

Remarks* by

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NIH Hematology Oncology Fellowship Commencement
National Institutes of Health

June 21, 2019

It's wonderful that family and friends are here. Without them it would be much, much harder to do this. So, I really would like to thank family and friends, as well.

I have had quite a few graduations myself. Most of them were a while ago. But, what has really struck me are my expectations going forward and how wrong I have been about them. For example, when I graduated from medical school, I assumed that I would simply follow in my parent's footsteps. Both my parents were primary care physicians and I thought that I would become an internist, live in New York, and do that. But, in part because of the Vietnam War, I ended up getting training in research here at NIH. Seven years after I graduated from medical school, I started in the research laboratory at NCI and they have not been able to get rid of me.

So, I think that being open to possibilities really is important. My sense is that we all have three goals when it comes to finding the right profession. The first is to find a profession that allows us to make a difference. Second is to find a profession that gives us satisfaction. And the third is to be paid for doing it.

It's really not straightforward to figure out how you are going to achieve all three areas, which seem perhaps to be easy on the one hand, but not so straightforward on the other. I'd like to spend a few minutes talking with you about some of the things that I learned during this time and I hope some of it may be relevant to you.

*This text is the basis of oral remarks by Dr. Douglas R. Lowy, acting director, NCI. Please use with the understanding that some material may have been added or omitted during final presentation

The first thing is to find out who you are.

I trained and have boards in two different specialty areas—in internal medicine and in dermatology. But it turned out that clinical medicine, while it was something that I think I was good at doing, it didn't give me quite the satisfaction that I have found from doing research. I really like having time to think. And when you are doing work with clinical problems, you really need to make a lot of split-second decisions. In addition, one of the great things about doing research is to be open to the possibilities that you're making mistakes, et cetera. It's very different when you're taking care of patients, where making a mistake is something that you absolutely want to try to avoid. So, having the chance to really think about what I am doing is something that I have found to be very satisfying about doing research.

In learning about yourself, I think it's important to understand your limitations. What are you not so good at doing?

For example, I tend to procrastinate. And I've tried hard to overcome that problem. So, I have asked people whom I work with to help, and to remind me, "Doug, you have a deadline and you've got to do this by the end of this afternoon," and that sort of thing. So, this is a very important area: figure out not only what you're good at, but also find ways to improve yourself.

It comes down to doing something that you're both good at and are paid to do. When I was growing up, I wanted to be a quarterback for a national football league team. There were only two problems: I lacked the size and I lacked the talent. I would probably have had to pay them to play, plus I'm not sure that they would have permitted it. So, I had to find plan B. Being a physician and doing research has been a very fulfilling plan B. I don't regret not having exposed myself to traumatic brain injury or things like that.

In terms of trying to make a difference, there are a wide range of ways to do that.

I still hold my parents in very high esteem. I don't see any higher calling than taking care of patients and trying to help them feel better and actually get better. But for me, doing research has been really important.

Another area is prioritization and decision making.

Many of us try to do too many things and, as a result, we don't do any of them in sufficient depth. It's really hard because all of you have lots of talents and abilities. Deciding what you are going to do and prioritizing that is very important in terms of accomplishment. There is always another area to think about, but the real question is, how are you going to be able to do something in sufficient depth that it has the kind of impact that you would like it to have? For the people with whom I work in the Center for Cancer Research, in some ways I think that the principal investigators' single biggest problem is prioritization.

Prioritizing means at least two different things. If you want to start something new, that's fine. But what are you going to do less of? Many people start doing more and more things, but they don't dial back on anything else. There are only so many hours in the day.

Be open to new opportunities.

I was perfectly happy running a research lab in the Center for Cancer Research. When Harold Varmus became the Director of the National Cancer Institute, he asked me if I would become the Deputy Director of the Institute. I had almost no interaction with the extramural community other than my having been on a study section for several years. It was with some trepidation that I said yes.

But, it has been an exhilarating experience to see all of the possibilities that come to fruition at NCI. I'm sure this is true for all of the other institutes and centers here at NIH, where you can do something beyond your own laboratory research. When Harold left in 2015, it was clear, since I was the Deputy Director, that I was going to be asked to become the Acting Director. Again, I really wasn't sure if I was up to the task but NCI and all of NIH have wonderful people. They all said, "Doug, we will help you." And they did. Being the Director of NCI is nowhere near as hard as I thought it would be because there are people here who can help you in their domains.

The next area is to try not to be siloed.

More and more, what we do is a team effort. We sometimes joke at NCI that we should be called the NC-We instead. Sorry, that was not a very good joke. But team science has become so much more important than it was before.

The same thing is true when a patient comes in and has a clinical problem. Instead of treatment being recommended by just one person, it is more common that a team of people, with partially nonoverlapping expertise, determine what should be done. This enables us to be able to play to our strengths and do the things that we do well.

It's important to try to be in an environment which is supportive and interdisciplinary, so that you can leverage the skills of people who have expertise that is different from your own. I like to think that, contrary to mathematics, the whole is greater than the sum of its parts when we're taking care of patients and when we're doing biomedical research, because it's by coming together and working together that we can really achieve the most.

Sometimes we focus too much on what already is. Focusing on what might be is at least as important.

When you're here at NIH, the ability to change things and do things differently is extraordinary. Part of the problem is the way that we do research, especially when we're

looking at clinical problems. We're always looking at past experience. But it's important to wonder about the future. Where are likely to be in 5 years? And think about what might get you there. Wayne Gretzky, the great ice hockey player, was asked, "Why do you score so many goals?" He said, "I skate to where the puck will be, not to where it is right now."

This brings me to an experience with the HPV vaccine. The vaccine is working well, but the big clinical issue is cervical cancer, which is one of the most common cancers of women in low- and middle-income countries. The vaccine requires multiple doses, and these were not getting out to young women in low and middle-income countries.

I had the heretical hypothesis that maybe one dose of the vaccine would be sufficient. Not that we need to have only one dose here in the United States, although that would save money, but that if one dose were sufficient to confer long-term protection, that could really be a game-changer in low and middle-income countries. Logistically, giving just one dose could make a very big difference.

When I first articulated this, there was a tremendous amount of push-back in the vaccine community, because there really isn't precedent for a single dose of a subunit preventive vaccine. But, data from the clinical trial that has been conducted in Costa Rica suggest that one dose may be sufficient. So, with help from the Bill and Melinda Gates Foundation, NCI, together with colleagues in Costa Rica, are actually doing the clinical trial to test this hypothesis.

We don't know what the answer is going to be, but we're cautiously optimistic that it will turn out that one dose is sufficient. If that happens, the World Health Organization presumably would endorse this and it could make an enormous difference for patients in low- and middle-income countries. In the United States, it could save a great deal of money and lead to higher uptake of the vaccine.

Expect to be wrong sometimes.

It's hard because, as physicians, we are trained that we're not supposed to be wrong. We're supposed to be right. But, if we're continually believing just our own hypotheses, we are very likely to miss new information. One of the things that I have found to be most useful is actually to work with PhDs. PhDs don't have the same training that we have. When their hypotheses are wrong, instead of saying an expletive they say well, maybe this is going to be interesting.

For example, we're trying to use virus-like particles for treatment of early ocular melanoma by farming them with a light-sensitive dye. We were talking in the lab yesterday about depleting different immune cells in the mouse studies that we're doing. We got a totally paradoxical result of NK cells, natural killer cells that are supposed to be helping to provide the protection that we see in this model. Paradoxically, when we depleted the NK cells, there was more protection rather than less protection.

Being the MD that I am, I said, "Let's not worry about that." John Schiller, my long-standing colleague, being the PhD, said, "Now, this is interesting." Being open-minded and being willing to recognize that maybe we are wrong, can really open our minds to new things.

All of you have long and, I hope, distinguished careers ahead of you. A lot can happen in 40 years. I expect that your careers will last for 40 years. The changes that will happen in biomedicine are going to be extraordinary.

When I started, the options, in terms of treatment, were really quite limited. Now, the FDA is approving almost one drug or one new indication every week. The options for doing things at the level of clinical treatment, clinical trials, or at the more basic levels really are extraordinary. We don't understand everything about cancer. But, we certainly understand much more than we did, and this is leading to a lot of innovations and opportunities for treating and preventing cancer in ways that we simply couldn't do before.

New knowledge is going to be extraordinarily important, so that 10 years from now, we're not stuck with the armamentarium that we have in 2019. And you are really in a very privileged position, where you are going to be able to help more people than ever before and participate in discoveries that are going to enable that.

So, congratulations to all of you and I wish you all the best!