give intrathecally, and having Jay point at me and say "Give it." He probably wouldn't remember that, but the fact of the matter is that he did. And I just remember it so well, because it was such a vivid departure from what you normally did. He was at once a very commanding and very terrifying figure.

PG: *Well here's kind of a—speaking of commanding and terrifying figures—Mary Lasker, here's a wealthy socialite who uses the methods of public relations to declare the War on Cancer, and she promises the cure by the bicentennial, she and her friends.*

Do you think she actually knew this couldn't be done?

VTD: I don't know. She was a very smart woman.

I never said to her, "Mary, we'll do our best, but you know it can't be done." That would have been foolhardy, because Mary didn't like people who were negative. So we didn't approach it that way. My feeling is she did know. But she never said she knew. She always felt that the end justified the means.

That's how she operated. We all kind of operated on the assumption and didn't have to explain it, because everyone knew it couldn't possibly be done. We couldn't get money going to the labs until 1974, two years before the bicentennial. I mean it was an impossible feat. But some people in the press and some people in Congress did really believe it. And they never let us forget it.

PG: *This expectation, which some people in the media, as you said, took literally—and how else are you going to take it? This caused serious problems for you at NCI. In retrospect, was it worth it to build up expectations like this?*

VTD: I think the War on Cancer was worth it. Whether it would have happened if she said this would

happen over 10 or 20 years, I don't know. I think the War on Cancer was a grand experiment and it worked.

The NIH was very much against it. But so many things at the NIH now happened because of the War on Cancer. It was a transformational program for the whole institution.

So I think the program was worth it. I think a little bit more honesty would have been better; it would have taken a little bit of heat off us, but I can't answer that question with any surety.

PG: *It's an opinion, of course. I guess what's also amazing is this bit about you being called in to give a science lecture to Sen. [Warren] Magnuson's chauffeur, so that he would bring it up with Mrs. Magnuson, who would then bring it up with the senator. [Magnuson, a Minnesota Democrat, was a powerful appropriator.] So the whole message was surrounding him.*

VTD: That was only one of several. I used to be invited on a regular basis to [Washington hostess] Deeda Blair's house for lunch, and that was Mary Lasker's tactic. Mary used to come to Washington and stay at Deeda's house.

That was a favorite tactic of hers. She never did leave any stone unturned. Because all through the lunch, I didn't know who he was, and so forth. It was a big black car that pulled up in front of the house, so when Mary told me that that was Maggy's driver, I was quite shocked, and she saw it. She looked at me and put her hand up, and said, "Wait a minute, he drives Maggy's wife around all day and she puts her head down on the pillow at night next to Maggy." I would shake my head at this woman. She was so thorough.

PG: *It's amazing that we're still in dialogue with Mary Lasker, and in some ways this book is. You end with an analysis of your thoughts of Mary Lasker. But I guess there is something about her thinking that is still there. What do you think of the more recent plan to end suffering and death due to cancer by 2015, which is almost over? Should future deadlines be less specific, or should this be a game that any of us should play?*

VTD: Well, you know we set goals for the year 2000. We published a monograph about the way this could happen, and then tried to remind people that they were goals, not estimates.

Goals we have to sit down and say—and let's use mammography as an example—when we sat down in 1984, 14 percent of women who were supposed to be screened by mammography were being screened. We thought we had to get up to 70 percent before 1990 to be able to decrease mortality in women with breast cancer by a significant degree by the year 2000. So we would have to set up programs to support the use of mammography screening, and also get on the bully pulpit and do it.

DeVita with former President Richard Nixon. "I asked him what he thought were the greatest achievements of his presidency," DeVita said. "He said going to China and signing the National Cancer Act."

So it wasn't a matter of saying, okay, we're going to drop mortality because we're going to screen more people—these were goals, not estimates. So I think the mistake is when you make a pronouncement or a prediction of what will happen, and don't back it up with information about how you get there.

We said in that monograph that [former director of the NCI Division of Cancer Prevention and Control] Peter Greenwald and I published, if you did everything that you could do in the country simultaneously, which we knew was impossible, you could get a 50 percent reduction in mortality. We thought, realistically, if we got 25 percent we'd be very pleased. And I think the actual figure was something like 16 percent.

You have to keep in mind that, at the time we did that, my advisors at the NCI were telling me that the incidence and the mortality rate was a straight line going straight up to the year 2000. They said there was not going to be any decrease; there was no way we could decrease it. So getting any decrease in mortality by the year 2000 was an achievement.

But it was a goal, it wasn't an estimate.

PG: *The year 2015 was also a goal and an estimate.*

VTD: Yeah, but there was nothing to it.

DeVita with Mary Lasker.

There was no "To end death and suffering, we have to do the following five things…"

And we have to identify what you mean by death and suffering. Death is clear: mortality statistics—but suffering?

It was so vague that—and you're referring to [former NCI Director Andrew] von Eschenbach's goal—it was so unclear what he actually meant, that it was clear to everybody that nothing of value that would ever come of it.

And, to be honest, I like Andy, but it sort of discredited us setting goals.

I think the American Cancer Society goals were very realistic. They looked at what the trends were and what programs they had in place and what they could manipulate—and most of the disease-specific goals were reached, or are very close to being reached.

I think they're helpful if you do that. And one of the reasons I did it, because the government is in the habit of spending money without any benchmark as to how well you're doing. So I think you need to set benchmarks.

So I like goals, but you have to be very careful. We took a lot of criticism when we set up goals for the year 2000 in 1984.

PG: *I hope you don't mind a small tangent here. This is a tangent because of Mary Lasker—what are your thoughts on the current state of the American Cancer Society, and how does it become as relevant as it was in her days?*

VTD: I think the new CEO is a terrific guy. I like Gary [Reedy] a lot. I think he will do a terrific job. But they had started to lose their way, I think, over a number of years. I think they need to be very careful about retaining their supporters. Most of their support comes from people who give small donations.

I was there when we did the transformation of the ACS and we centralized much of it. And the main concern was that they would lose contact with supporters. I haven't kept in touch with how well they're doing in terms of income over the last couple of years, so I don't know whether it's continued to go down—it went from a billion dollars down to about $800 million, which is a big drop.

And my beef with them always—and they had, supposedly, before I left, set up programs to correct this—my beef with them is that I didn't think they put enough money into support of basic research and the grant program.

PG: *I remember when Mary bought it from the surgeons, she sent them huge amounts of money—what was it, 75 percent? It's in your book.*

VTD: No, no, no, she actually said something like 25 percent. And for a long time, the American Cancer Society contributed 20 to 22 percent of their money to extramural grants; grants that go to scientists on the outside. Now they're down to 10 percent, and I think that's a mistake.

And we set in motion a plan to double that over 10 years as I left the board. I hope they're staying with it.

When you listen to the advertising of the American Cancer Society, they talk about how many Nobel laureates they support and so forth. And then you look at how 10 percent of their money goes to support extramural grants—there's a very severe mismatch there.

If I know Gary, he will change that, but it's going to take some time.

PG: *Let's go back to your book, but thanks for the tangent.*

In a version that didn't make it into law, the National Cancer Act would have taken approval authority for cancer drugs out of the FDA and put it in the institute. Do you think this schema would have worked better than what we got?

VTD: Yes… Do you want an explanation?

PG: *Please.*

VTD: I have made the case many times to the FDA, pleaded with them, that cancer patients were different.

They're different from patients with hypertension; they're different than patients who have high cholesterol, anemia, or diabetes. They're different than patients with arthritis.

These people have chronic diseases that are not curable—when you have arthritis you have it for your entire life, but you can manage it. And the people live and in many cases do live a normal life.

Cancer is the most curable chronic disease and it's the most fatal chronic disease. You need to deal with patients who are facing death in six months to a year differently than you deal with developing drugs for patients who have arthritis.

The FDA has always said, "No, if we do it for you, we have to do it for everybody else"—and that's nonsense, that assumes that you have no judgment at all, and that you just follow the line. So we never did it.

I think if we moved the drug development approvals to the NCI, where we have expertise, it would have been a major change into how we develop drugs. And as I point out in the book, I think one of the main problems getting in the way of progress right now is the fact that everything is centralized at the FDA and the NCI.

Cancer centers were developed to be small replicas of the NCI, to be independent scientific bases that could apply what they learned in practice. And they need to have the flexibility to move very quickly, especially in the early-phase clinical trials.

So I think now, today, the NCI and the FDA should delegate all authority for phase I and II trials to the cancer centers, and let them make all their adjustments based on their own expertise. The NCI and the FDA retain the right to come in and audit at any time, but all the cancer centers have really spent years getting their trial programs up to snuff—and when they're reviewed, it's a big part of the review to see if they have their clinical trials program in shape.

So they're there now, and they could do that. I think it was a problem then, and I think it's a problem now.

PG: *In the book you refer to the Frances Kelsey syndrome, describing the FDA stance as exceedingly risk-averse.*

I cover FDA closely, and I see the agency approving drugs at a pretty rapid rate these days. I can barely keep track. I think their philosophy is influenced by evolving science in cancer, and it seems to be really moving towards activism. Do you see it otherwise?

VTD: Yes I do. Do you want an explanation for that, too?

PG: *Please.*

VTD: I am giving a talk to the fellows here, and I do it every year, and I'll be going over the book.

One of the things I'm going to say to them is that, you think you're the doctors of the patients, but you're not. The FDA is the doctor. You don't do anything that the FDA doesn't approve.

And the thing that struck me recently was the approval of the use of two checkpoint inhibitors, the anti-PD-1 and the anti-CTLA4 together. The FDA approved the combination, and nobody noticed.

Now you have the FDA approving the use of approved drugs in combination—where these drugs are both approved for the disease, and now you have to go to them to get approval for a protocol and approval for the use of that.

If that had been in place when we were developing MOPP, if we were persistent it would have taken us a minimum of 10 to 15 years to develop the MOPP program. You don't realize it, but it's a very subtle thing, but the FDA has sort of paralyzed clinical investigation because no one can do anything without going through these myriad approval processes. I think it's ludicrous.

There's another one I can't recall, but I just saw it, another approval of another drug combination. I can see the FDA approving drugs that are packaged in one pill or two drugs given together as a formula, but to take drugs that are approved individually for the diseases, and to require investigators to get approval for the testing and the approval to use them in practice, I think is a very serious backward step.

Basically you're having them approve the combination of radiation therapy or chemotherapy or a targeted therapy. In fact, I've heard rumbles about having to do it. These guys are so far away from the patient that they have no business doing that.

PG: *But off-label use is fine though.*

VTD: Off-label use—okay, then tell me why the combination of ipilimumab and nivolumab was approved by the Food and Drug Administration?

PG: *I'm just going to take a stab at it, and I'm probably going to guess it wrong, but I think the rationale would be so it would get on the label, because the sponsors wanted it on the label so they could get paid.*

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VTD: Well I think you did quite well. It's a vicious cycle.

If the drugs are approved, and the FDA doesn't approve combinations, they'll get paid; if it works the insurance companies will pay for them.

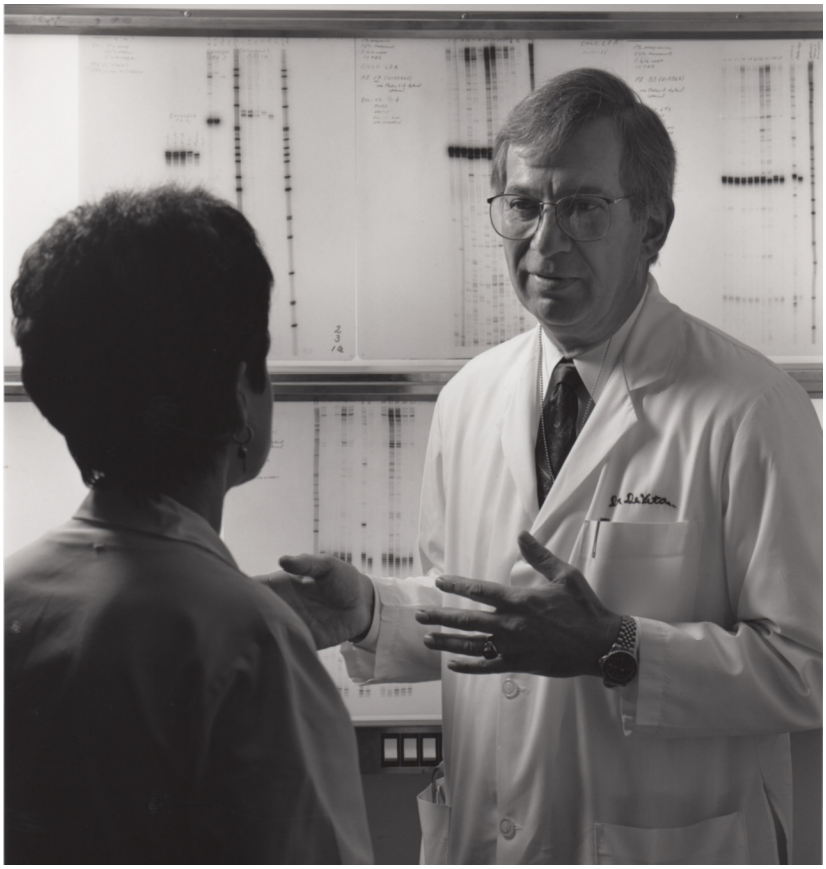
But do you realize how much longer it takes to get these things—it also inhibits the process. I can't do something if I have to send it to the FDA, I have to send it to the IRB, to my cancer center approval committee, and then I have to send it to the NCI.

So you go through these various approval processes and you're thinking about the protocols—and I have to send it to the IRB, but they don't like these kind of protocols, so I'm not going to put this together. It slows down the process tremendously.

The sad thing about it is that we've just come to accept it. It's not necessary for patient safety. It's just totally unnecessary.

PG: *So you're exactly where Jay Freireich is on this issue?*

VTD: I haven't discussed it with Jay Freireich, to be honest with you. But I'm not surprised if we are. I'm sort of a clone of Jay Freireich.



DeVita talking over lab results with a researcher at Yale. On the viewbox are her electrophoretic gels, which separate molecules by size and electric charge.

PG: *You've criticized FDA for excessive reliance on the overall survival metric, which requires randomized trials, but this reliance has made it possible to approve drugs based on metrics of slowing disease progression.*

Is it wrong to rely on randomization in the regulatory setting? And I guess before I shut up, you seem to admire Bernie Fisher for his reliance on randomization in clinical research, but you seem to be less admiring of Chuck Moertel pushing FDA towards reliance on survival, so is there a difference?

I think both of these guys are giants in exactly the same way, and I could be wrong. Am I?

VTD: They're both great friends of mine. The late Chuck Moertel—I used to tell people that when things got hot, and I looked around to see who was still standing to give me a hand, and Chuck Moertel [director of the Mayo Clinic Cancer Center and member of the FDA Oncologic Drugs Advisory Committee] was always there.

And he's a great friend of mine, but he was totally wrong about what he did. And it wasn't randomized trials, and it wasn't even just the survival, he approached it from a very negative point of view. I guess it was Henry Kaplan [radiologist who pioneered radiation therapy] who used to say to me, "If it's not worth doing, it's not worth doing well."

Chuck Moertel would design randomized trials that were ridiculous in terms of how he used 5-fluorouracil. He would use 5-fluorouracil five days every six weeks, because that's the way the referral system at the Mayo Clinic worked. And it was magic.

I actually wrote a piece, he and I wrote—he was a thespian, he was a great actor, and he would deliver these speeches and wow the audience, and I used to write these counter-speeches—and I wrote one about the ability to believe in magic. So what good was the randomized controlled trial when the premise behind the trial was completely insane? And nor would any human investigations committee know that.

Because most of them just don't have the kind of staffing that would say, "Wait a minute, it's a

randomized trial, but the trial itself is crazy. That's where guys like Chuck Moertel were saying let me look at survival as an endpoint. I admire Bernie Fisher [pioneering breast cancer researcher and founder of the National Surgical Adjuvant Breast and Bowel Program] a great deal—and look, I believe randomized controlled trials are a gold standard, and absolutely necessary under certain circumstances, but not under every circumstance.

PG: *But this case, right now, the reason you see this huge number of approvals is because of the randomized trials, which are allowing you to see whether drugs are actually slowing down disease progression.*

VTD: No I don't think so. I think it's because they're targeted therapies. And they're easier for the FDA to swallow, because they have a specific target to shoot at. As a matter of fact, if they weren't targeted therapies, most of these drugs wouldn't get approved by the FDA, because by themselves they're often very poor. They need to be used in combination with some other drug. So I think that it's more of an illusion.

Mind you, what I said before: phase I and phase II trials should be delegated to the cancer centers. Most of them are not randomized; some of them are. The phase III trials, which are randomized, are different. They're bigger studies and they're the studies that go for NDA approval, and I think these should still be under the purview of the FDA and the NCI. Yes, I'm very happy that the FDA is approving drugs more rapidly, but we're in a situation now where we have proof of principle.

In general, the combinations of drugs are equal or are better than using them alone. We really want to encourage that kind of research, and that's not being encouraged by the Food and Drug Administration. They want you to get individual drug data for approval. That was the point that I made, among a number of other things, in that FDA chapter.

PG: *There are these wonderful anecdotes in the book. Which one would you say, if you were to look at all of it, what would be the most spectacular mistake you've made as a physician or as a policymaker?*

VTD: I used to keep track, honestly, of major decisions, and I calculated that about 80 percent of the time, I made a really good decision. And 20 percent of the time I didn't. I've made so many decisions I can't even tell you which one was which at the moment. I don't really recall any of the spectacular mistakes, do you?

PG: *No. I didn't see any in the book. So 80-20 is pretty good!*

VTD: I thought it was pretty good. I would say 20 percent of the time I wish I could do it over again. They weren't always disastrous, but they weren't always the most productive things. I used to keep track of the total and I don't have a list of them anymore, but that's pretty good. Fifty-fifty you can just do with a coin.

PG: *Fifty-fifty is pretty good. I'm striving for that.*

You've seen the development of this field, both as a heroic doc and as a policymaker. Now that you are seeing it as a prostate cancer survivor, how is it different?

VTD: I recapped a lot of the problems I've had, if I hadn't been who I am, I'd be dead by now. It shows me we have a long way to go to navigate patients through a field like cancer treatment, which is evolving so rapidly. The thing about the field now is that there are so many things happening.

When they happen they don't happen universally at the same time across the country. When you get a new anti-PD1 inhibitor, it's imported from a center or maybe a group of five centers; it's not universally available across the country.

I just found out first hand, in my own case—my sister developed non-small cell lung cancer. She was a candidate for the PD1 inhibitors, and no matter what I did, I could not get her doctors to get access to it, even though she was an eligible patient study-wise: she had failed her first round of combination doublets for non-small cell lung cancer.

She died in May without access to drugs that were approved a few months later. And part of the problem was the doctors did not want to buck the system and get in trouble with their human investigations committee or get in trouble with the FDA to be able to do it. It was a big disappointment on my part.

PG: *This book is really entirely about you fighting the establishment and the conservatives in the medical field.*

VTD: Well, it's a description of those things. I have played some role. I didn't fight everything.

I've been in a unique position. Partly the War on Cancer happened because of what we were doing. I watched it grow, and then I ran it at the NCI. And then I came out of the NCI and I watched it from a private cancer center and a university cancer center.

There are very few people who have been in that position. But I felt I owed it to the field to give a description of how I saw it, from the beginning to watching it from the outside—watching the field go through some very exciting times.

PG: *And that was why I couldn't put the book down. Thank you.*

Book Review

DeVita's History of Oncology Told with Candor and Optimism

(Continued from page 1)

In scientific terms, Siddhartha Mukherjee's book has the limitations of a retrospective study; Vince DeVita's book is more like a prospective clinical trial.

I trained at the NCI in the 1980's. I openly admit that Otis Brawley the medical oncology fellow was intimidated by the mere mention of "Dr. DeVita."

I have since realized that he is a nice, supportive, even approachable man with an intensity of purpose. The intensity was and is fueled by the serious fact that people die from cancer, and it is our calling as research physicians to stop the dying.

Indeed, our common values of respect for truth, orthodoxy to scientific principles and support of research, all derive from having watched people die from this disease.

The first half of the book tells a number of touching and surprising personal stories of a young DeVita. Many involve the founding fathers of medical oncology, including Gordon Zubrod, Tom Frei, Jay Freireich, George Canellos, and Paul Carbone.

THE DEATH OF CANCER
After Fifty Years on the Front Lines of Medicine, a Pioneering Oncologist Reveals Why the War on Cancer Is Winnable–and How We Can Get There.
By Vincent T. DeVita, Jr. and Elizabeth DeVita-Raeburn; Illustrated. 336 pp. Sarah Crichton Books, Farrar, Strauss & Giroux. $28.00

These are men oncologists of my generation have been taught to look up to. Eventually, I would come to meet all of them and become friends with some. Even now, having met them makes me feel like the Forrest Gump of medical oncology.

I was very ready and prepared to hear about the eccentricity of Tom Frei and the outrageous behavior of Freireich. They pushed the envelope, and exhibited a total devotion and disciplined approach to the care of patients and development of treatments.

I could easily see Jay Freireich enjoying himself at a party one evening and being on the wards the next morning knowing about abnormal lab results before the fellow who ordered it. I am, however, startled at the thought of Tom Frei walking on his hands to entertain guests at an NCI party.

The above were stories of DeVita as a fellow. It is equally fascinating to hear of DeVita's trials and tribulations on senior staff at NCI and later as NCI director. This includes: his survival of the Reagan Administration inquisition of Democrats in government and his clashes with Sen. Ted Kennedy.

As director in the 1980s, he tried to reduce waste in the NCI funding programs. He battled the bad doctor habit of rejecting paradigm shifting research findings, such as those of Bernard Fisher's breast cancer studies—and he recounts the struggles to get Fisher's results published.

This book contains important lessons about moderating and creating reasonable expectations as we try to increase support for cancer research. Many members of Congress unrealistically expected the National Cancer Act of 1971 to result in a cure for cancer by the 1976 bicentennial.

DeVita became director a decade after passage of the act, and he had to deal with the fact that many were miffed that cancer had not been cured for much of his directorship.

DeVita has much to say about the NCI-designated cancer centers, cancer research and treatment today. He offers ideas on how to jump-start the National Cancer Program. He calls for a new National Cancer Act—and the naming of a federal cancer czar.

And he is critical of the FDA's regulation of cancer drugs throughout the last five decades. At one point, he says, "the air pumped into the FDA building must have some kind of regulatory gas in it."

This is where I have some disagreement with a man I have tremendous respect for. There is a greater need for a strong FDA with rigorous evaluation of drugs. I believe FDA, over at least the past twenty years, has been far better than it was in the 1970s, when a heavy-handed agency delayed approval of cisplatin for testes cancer treatment for more than three years.

I concur that there has been overreliance on phase III clinical trials. These studies provide for drugs that give us clinically mediocre two-month or three-month increases in median survival.

Drugs that really move the needle show usefulness without such large trials. This is going to be even more important as oncology moves toward precision medicine.

Think of imatinib for CML or crizotinib for ALK-positive lung cancer. The future is precision medicine, studies like the Lung-MAP and bucket trials. The move toward precision medicine is a dividend of the National

Cancer Act of 1971.

One final note about an extraordinary book and an extraordinary story:

I appreciate the admission that big jobs such as NCI director can cause mild depression. From time to time, DeVita's therapy was to "put time aside to make regular rounds on the cancer floors." This reminded him why he was doing what he was doing.

This again points to seriousness of our jobs as oncologists.

A large proportion of the people we care for die of this disease. This was a theme throughout the book, reinforcing the need for intensity, the commitment to basic principles, and to orthodox science.

DeVita-the-writer is as optimistic as DeVita-the-doctor. He reminds us that we cannot do what we do if we are not optimistic about the death of cancer.

Brawley is the chief medical officer of the American Cancer Society.

Judge Rebukes Brigham For Placing Morcellation Critic Under Guard While Wife Underwent Cancer Surgery

(Continued from page 1)

Earlier this week, Brigham provided care to Amy Reed, who needed urgent surgery for a cancer recurrence. However, her husband, Hooman Noorchashm, had to submit to being searched and accompanied by a security guard.

Both Reed and Noorchashm are physicians. She is an anesthesiologist who was formerly employed at Beth Israel Deaconess Medical Center, and he is a cardiothoracic surgeon who had practiced at Brigham.

The decision to subject the couple to enhanced security procedures was made by Ron Walls, executive vice president and chief operating officer at Brigham.

On Nov. 2, after Reed and Noorchashm were searched at the entrance to Brigham, and Noorchashm was put under surveillance, their attorney went to court seeking a restraining order against Brigham for engaging in a "retaliatory action" that was brought on by the couple's public criticism of Brigham leadership in the controversy over power morcellation.

The motion, filed in the Superior Court Department of Suffolk County that day, states that Reed and Noorchashm were subjected to a "humiliating and distressing physical search" at the Harvard-affiliated hospital.

On Nov. 3, at 4 p.m., Superior Court Judge Elizabeth Fahey ordered Brigham to lift all security requirements.

"Allowed as a Temporary Restraining Order, finding that both plaintiffs will suffer irreparable harm," Judge Fahey wrote.

After the ruling, Brigham attorneys notified the couple's attorney Tom Greene that they will not contest the injunction.

"Brigham had filed affidavits of some security personnel to try to make the point that Hooman posed a security threat," Greene said to The Cancer Letter. "The judge basically didn't buy it. Brigham wanted the security restrictions to remain in place, I argued they shouldn't, and she agreed, and she lifted them.

"There was no justification to have these restrictions in place. Hooman and his wife had visited Dana-Farber and Brigham probably more than a dozen times in the past two years, and they were never required to check in or be shadowed by security personnel, so why now?"

Over the past two years, the couple's advocacy led to FDA restrictions on the use of power morcellators and largely ended insurance coverage of the procedure. The Government Accountability Office and the Federal Bureau of Investigation are looking into claims of corporate negligence in reporting adverse events.

"My wife and I, today, were subjected to a useless search immediately prior to her going into the operating room," Noorchashm wrote in a Nov. 2 email to Walls, executive vice president and chief operating officer at Brigham. "And I will tell you that it was all posturing your leadership had designed to intimidate, because anyone with half a wit would immediately see who my wife and I are.

"That you subjected my wife and I to a security check on a day like this is unbecoming of your MD and of your Harvard professorship."

The documents, including the complaint, Brigham's opposition, Fahey's ruling, and Walls's letter to Noorchashm are posted here.

A mother of six, Reed, 42, is battling a third recurrence of leiomyosarcoma, an aggressive uterine cancer, which has spread to the upper section of her right lung. Reed, an assistant professor of anesthesia and critical care medicine at the Hospital of the University of Pennsylvania, had undergone surgery and radiation for the past two recurrences, both on her spine.

The metastases can be traced to an Oct. 17, 2013 hysterectomy—performed with a power morcellator

at Brigham—that disseminated Reed's undiagnosed sarcoma (The Cancer Letter, July 4, 2014).

"Dr. Reed's doctors, both at the University of Pennsylvania and the Brigham & Women's Hospital believed that it was imperative that the uLMS [lung] tumor be removed from Dr. Reed as soon as possible," the complaint states. "The thoracic surgeons at HUP expressed reservations about performing the operation due to its proximity to major vessels.

"BWH's thoracic surgery division is world-renowned and is capable of resecting Dr. Reed's tumor in a routine fashion. Dr. Reed is expected to stay at BWH for a total of four to five days following the surgery."

Reed's lung metastasis was removed Nov. 2 at Brigham under the care of Scott James Swanson and Suzanne George. Swanson is co-director of Minimally Invasive Thoracic Surgery at Brigham and chief surgical officer at Dana-Farber Cancer Institute. George is an assistant professor of medicine at Harvard Medical School and clinical director of the Center for Sarcoma and Bone Oncology at Dana-Farber.

According to Noorchashm, Swanson and George had no prior knowledge of Walls's decision.

"In the many times I have cared for Amy, with you at her side, I have never felt threatened or unsafe or have required any unusual security procedures," George wrote to Noorchashm when informed of the security measures. "I cannot speak for BWH policies, but only from my personal experience and interactions with Amy as a patient and you as her family."

Brigham initially intended to appeal Judge Fahey's decision, a Brigham spokesperson said to The Cancer Letter.

"Dr. Noorchashm and his wife left the hospital before we had the opportunity to do so,"the spokesperson said. "We believed that the appellate court would have allowed the hospital to continue with the security measures we had put in place."

The security measures were intended to "adequately address the fears and anxieties of hospital faculty who felt targeted by Dr. Noorchashm, [and balance that] with the desire to treat Dr. Noorchashm with professionalism and discretion," the spokesperson said. "When members of the hospital's security team perceive a threat, it is not unprecedented for the hospital to implement security measures in order to ensure the safety of faculty, staff, patients and visitors."

It is unclear whether Reed and Noorchashm will be subjected to similar security measures in the future.

"The hospital does not have a statement to share regarding this," the spokesperson said.

Searched at the Door, Followed by Guard

Four days before Reed's surgery, on Oct. 29, Brigham COO Walls sent a letter to Noorchashm, describing security measures that would apply to him:

"In light of concerns created by your on-going communications with BWH staff, your presence will be subject to the following standards and expectations:

• "Upon arrival at the hospital, you will present to the information desk at 75 Francis St. and identify yourself.

• "A plain-clothed Security officer will escort you to a discreet location where you will be subject to a security screening.

• "A plain-clothed Security officer will escort you at all times while you are on BWH property, with the exception of when you are in your wife's inpatient room, or in conference with members of the care team, at which time the officer will remain outside the door."

Brigham's policy on patient rights states that patients have a right to a "prompt response to all reasonable requests and a right to personal dignity and to a reasonable extent, privacy," the complaint states.

Brigham has violated both of these patient rights with regard to its treatment of Reed, the complaint states.

"BWH has refused reasonable requests from Dr. Reed and her husband Dr. Noorchashm to lift the arbitrary security requirements the institution has imposed, despite the fact that no such restrictions were required on any of Drs. Reed or Noorchashm's previous visit to the hospital," the couple's complaint stated.

Earlier this year, in an unrelated incident, Michael Davidson, a Brigham cardiovascular physician, was shot and killed by Stephen Pasceri, who apparently believed that a post-operative drug Davidson had prescribed caused his mother's death.

Brigham's attorneys did not refer to the incident during the Nov. 3 hearing, a Brigham spokesperson said.

"Counsel for the hospital explained to the court that the BWH community had been recently traumatized by violence in the workplace, and as a result the hospital is very sensitive to providing a safe facility for patients, visitors and staff," the spokesperson said to The Cancer Letter.

Noorchashm, a cardiac surgeon at Thomas Jefferson University Hospital, requested that Brigham revoke the security requirements, because he has no intention of harming anyone. Noorchashm said that nothing he has ever said or written in any way constitutes a violent threat.

"I assure you that I pose no physical danger to anyone at BWH—most on the cardiothoracic service

are my friends and esteemed colleagues," Noorchashm wrote to Walls Oct. 31. "We are there at a very difficult time, by choice, for help from the physicians and surgeons we trust.

"I assure you that the strain and duress this BWH corporate imposition is causing on your patient, Dr. Amy J. Reed, and our entire family is unwarranted and unnecessary. And if you choose to persist, it will likely cause extreme psychological duress for my wife and other members of the extended family."

Walls replied to Noorchashm, saying that his decision is consistent with his mandate to protect Brigham.

"You must understand that nothing relieves me of the responsibility I have to ensure the safety and security of the patients, family members, visitors and staff who enter our doors every day," Walls wrote. "This requires me to use my best judgment and, after a careful review of your prior communications with hospital staff, I stand by the decision with respect to your upcoming visit."

On Nov. 2, Brigham security staff searched Reed's belongings immediately prior to her surgery. Noorchashm was subjected to a physical search, and a member of Brigham's security team accompanied him at all times—except when he and Reed were in private care meetings with physicians.

Since Reed's initial morcellation surgery in late 2013, Noorchashm has widely and publicly criticized Brigham's leadership for ignoring and "stonewalling" the couple's attempts to address the harm that power morcellators pose to public health. Noorchashm has sent multiple acrimonious emails berating top physicians at the institution for their "corruption," "atrocious complacency" and "failure" to prevent harm to his wife (The Cancer Letter, July 4, 2014).

"Dr. Walls' letter explicitly contains a threat against Dr. Noorchashm in retaliation for his exercise of his constitutional [First Amendment] rights," the complaint stated.

Brigham argued in court filings that Noorchashm's emails represent "a credible threat to the safety of BWH employees," citing multiple complaints from hospital staff members who are concerned about their security. The filings include several colorful emails from Noorchashm to Brigham leadership:

"I have all the time in the world to mince words with you," Noorchashm had written in a March 15 email to hospital president Elizabeth Nabel and Robert Barbieri, the head of obstetrics and gynecology at Brigham. "But I assure you that the longer you wait to take full responsibility, to apologize, to make good on your failure, the harder you will fall in full public view. I will make sure of this."

The hospital filed affidavits from Greg Foley, a retired state trooper, Robert Chicarello, director of security at Brigham, and John Pierro, senior vice president of facilities and operations at Brigham:

• "I believe that Dr. Noorchashm's presence at the Brigham and Women's Hospital presents a definite safety risk to Brigham and Women's Hospital physicians and staff as well as to members of the general public," Foley wrote.

• "In my professional opinion, and in consultation with members of law enforcement and others, the email messages are of a kind and nature that I perceive as exceptionally hostile and which demonstrate a will and desire to disrupt the safety, security and peaceful access of hospital staff, patients and visitors," Chicarello wrote.

• "The risks of harm to BWH employees, patients and staff has been assessed and would be considered heightened, should these security safeguards not be allowed to remain in place," Pierro wrote.

Brigham officials declined to provide examples of Noorchashm's communications that in their judgment could be construed as physical threats. "The hospital does not intend to respond," a spokesperson said Nov. 2 to The Cancer Letter.

Brigham officials are bullying Noorchashm and Reed, said Richard Kaitz, a Boston real estate lawyer whose wife, Erica, died in December 2013 from leiomyosarcoma upstaged by power morcellation at Brigham (The Cancer Letter, Nov. 21, 2014).

"I am completely outraged. This is nothing other than pure, unadulterated harassment," Kaitz said to The Cancer Letter. "Hooman worked at Brigham for almost a year after Amy's morcellation. They know Hooman; they know he's not a threat. He's the furthest thing from a physical threat to walk this earth!

"I'm absolutely and completely appalled. To do this to a guy when his family is down and undergoing serious medical issues requiring lifesaving treatment at Brigham—it is the height of arrogance, aggression, and bullying."

Kaitz filed a lawsuit against Brigham earlier this year, alleging that Brigham physicians knew of the risks of the device and are responsible "for the wrongful death of Erica Kaitz, and the conscious pain and suffering she experienced prior to her death, due to Dr. [Jon] Einarsson and BWH's medical malpractice and their failure to obtain informed consent."

NCI Funds Eight SPORE Grants

NCI awarded eight new, competing and renewed grants as part of its funding for its Specialized Programs of Research Excellence. The grantees will receive $2,185,000 per year for five years.

Of the 36 applications submitted for the 2015 fiscal year—with the eight grants coming to a 22.2 percent success rate—four funded studies were brand new to the SPORE program and four were renewal applications. Each of the renewed grants included a new principal investigator or new multiple PIs.

"The SPORE program is 23 years old and has been evolving since day one, based upon recommendations for NCI advisory groups and the evolution of science, itself," said Toby Hecht, associate director of the Translational Research Program in the NCI Division of Cancer Treatment and Diagnosis.

"We expect this evolution to continue to keep the program up-to-date and relevant," said Hecht. "One interesting change that will be taking place this year is giving a funding incentive to awarded applications that include translational cancer research in qualified early detection, prevention, and population science projects—areas that are underrepresented in the NCI portfolio."

The four new SPOREs and their lead investigators are:

• **Wade Clapp,** of Indiana University, and **Kevin Shannon**, of University of California, San Francisco, for developmental and hyperactive RAS tumors. This is the SPORE program's first pathway-based grant.

Clapp is the Richard L. Schreiner Professor, chairman of the Department of Pediatrics and a professor of microbiology at Indiana University. Shannon is the Auerback Distinguished Professor of Molecular Oncology in the UCSF Department of Pediatrics and an American Cancer Society Research Professor. He is also director of the UCSF Physician Scientist Scholar Program.

• **Leif Bergsagel** and **Vincent Rajkumar**, of the Mayo Clinic, in multiple myeloma. Bergsagel is co-director of the Hematologic Malignancies Program at the Mayo Clinic Comprehensive Cancer Center and a professor of medicine at the Mayo Clinic College of Medicine. Rajkumar is chair of the Myeloma Amyloidosis Dysproteinemia Group at the Mayo Clinic, chair of the Eastern Cooperative Oncology Group Myeloma Committee and co-chair of the International Myeloma Working Group.

• **Roy Herbst**, of Yale University, in lung cancer. Herbst is chief of Medical Oncology at Yale Cancer Center and Smilow Cancer Hospital, and associate director for translational research at Yale Cancer Center.

• **Sue O'Dorisio**, for the first and only SPORE grant in neuroendocrine tumors. O'Dorisio is a distinguished professor in pediatrics at the University of Iowa.

The developmental and hyperactive RAS tumor SPORE involves researchers at NCI's Pediatric Branch and eight academic institutions. Its overall goal is to implement targeted treatments for tumors characterized by mutations of the NF1 tumor suppressor gene.

In contrast to most other SPORE efforts supported by the NCI, this project does not focus on a particular type of cancer. Persons with NF1 have a markedly increased incidence of developing specific tumors, which are frequently diagnosed in children, adolescents and young adults.

The program encompasses four integrated projects and three cores: administrative core, a biospecimen and pathology core, and an omics core. The main projects are:

Project 1: Molecular, Developmental, and Genetic Evaluation of Plexiform Neurofibromas to Inform Clinical Trials

Project 2: Targeted Therapies for Malignant Peripheral Nerve Sheath Tumors

Project 3: A High Content Clinical Trial of the MEK Inhibitor Trametinib in Juvenile Myelomonocytic Leukemia

Project 4: Subsequent Malignant Neoplasms Among NF1 Cancer Survivors

The program plans to re-purpose drugs that are being developed to block the biochemical effects of RAS gene mutations, which are found in about one-third of all cancers.

Because the protein made by the NF1 gene interacts directly with Ras and controls its activity, drugs that are being tested in cancers with RAS gene mutations should also be systematically evaluated in malignancies driven by NF1 inactivation, according to this project's abstract.

The Mayo Clinic multiple myeloma SPORE includes four major translational research projects, a developmental research program, a career enhancement program, a biostatistics/bioinformatics core, a biospecimen core, and an administrative core. Project investigators are located at all three Mayo Clinic sites, in Arizona, Minnesota and Florida.

The main projects are:

Project 1: Oncolytic Virotherapy using Vesicular Stomatitis Virus

Project 2: Immunomodulatory Therapy with SMAC Mimetics

Project 3: MYC in Progression and Treatment

Project 4: Clonal Evolution

Journalist and Mayo Clinic Trustee Tom Brokaw will serve as a patient advocate to the SPORE. Brokaw was diagnosed with multiple myeloma at the Mayo Clinic in 2013.

The Yale SPORE in lung cancer seeks to improve overall survival by developing therapeutics and personalized prevention strategies based on targetable pathways involved in the progression of lung cancer and the acquisition of resistance to therapy.

The project has five specific aims:

1: Develop and test novel therapeutics by discovering the mechanisms underlying the response and resistance to anti-PD-1 and anti-B7-H1 (PD-L1) therapies;

2: Evaluate the potential of non-coding microRNAs as targeted therapies;

3: Understand and target the EGFR pathway in mutant/resistant lung cancer;

4: To develop and test the efficacy of a new personalized approach to gain-framed messaging to improve smoking cessation in Americans with asymptomatic lung nodules who continue to smoke; and

5: To develop new research directions and nurture the next generation of translational investigators in lung cancer through a developmental research program and a career development program.

The University of Iowa SPORE in neuroendocrine tumors includes four major projects and four cores that will explore the genetics of the tumors, their molecular makeup, and new approaches to diagnosis and treatment. This is the first and only SPORE grant to fund research on neuroendocrine tumors.

The main projects are:

1: Theranostics in Neuroendocrine Tumors

2: Molecular Mechanisms and Biomarkers of Neuroendocrine Tumors

3: Genetic Studies of IIeal Neuroendocrine Tumors

4: New Approaches to Improving the Effectiveness of Radionuclide Targeted Treatments in Neuroendocrine Tumors

More detail on the individual projects is available here.

The 2015 competing renewal SPOREs and their lead investigators are:

• **William Catalona**, in prostate cancer. Catalona is a professor in the Department of Urology at Northwestern University Feinberg School of Medicine, and is director of the Clinical Prostate Cancer Program at the Robert H. Lurie Comprehensive Cancer Center.

• **Robert Ferris** and **Jennifer Grandis** in head and neck cancer. This grant is co-funded by the National Institute of Dental and Craniofacial Research.

Ferris is vice-chair for clinical operations and chief of the Division of Head and Neck Surgery, as well as co-leader of the Cancer Immunology Program at the University of Pittsburgh Cancer Institute. Grandis is associate vice chancellor for clinical and translational research, director of the Clinical and Translational Science Institute, and a professor in the Department of Otolaryngology at the University of California, San Francisco.

• **David McDermott** and **William Kaelin**, of Dana Farber Cancer Institute, in kidney cancer.

McDermott is the leader of the Dana Farber/Harvard Cancer Center Kidney Cancer Program and is director of the Biologic Therapy and Cutaneous Oncology Programs at Beth Israel Deaconess Medical Center, as well as an associate professor of medicine at Harvard Medical School.

Kaelin currently serves as associate director of basic science at Dana-Farber/Harvard Cancer Center, and is a professor in the Department of Medicine at Dana-Farber and at the Brigham and Women's Hospital.

• **Scott Kaufmann**, of the Mayo Clinic, in ovarian cancer.

Kaufmann is chair of the Division of Oncology Research and associate director of the Medical Scientist Training Program at the Mayo Clinic College of Medicine, and co-chair of the Developmental Therapeutics Program at Mayo Clinic Cancer Center.

The Northwestern University Prostate Cancer SPORE aims to identify patients who have aggressive prostate cancer versus those who have indolent disease through population genetic studies; to develop therapies for castration-resistant prostate cancer, such as combination therapy to re-sensitize patients to androgen deprivation or novel molecular therapeutic approaches; and to develop and validate biomarkers that will avoid overtreatment of patients who receive a diagnosis.

One project will focus on early diagnosis and

three will focus on CRPC. The SPORE first received NCI funding in 2001. The researchers' work has contributed to implementation of clinical trials, FDA approval of a PSA assay, participation in inter-SPORE and Department of Defense national clinical trials, and involvement in national active surveillance initiatives.

The four main projects of this SPORE are: Impact of germline genetic variants on failure of active surveillance for prostate cancer; GR transcriptional activity and the evolution of enzalutamide resistant CRPC; EPHB4 receptor kinase as a target in prostate cancer; and Targeting FOXA1 Downstream Pathways: A novel therapeutic strategy for CRPC.

The University of Pittsburgh SPORE in head and neck cancer contains four projects, which aim to evaluate a chemoprevention strategy using broccoli seed preparations to reduce the morbidity and mortality of head and neck squamous cell carcinoma recurrence and second primary tumor formation, and to develop a safe and effective STAT3 targeting approach that combines systemic delivery for metastatic disease with enhanced delivery to the tumor using a novel microbubble/ultrasound approach.

The SPORE also plans to optimize the therapeutic benefits of cetuximab by combining the antibody with the immunotherapeutic ipilimumab, which targets suppressive regulatory T cells that appear to limit cetuximab-mediated antitumor activity—and to reduce the morbidity and health care costs of over-treating low-risk thyroid nodules and identify differentiated thyroid cancer patients that require aggressive therapy using a novel NGS-based strategy.

Three of the SPORE's four proposed projects are studying head and neck squamous cell carcinoma, and two projects are dedicated to improving HNSCC treatment using either a novel STAT3 decoy oligonucleotide initially developed in the SPORE program, or an immunotherapy strategy building on promising findings from the current funding period. A new HNSCC project will focus on chemoprevention.

The renewal application now includes a project studying differentiated thyroid cancer, which plans to use a next-generation sequencing approach to improve the sensitivity and specificity of fine needle aspirate biopsies with the goal of reducing unnecessary surgeries for indolent disease.

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The Dana-Farber/Harvard Cancer Center kidney cancer SPORE grant explores angiogenesis inhibition, immune modulation, and inhibition of molecular pathways. This SPORE, funded since 2003, is previously responsible for the identification of a gene whose inactivation accounts for approximately one-third of Wilms tumors.

This SPORE includes Beth Israel-Deaconess Medical Center; Dana- Farber Cancer Institute; Harvard Medical School; Harvard School of Public Health; Brigham and Women's Hospital; Massachusetts General Hospital; and the Children's Hospital of Boston. The Whitehead Institute at MIT and Georgetown-Lombardi Cancer Center are collaborating institutions.

The SPORE consists of four projects that address strategies for targeting HIF2α, the dominant oncogenic driver of clear-cell RCC; exploring angiogenesis inhibitor resistance mechanisms; and improving the therapeutic index of agents targeting both the mTOR and immune checkpoint pathways.

The projects are supported administrative, biostatistics and tissue acquisition and pathology cores, as well as a career development program and a developmental projects program.

The Mayo Clinic SPORE in ovarian cancer contains four main projects, supported by administrative, biostatistics, biospecimen and animal model cores:

Project 1, Novel Determinants of PARP Inhibitor Sensitivity in Ovarian Cancer, assesses biomarkers of response in both BRCA1/2-mutant and BRCA1/2-wildtype ovarian cancers.

Project 2, Targeting Protein Kinase C-Iota for Ovarian Cancer Therapy, proposes to 1) dissect the mechanism by which PKCι regulates ovarian cancer TIC behavior and assess the effect of PKCι inhibition on the ovarian cancer TIC phenotype; 2) assess the effect of PKCι inhibition on signaling and growth of HGSOC cell lines and validate potential pharmacodynamic and predictive biomarkers of PKCι inhibitors in patient-derived ovarian cancer xenografts in vivo; and 3) in humans, assess the ability of a highly potent and specific PKCι inhibitor to inhibit PKCι signaling in clinical OvCas in vivo through analysis of paired pre- and post-treatment biopsies obtained from ovarian cancer patients enrolled in the expansion cohort of the associated clinical trial.

Project 3, Metformin as a Metabolic Therapeutic in Ovarian Cancer, proposes to elucidate the mechanisms by which metformin affects tumor cell growth and

chemoresistance; use patient-derived ovarian cancer xenografts to study pharmacodynamic markers of metformin action; and use serum and tissue samples from a randomized phase II clinical trial of standard therapy to understand the mechanisms of metformin antineoplastic action in the clinical setting.

Project 4, Development of a Th17-Inducing Dendritic Cell Vaccine for Ovarian Cancer, aims to complete a recently opened clinical trial to determine whether FRα-specific Th17 T cell responses can be safely generated in ovarian cancer patients following their adjuvant chemotherapy. This trial will be performed in the setting of minimal residual disease, where immunotherapy might be most effective, according to the SPORE's abstract.

A breakdown of all funded SPOREs in 2015:

Organ Site or Highly Related Groups of Cancers	FY 2015
Breast	5
Prostate	7
Lung	4
Gastrointestinal	4
Ovarian	4
Bladder	1
Skin	4
Brain	5
H&N/Thyroid	4
Lymphoma	3
Cervical	1
Kidney	1
Leukemia	2
Myeloma	2
Pancreatic	2
Sarcoma	1
Neuroendocrine	1
Pediatrics/RAS	1
Total SPOREs	52
Total non-competing awards	42
Annual Budget	$106.0M

(Source: NCI)

At least half of all funded SPOREs involve more than one institution and 16 percent involve more than two; 20 percent have multiple PIs. All funded SPOREs currently reside in cancer centers, although that is not a requirement of the program.

According to NCI's Hecht, the SPORE program is the only NCI grant mechanism that is dedicated entirely to translational research, and requires each scientific project to achieve a human endpoint during the five-year funding period.

Funding Opportunity

NCI Taking Applications for Research Specialist Award

NCI is taking applications for its Research Specialist Award, which is designed to encourage the development of stable research career opportunities for scientists who want to pursue research within the context of an existing cancer research program, but not serve as independent investigators.

These scientists include researchers within a research program, core facility managers, and data scientists. The Research Specialist Award is intended to provide desirable salaries and sufficient autonomy so that individuals are not solely dependent on grants held by Principal Investigators for career continuity.

According to the announcement, before submitting the application, the research specialist must identify a primary support unit director who, together with the research specialist, is responsible for planning, directing, monitoring, and executing the proposed research. The unit director should be an active NCI-funded investigator in the area of the proposed research and be committed both to the research specialist and the specialist's research.

Letters of Intent are due by Jan. 9, 2016, with final applications due Feb. 9, 2016. The earliest start date for the grant is October 2016. The full text of the Funding Opportunity Announcement and details on how to apply are available on the NIH grants website.

In Brief

Edith Perez Steps Down as Vice Chair of Alliance Clinical Trials Network

EDITH PEREZ was named vice president and head of **Genentech/Roche BioOncology U.S. Medical Affairs**. Perez stepped down as vice chair of the **Alliance for Clinical Trials in Oncology**.

Perez's primary focus at Genentech and Roche will be to develop and implement medical strategies to optimize the utilization of cancer medicines and to lead a broad spectrum of oncology medical affairs activities including phase IV trials, medical education, publications, medical communication, advisory boards, promotional material review and product launches.

She will remain a professor of medicine at the Mayo Clinic, where she will continue to pursue basic and translational research in breast cancer.

Perez has been a key Alliance leader since 2010, when she joined in planning and implementing the merger of three cooperative groups that created the Alliance.

In addition to her role as vice chair, she served as vice president of the Alliance Foundation. Perez also worked closely with the Alliance Patient Advocate Committee, serving as an advisor and facilitating the implementation of initiatives such as published plain-language summaries of Alliance studies for patients and the general public.

As the principal investigator of one of the landmark trials for the adjuvant treatment of breast cancer by using Herceptin in combination with chemotherapy, she helped paved the way for the 2005 discovery that changed how treatment is managed for patients with HER2-positive breast cancer.

She also holds positions with the American Association for Cancer Research, the American Society of Clinical Oncology, and NCI and continues to serve on the editorial boards of multiple academic journals and has authored more than 700 research articles and abstracts.

NCI recognized 11 investigators nationwide with its **Cancer Clinical Investigator Team Leadership Awards**.

The awards support clinical investigators at NCI-designated cancer centers who participate in NCI-funded clinical trials. Established in 2009, the awards are intended to help retain investigators in academic clinical research careers. The award provides partial salary support for 2 years for the recipient to engage in activities and efforts related to the award.

The 2015 recipients are:

- **Leora Horn**, of Vanderbilt-Ingram Cancer Center
- **David Hyman**, of Memorial Sloan-Kettering Cancer Center
- **Matthew Katz**, of MD Anderson Cancer Center
- **Edward Kim**, of UC Davis Comprehensive Cancer Center
- **Frederick Lansigan**, of Norris Cotton Cancer Center at Dartmouth-Hitchcock Medical Center
- **Charles Leath III**, of University of Alabama at Birmingham Comprehensive Cancer Center
- **Elizabeth Plimack**, of Fox Chase Cancer Center
- **Andrew Poklepovic**, of Massey Cancer Center at Virginia Commonwealth University
- **Yvonne Saenger**, of Columbia University's Herbert Irving Comprehensive Cancer Center
- **Emma Scott**, of Oregon Health & Science University Knight Cancer Institute
- **Liza Villaruz**, of the University of Pittsburgh Cancer Institute

For details of the 2016 program announcement, open through Dec. 4, visit the NCI website.

THE AMERICAN ASSOCIATION FOR CANCER RESEARCH launched an international genomic and clinical data sharing initiative, known as AACR Project Genomics, Evidence, Neoplasia, Information, Exchange—or GENIE.

The initial phase of the project, which is being conducted in partnership with seven global leaders in genomic sequencing for clinical utility as well as two informatics partners, will aggregate participants' clinical-grade sequencing data.

The seven founding members of the consortium and phase one participants are: The Center for Personalized Cancer Treatment, in Utrecht, Netherlands; Dana-Farber Cancer Institute; Institut Gustave Roussy; Johns Hopkins University's Sidney Kimmel Comprehensive Cancer Center; Memorial Sloan Kettering Cancer Center; Princess Margaret Cancer Centre; and Vanderbilt-Ingram Cancer Center.

The two informatics partners are Sage Bionetworks, of Seattle, and cBioPortal, of New York.

"Numerous factors are driving an increase in the amount of genomic data available for analysis; however, these data are typically insufficient in number or lack the necessary clinical outcomes data to be clinically meaningful," said Charles Sawyers, chair of the Project GENIE Steering Committee. "Thus, to effectively benefit patients, the genomic and clinical outcomes data from as many institutions as is practical should be combined through a data-sharing initiative."

The project will pool existing and ongoing CLIA- and ISO-certified sequencing data from the participating institutions into a single registry, and link the data with select clinical outcomes. All project data will be made open-access following defined periods of project exclusivity, and the initial genomic data set will be publicly available Nov. 6, 2016.

The GENIE registry already contains more than 17,000 genomic records.

CANCERCARE announced the availability of co-payment assistance for pancreatic cancer patients

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through the **CancerCare Co-Payment Assistance Foundation**.

People receiving assistance from CCAF also have access to the full array of CancerCare services, including counseling, support groups, resource referrals, publications, education and financial assistance with treatment-related expenses such as transportation and child care.

"We are thrilled to provide this crucial co-payment assistance to people coping with a pancreatic cancer diagnosis," said Patricia Goldsmith, CEO of CancerCare. "Pancreatic cancer can be an especially challenging diagnosis to treat, and the CancerCare Co-Payment Assistance Foundation is committed to easing the financial burden so that patients can focus on managing their diagnosis and maintaining quality of life during treatment."

SRI INTERNATIONAL was awarded a contract of up to $9 million to provide preclinical development services to the **NCI PREVENT Cancer Program**.

Under the contract, SRI will provide scientific expertise, modern testing and support facilities, and analytical instrumentation to conduct a wide variety of preclinical pharmacology and toxicology studies to evaluate potential cancer prevention drugs.

The PREVENT Cancer Drug Development Program is an NCI-supported pipeline to bring new cancer preventing interventions and biomarkers through preclinical development towards clinical trials. PREVENT enables milestone-driven progression of novel cancer preventive chemical or biological agents and biomarkers from the laboratory bench towards proof-of-principle clinical testing and registration or validation.

The current contract calls for SRI to deliver high-quality laboratory data to support NCI-PCP's efforts to develop promising therapeutic candidates such as vaccines and cancer chemopreventive agents that will inhibit, delay or reverse manifestations of cancer. SRI will be responsible for managing therapeutic candidates from conception to submission of an Investigational New Drug application to FDA.

Drugs and Targets

TCGA Researchers Identify Seven Subtypes of Prostate Cancer and Two Drivers of Papillary Renal Cell Carcinoma

Researchers from The Cancer Genome Atlas Network recently published two studies—one identifying seven distinct molecular subtypes of prostate cancer, and one exploring the genetic drivers of papillary renal cell carcinoma.

A comprehensive analysis of 333 prostate cancers identified key genetic alterations that may help improve classification and treatment of the disease, revealing seven new molecular subtypes of prostate cancer based on known and novel genetic drivers of the disease. These subtypes may therefore have prognostic and therapeutic implications, according to researchers.

Of the seven subtypes, four are characterized by gene fusions (in which parts of two separate genes are linked to form a hybrid gene) involving members of the ETS family of transcription factors (ERG, ETV1, ETV4, and FLI1), and the other three are defined by mutations of the SPOP, FOXA1, and IDH1 genes.

Notably, the IDH1 mutation was identified as a driver of prostate cancers that occur at younger ages. Although 74 percent of the analyzed tumors could be categorized into one of the seven molecular subtypes, the remaining 26 percent of prostate tumors in this analysis could not be categorized because molecular alterations driving their growth were not identified.

Another finding from the analysis was that gene expression profiles differed based on whether the tumors were driven by gene fusions or by mutations.

Within the mutation-driven tumors, the SPOP and FOXA1 gene subtypes shared similar patterns of DNA methylation, a chemical modification of DNA that inhibits gene expression; somatic copy-number alteration and messenger RNA expression. These genomic commonalities suggest that mutations in SPOP and FOXA1 genes cause similar disruptions in the cell to bring about cancer.

Additionally, the SPOP and FOXA1 subtypes showed the highest levels of androgen receptor-mediated gene expression, suggesting potential preventive and therapeutic possibilities targeting androgens, which are male sex hormones that can stimulate the growth of prostate cancer.

The researchers, led by Chris Sander, of Memorial Sloan-Kettering Cancer Center, published

their results online in the journal Cell.

In the second study, a comprehensive genomic analysis of 161 tumors from people with papillary renal cell carcinoma provided insights into the molecular basis of this cancer and may inform its classification and treatment.

PRCCs are divided into two main subtypes, Type 1 and Type 2, which are traditionally defined by how the tumor tissue appears under a microscope. Findings from this genomic analysis, carried out by investigators from The Cancer Genome Atlas Research Network, have confirmed that these subtypes are distinct diseases distinguished by certain genomic characteristics.

Researchers found that Type 1 PRCC is characterized by alterations in cell signaling involving the MET gene that are known to drive cancer cell growth, the growth of tumor blood vessels, and cancer metastasis or spread. MET gene mutations or other alterations that affect its activity were identified in 81 percent of Type 1 PRCCs examined. This finding suggests that it may be possible to treat Type 1 PRCCs with specific inhibitors of the MET cell signaling pathway, including the MET/VEGFR inhibitor foretinib, which is currently being tested in phase II clinical trials in PRCC and other cancer types.

Type 2 PRCC was found to be more genomically heterogeneous. A specific characteristic, referred to as the CpG island methylation phenotype, was found almost exclusively in Type 2 PRCC and defined a distinct Type 2 subgroup that was associated with the least favorable outcome.

CIMP is marked by increased DNA methylation, which is a chemical modification of DNA that inhibits gene expression. Across all Type 2 PRCCs examined, 25 percent demonstrated decreased expression of CDKN2A, a tumor suppressor gene that helps regulate the cell cycle. Loss of CDKN2A expression was also associated with a less favorable outcome.

The researchers in this study were led by Paul Spellman, of Oregon Health and Science University, and Marston Linehan, of NCI. Their findings were published in the New England Journal of Medicine. TCGA is a collaboration jointly supported and managed by NCI and the National Human Genome Research Institute.

FDA granted Breakthrough Therapy Designation to pexidartinib (formerly PLX3397) for the treatment of tenosynovial giant cell tumor where surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity.

Currently, there is no FDA-approved systemic therapy for the treatment of TGCT. The designation was granted based on results from an extension cohort of a single-arm, multi-center phase I study that assessed the safety and efficacy of pexidartinib. Results of this study were published in The New England Journal of Medicine.

A pivotal phase III trial of pexidartinib called ENLIVEN is currently enrolling patients with symptomatic TGCT for whom surgical removal of the tumor would be associated with potentially worsening functional limitation or severe morbidity.

Pexidartinib is an oral small molecule that potently and selectively inhibits colony stimulating factor-1 receptor, which is a primary growth driver of abnormal cells in the synovium that causes TGCT. Pexidartinib has not been approved by FDA or any other regulatory authority for uses under investigation.

In addition to Breakthrough Therapy Designation, pexidartinib has been granted Orphan Drug Designation by FDA for the treatment of PVNS and GCT-TS. Pexidartinib also has received Orphan Designation from the European Commission for the treatment of TGCT. Pexidartinib is sponsored by Daiichi Sankyo Inc. and Plexxikon Inc., a member of the Daiichi Sankyo Group.

MD Anderson Cancer Center entered into a collaboration with CytomX Therapeutics to research Probody-enabled chimeric antigen receptor natural killer cell therapies, to be known as ProCAR-NK cell therapies.

MD Anderson will develop allogeneic umbilical cord blood and peripheral blood derived NK-cell therapies and combine it with CytomX's Probody technology to address new targets for this novel modality in cancer immunotherapy. Designed for more precise binding to tumors and reduced binding to healthy tissue, the therapies will be created against targets for which safety and toxicity have traditionally been limiting factors for CAR cell therapies.

Under the collaboration, CytomX and MD Anderson will develop ProCAR-NK cell therapies against multiple targets, and CytomX will have the option to license therapeutics that demonstrate preclinical proof of concept for clinical and commercial development.

From MD Anderson, the collaboration will be led by Katy Rezvani and Elizabeth Shpall, professors in the department of Stem Cell Transplantation and Cellular Therapy.