

Gordon B. Mills, MD, PhD

Interview Session One: May 23, 2016

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Chapter 00A

Interview Identifier

Codes

A: The Administrator

Tacey Ann Rosolowski, PhD

[00:00:01]

All right, we are recording, the counter is moving. It is about sixteen minutes after nine, on the twenty-third of May, 2016, and I'm in the Zayed Building on the main campus of MD Anderson, interviewing Dr. Gordon B. Mills, for the Making Cancer History Voices Oral History Project, run by the University of Texas, MD Anderson Cancer Center. It's housed in the Research Medical Library, and I should say my name is Tacey Ann Rosolowski, I'm going to be conducting the interview today. Dr. Mills joined the faculty of MD Anderson in 1994, as a professor, and chief of the section of molecular therapeutics. And I guess we've already tacitly agreed, you're going to correct me as I go along through this. Okay, good, so, so far so good, all right. In 2006, he founded the Department of Systems Biology, and has chaired the department since that time. Now, there was a detail that I found, it was a little confusing. It says this is the first Cancer Systems Biology Department, and the second Systems Biology Department in the United States. Now, could you clarify that for me?

[00:01:12]

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Gordon B. Mills, MD, PhD

[00:01:12]

That's correct.

[00:01:13]

Tacey Ann Rosolowski, PhD

[00:01:12]

It's correct.

[00:01:13]

Gordon B. Mills, MD, PhD

[00:01:14]

To my knowledge, dedicated to cancer specifically.

[00:01:18]

Tacey Ann Rosolowski, PhD

[00:01:18]

Wow. So the first Systems Biology Department here at MD Anderson, or in the U.S.?

[00:01:22]

Gordon B. Mills, MD, PhD

[00:01:23]

In the U.S.

[00:01:23]

Tacey Ann Rosolowski, PhD

[00:01:23]

In the U.S. Wow.

[00:01:25]

Gordon B. Mills, MD, PhD

[00:01:25]

So the first Cancer Systems Biology Department, or Systems Biology Department dedicated to cancer.

[00:01:33]

Tacey Ann Rosolowski, PhD

[00:01:33]

Got you, okay. And then in general.

[00:01:34]

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Gordon B. Mills, MD, PhD

[00:01:35]

And in reality, I didn't even know that until it was pointed out to me in a scientific advisory board review from outside individuals, where this to me was an obvious thing that needed to be done. I did not realize it was the first attempt to do this in a cancer specific manner, but it has worked and worked well.

[00:02:01]

Tacey Ann Rosolowski, PhD

[00:02:01]

Well, I'm going to be very interested in talking more about that.

[00:02:04]

Gordon B. Mills, MD, PhD

[00:02:03]

There is a little bit of perhaps background, that can be added into that. I was actually recruited here to chair the Department of Molecular Oncology, which is established in 1995. That then changed due to retaining an absolutely outstanding scientist at MD Anderson, who wanted to use the word molecular oncology in the title of their department, so we renamed ours to Molecular Therapeutics. Then, with the recruitment of Garth Powis, that really was the push to say that since we had a Department of Experimental Therapeutics, we needed to step back, decide what our department should be, what our theme should be, and what was the major opportunity within the institution and worldwide, and it had become very clear that a systems biology approach to cancer was needed, and further, that it was an opportune time to build such a department.

[00:03:17]

Tacey Ann Rosolowski, PhD

[00:03:17]

Cool. Well, I'll be very interested in kind of tracing that whole history, thanks for that preview. Oh, another question. The Department of Systems Biology, housed in the Division of Cancer Medicine?

[00:03:31]

Gordon B. Mills, MD, PhD

[00:03:32]

Mm-hmm. [Affirmative]

[00:03:32]

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Tacey Ann Rosolowski, PhD

[00:03:32]

Okay. Now, I also saw somewhere that it's housed in Basic Science Research.

[00:03:36]

Gordon B. Mills, MD, PhD

[00:03:35]

So, last year, we moved from the Division of Cancer Medicine, to the Division of Basic Science or the Division of Science. It's actually Division of Science, not basic science, and the reason for that really, was multifold, but two key pieces. One, we had already developed very strong relationships with the clinical side, and it was clear that we are a department that sits between the sciences and the patient, and that one of the opportunities that we could then build on, was putting a stronger relationship with our sciences departments, as that interface, and that that would be better served by being within the Division of Sciences than within the Division of Cancer Medicine. We retain strong relationships across the Division of Cancer Medicine, so it was an extension rather than a subtraction, and I think it's an important concept, that this department really is very much in-between the basic and the translational aspects of patient management, at the MD Anderson Cancer Center, and the precepts are needed on both sides.

[00:05:00]

Tacey Ann Rosolowski, PhD

[00:05:00]

Okay. All right, the next title, you served as co-director of the Zayed Institute for Personalized Cancer Therapy, since 2010, correct?

[00:05:11]

Gordon B. Mills, MD, PhD

[00:05:11]

That's true, with Dr. John Mendelsohn is the director.

[00:05:14]

Tacey Ann Rosolowski, PhD

[00:05:15]

And administrative director of the Kleberg, am I saying that right, Kleberg?

[00:05:19]

Gordon B. Mills, MD, PhD

[00:05:19]

It's Kleberg actually.

[00:05:19]

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Tacey Ann Rosolowski, PhD

[00:05:20]

Kleberg. Kleberg Center for Molecular Markers. And is that also since 2010? Okay, please tell me the details on that, because I also saw 2006?

[00:05:33]

Gordon B. Mills, MD, PhD

[00:05:33:[00]

Two-thousand and six, I think is correct. Let me find out for you.

[00:05:38]

Tacey Ann Rosolowski, PhD

[00:05:38]

There were some different choices of dates on different sources.

[00:05:42]

Gordon B. Mills, MD, PhD

[00:05:42]

Trust me. Partly, I don't care. I am one of the people that as far as I can tell, cares about these types of things less than anyone else in the institution. Titles are not all that important, but if I pull up my CV and a bio, it will all be there and we can get the dates right.

[00:06:01]

Tacey Ann Rosolowski, PhD

[00:06:03]

All right, because I um... Let's see.

[00:06:08]

Gordon B. Mills, MD, PhD

[00:06:08]

Let's see, the Kleberg started in 2004.

[00:06:11]

Tacey Ann Rosolowski, PhD

[00:06:12]

Okay, 2004, and that does say. Okay, so is there a difference between director and administrative director?

[00:06:17]

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Gordon B. Mills, MD, PhD

[00:06:18]

No. I'm actually director, and I think administrative director is correct.

[00:06:21]

Tacey Ann Rosolowski, PhD

[00:06:23]

Okay. All right. I think I got that off of the website.

[00:06:25]

Gordon B. Mills, MD, PhD

[00:06:25]

It's okay.

[00:06:26]

Tacey Ann Rosolowski, PhD

[00:06:26]

Okay, well this is good, that we're correcting it all. Then, you were also co-head of the Women's Cancer Moon Shot, and that's since 2013.

[00:06:36]

Gordon B. Mills, MD, PhD

[00:06:37]

Yes.

[00:06:37]

Tacey Ann Rosolowski, PhD

[00:06:38]

Okay, great. Well, I just --

[00:06:40]

Gordon B. Mills, MD, PhD

[00:06:40]

You haven't even touched on my other administrative roles, that are probably as important.

[00:06:46]

Tacey Ann Rosolowski, PhD

[00:06:46]

Well, why don't we actually wait to process a few of those, when we're actually talking about them in detail.

[00:06:51]

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Gordon B. Mills, MD, PhD

[00:06:48]

Sure. Good enough.

[00:06:51]

Tacey Ann Rosolowski, PhD

[00:06:51]

I kind of wanted to hit the highlights, is that okay? Because I do have a section to talk about each on in detail.

[00:06:57]

Gordon B. Mills, MD, PhD

[00:06:57]

Okay, good. And the other highlight that is probably important is that I have served under three different presidents and have watched the institution grow and mature during that time.

[00:07:08]

Tacey Ann Rosolowski, PhD

[00:07:09]

Wonderful, thank you. All right, well I wanted to thank you for giving your time this morning, and I can tell, we're going to have a lot to talk about.

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Chapter 01

A: Educational Path;

An Education Designed to Keep Options Open

Story Codes

A: Personal Background;
A: The Researcher;
A: The Administrator;
B: Multi-disciplinary Approaches;

Tacey Ann Rosolowski, PhD

[00:07:09]+

I'd like to start, if we may, kind of in the traditional oral history place, which is I wanted to ask you where you were born and when, and please tell me a little bit about your family.

[00:07:34]

Gordon B. Mills, MD, PhD

[00:07:35]

I was born in Edmonton, Alberta, 1953.

[00:07:40]

Tacey Ann Rosolowski, PhD

[00:07:42]

Can you give me the date?

[00:07:42]

Gordon B. Mills, MD, PhD

[00:07:43]

August third. My family is a local family that had been in the Edmonton area for five generations on one side and four generations on the other.

[00:07:57]

Tacey Ann Rosolowski, PhD

[00:07:57]

Wow.

[00:07:58]

Gordon B. Mills, MD, PhD

[00:07:58]

Which is unusual. Really, I was the first person in my family to ever graduate from college and indeed, only one person had ever gone for one year before that, and it was another generation

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before anyone else graduated from college.

[00:08:18]

Tacey Ann Rosolowski, PhD

[00:08:19]

What was the family professions?

[00:08:20]

Gordon B. Mills, MD, PhD

[00:08:21]

They were blue collar workers and quite successful in those roles. My father was a plumber and had established a company. He retired at forty-eight because he could, and because it became clear that neither I, nor my sisters and their husbands, were going to take over the company, so he said, I don't need to run it anymore, and he worked when and as and if he wished, without the stress of running a company until he passed away two years ago.

[00:08:56]

Tacey Ann Rosolowski, PhD

[00:08:56]

Wow. Can you tell me your parents' names?

[00:08:58]

Gordon B. Mills, MD, PhD

[00:09:01]

Sorry, there's only a smile. My mother's name is Aileen. A-I-L-E-E-N. That is a name that was not what she was born with in that it was inserted in school. Her name was actually Aleen, A-L-E-E-N, and nobody was used to that. Then my father's name is Robert and that's also my son's name, and his middle name was Gordon, which is my first name, so there's a history.

[00:09:35]

Tacey Ann Rosolowski, PhD

[00:09:35]

That's nice. So you have siblings.

[00:09:37]

Gordon B. Mills, MD, PhD

[00:09:37]

I have three sisters. Two of them are still in Edmonton and one is in Cincinnati.

[00:09:44]

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Tacey Ann Rosolowski, PhD

[00:09:45]

And your sisters' names just for the record.

[00:09:47]

Gordon B. Mills, MD, PhD

[00:09:48]

Cathy, with a "C," Kelly, and Terri, T-E-R-R-I.

[00:09:54]

Tacey Ann Rosolowski, PhD

[00:09:56]

All right, thank you. So, what was the attitude about education in your family, and how did -- you know, you flowered into a person who was interested in the sciences. How did that all happen?

[00:10:10]

Gordon B. Mills, MD, PhD

[00:10:12]

It's completely unclear. My family clearly valued an education, but my father had made it through to grade nine and then went into trade school. That was a normal pathway for my family members. So, my interest in going further in school was completely supported but not understood. Indeed, I can note that my father asked me multiple times if I ever was going to get a real job, instead of just being a trainee or a student. So, when you do an undergrad, an MD, a PhD, a fellowship, a postdoc, it adds up, and he just did not completely understand why the process was so prolonged, but both parents were extremely proud and happy to see what I've accomplished.

[00:11:11]

Tacey Ann Rosolowski, PhD

[00:11:12]

Tell me about your early education. When did you start to know that you were drawn to certain areas?

[00:11:20]

Gordon B. Mills, MD, PhD

[00:11:21]

Oh, I would say that my initial excitement was reading about Pasteur and others, in terms of bacteriology, and the incredible change that had been made in outcomes in healthcare, with vaccines and better quality of water and simply things that totally have altered the lifespan of people. From that, I went into college in biochemistry, and watching my colleagues, my

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professors, struggling to get grants and feeling that they were really absolutely incredible and if they were going to struggle, I needed a backup. And so one day I walked over to the medical school and said, "What would it require to get into medical school?" The secretary said, "Well, the dean of admissions is in her office, she doesn't have an appointment," and the rest is history.
[00:12:28]

Tacey Ann Rosolowski, PhD

[00:12:28]

Right, right. So, tell me more about the classes you were taking in college. What was the array?
[00:12:35]

Gordon B. Mills, MD, PhD

[00:12:35]

I would say that the steps that I did in college and indeed, throughout my whole career, has been to keep as many options open as at all possible. So while I was doing an undergrad in the sciences and biochemistry as my specialization, my minor, and actually the majority of my classes, were in political science. And so the idea of breadth and not trying to decide early, where I was going, is something that I kept doing, and even when I did a medical degree, I kept my whole science background moving and did a PhD sort of along the way, again, keeping all possible doors open for as long as possible.

[00:13:28]

Tacey Ann Rosolowski, PhD

[00:13:28]

Why did you select political science as a minor?

[00:13:31]

Gordon B. Mills, MD, PhD

[00:13:33]

Because I enjoyed the classes. I took one class as my arts course, I did not like English, and so that became a much more interesting field and area in terms of how political science works, how interactions at both a personal and then a national and international level occur, you know, if I was to say I understood what I do now, is politics.

[00:14:05]

Tacey Ann Rosolowski, PhD

[00:14:06]

I was going to ask you about the connection.

[00:14:07]

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Gordon B. Mills, MD, PhD

[00:14:07]

Yeah. I don't think it was conscious at that time. I don't think that most of the things we do that benefited us massively in the future are conscious. I mean, I think that probably, the single most important course I ever took was typing, in college, because that's what we do now for a living, and I would love to say it was because I was prescient and knew the future, but in reality, it's probably because there were three males and twenty-seven females in the class.

[00:14:35]

Tacey Ann Rosolowski, PhD

[00:14:38]

Well, I don't think we do make those choices, but those choices do show a certain proclivity of mind or skills, and they often flower in interesting ways.

[00:14:46]

Gordon B. Mills, MD, PhD

[00:14:46]

Well, and I can say that that theme has continued. I would say that when I recruit people to my lab, and this is a little bit out of order, I tell them that our greatest strength and our greatest weakness are identical, that we are very broad, we have no fear, we will do anything that is needed, and our weakness is that we do things broadly and we may not be the best at any one of them. What we and where we gain is by integrating across many different areas, many different disciplines, and really, in the precept of systems biology, integrating that information into new concepts that are not apparent without the approaches.

[00:15:31]

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Chapter 02

A: Educational Path;

Medical School with a Path to Research and Team Science

Codes

A: Professional Path;
A: Inspirations to Practice Science/Medicine;
A: The Researcher;
D: Understanding Cancer, the History of Science, Cancer Research;
D: The History of Health Care, Patient Care;
C: Diversity at MD Anderson;
A: Personal Background;
A: Influences from People and Life Experiences;
C: Professional Practice;
C: The Professional at Work;
C: Collaborations;
A: Career and Accomplishments;
A: Professional Values, Ethics, Purpose;

Tacey Ann Rosolowski, PhD

[00:15:32]

Right, cross fertilization, absolutely. And just for the record, you got your BS in '75, at the University of Alberta, in Edmonton, is that correct?

[00:15:42]

Gordon B. Mills, MD, PhD

[00:15:42]

That's actually not a BS, it's a... oh, what's the formal term?

[00:15:48]

Tacey Ann Rosolowski, PhD

[00:15:48]

Oh, because the Canadian degrees are different?

[00:15:50]

Gordon B. Mills, MD, PhD

[00:15:50]

No. It's actually a bachelor of medical sciences.

[00:15:52]

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Tacey Ann Rosolowski, PhD

[00:15:53]

Oh, okay.

[00:15:53]

Gordon B. Mills, MD, PhD

[00:15:54]

B Med Science, and what that is, is that in the Canadian system and frequently here, you go into medical school after your second year of college, and then in your fourth year, as long as things are going well, they confer a bachelor of medical sciences, saying that this is equivalent of a bachelor of science.

[00:16:16]

Tacey Ann Rosolowski, PhD

[00:16:17]

And then you got your MD in '77?

[00:16:19]

Gordon B. Mills, MD, PhD

[00:16:19]

I did.

[00:16:20]

Tacey Ann Rosolowski, PhD

[00:16:20]

Okay. So tell me about that choice, to go to medical school. Why did you stay at the University of Alberta? And I didn't ask you why you selected that university for undergrad too.

[00:16:31]

Gordon B. Mills, MD, PhD

[00:16:32]

It's where I grew up and so it was something that I would say I didn't know better. But on the other side, I would say that despite the fact that I trained in a nonconventional program in the U.S., I did not go to Harvard, I did not go to Johns Hopkins, I did not go to Duke, I've done okay. I think it really does show that the benefit of where you go can be very important, but a lot of people at MD Anderson, and my guess is about half, came through a nontraditional medical program, and it says that it's the person, not the program that matters in many cases. So, it was my home university, it was a good university, and so I went there. I went into medical school, really with the idea, again, of saying that the breadth of having medicine as a background, to understand what was going on in a disease, but further, if my research program did not flower, it would be a way to make a living. And then to a degree, even the same concept when I went into

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obstetrics and gyne as my specialty, my interest had really become immunology, and one of the major aspects of pregnancy is understanding why the fetus is not rejected by the mother, and so this is a major immunological question.

[00:18:10]

Sort of along that way, I became much more interested in tumor immunology, why the tumor is not rejected, and further, in how one could trick the immune system into rejecting the tumor, which I think now, thirty-some years later, is becoming a real opportunity, and that led to sort of my process. While I would never recommend that somebody else do what I did, it worked. So during medical school, I did approximately eighty hours of research a month, at two and three in the morning, and went into obstetrics and gyne and did a year of clinical training and then finished a PhD, and then went back and completed my obstetrics and gyne training, and so these were separate. This was not an MD PhD program, these were bona fide MD programs, PhD programs, but were all mixed up, where I used every elective that was available, to look at research opportunities and move those forward, really based very much on our tumor immunology concepts.

[00:19:31]

Tacey Ann Rosolowski, PhD

[00:19:32]

I didn't ask you earlier, I mean obviously, you had an understanding very early, that research was where you wanted to focus your attention. Why? Why did you make that choice?

[00:19:44]

Gordon B. Mills, MD, PhD

[00:19:45]

At one point, it was not completely clear and again, as I mentioned earlier, one of my major goals was to keep as many opportunities open as possible, but by the time I was completing my PhD, during my obstetrics and gynecology fellowship, it became clear that if I treated the patient in front of me, that could have a great impact, but if I determined how to treat hundreds of patients, for other obstetricians and gynecologists, that would have a much greater impact. Further, unlike some of my colleagues, where it was absolutely required that they have the ego input of grateful patients, that was not nearly as exciting to me as saying I can have a much greater influence by doing research than I can by treating a single individual. It actually was an interesting challenge, because my medical school class was very clinically oriented, and to a degree, I think there was a resentment or a concern, that perhaps a slot in the medical school could be better filled by the individuals who would treat the one patient across from then, than those that were going to determine the direction of the future. Now, I think that that attitude has completely changed. I think we now value the impact of research in how we are going to improve patient outcome, but at that time, in that institution, it was a major discussion.

[00:21:32]

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Tacey Ann Rosolowski, PhD

[00:21:34]

I'm not surprised, I'm not surprised at all. I mean, there is a history to translational work and it's crossing a really -- there's a traditional, fairly big gap.

[00:21:45]

Gordon B. Mills, MD, PhD

[00:21:45]

And I think that I would say that now, there really isn't a discussion. I think that medical schools, with a few exceptions, really are trying to determine how to bridge that gap, and to train the people that will do both. I think again, out of order, I'm not sure what the future is. Is it the single individual who is going to be the triple threat of teaching, treating patients and doing research? Is it going to be teams, where you have a clinician who understands research, working with a PhD who understands clinical questions, or even much bigger teams? I would say that the biggest transition over the last five years, which again is after the development of the Department of Systems Bio, is really the understanding or the push on my side, that team science is going to be the future of making progress rapidly, to improve patient outcome, and that the day of the single professor, small lab, one postdoc, one trainee, one technician, focusing on a single molecule for life is wonderful and will give us the base science information that is necessary, but with the incredible explosion in information that we have that's available, we're going to need to figure out how to build, how to maintain, and how to reward teams, if we're really going to move all of this to our patients in an efficient manner.

[00:23:32]

Tacey Ann Rosolowski, PhD

[00:23:32]

Is there a particular kind of individual who is drawn to this? I mean, you mentioned something you say to recruits when they come. What kind of people do you like to recruit, what's their profile, if you will?

[00:23:44]

Gordon B. Mills, MD, PhD

[00:23:45]

I'm looking for people who understand what a team is. Indeed, one of my interview questions is tell me what team sports you played in college. It's very interesting, because the vast majority will say tennis or swimming, and those are not team sports. I want someone who has understood the concept that if you are playing on a football team or a baseball team, it is the weakest member of the team that is critical, and that you work with them, to build their strengths, to work around their strengths and weaknesses, and that it is the team that succeeds, it's not one person. That works for people who train in the United States. It's not quite the same when you're

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interviewing people from outside, where the culture of sports and team sports is different, but it is an important question to try and get an understanding of those people who want to be part of a team, and knowing that team will accomplish far more than a bunch of individuals.

[00:24:53]

Tacey Ann Rosolowski, PhD

[00:24:55]

Now, am I assuming correctly, that individuals from outside the U.S. have less of a culture of team sports?

[00:25:[00]

Gordon B. Mills, MD, PhD

[00:25:00]

Absolutely, and so that question is one that doesn't help a lot. And then you try and elicit the same concepts through different types of questions.

[00:25:10]

Tacey Ann Rosolowski, PhD

[00:25:10]

And what sort of questions do you ask to get at that?

[00:25:12]

Gordon B. Mills, MD, PhD

[00:25:13]

My first question to everyone is the same, with a slight difference in timeline, and that includes administrative assistants, all the way through to assistant professors, and that is, is tell me what the perfect job would be for you five, seven, ten years from now, depending on where they are in their training. There's no right answer, it really just is to start a conversation. And then the second part of that is tell me what would make you excited to get up in the morning and go to work, and that gives you a very good feeling of whether they say well, I want to be the boss and I want to run things and I'm going to have my own lab and I'm going to have five people reporting to me, versus I'm going to be part of a group that is going to make a difference. That comes all the way from administrative assistants, that says I'm going to be excited to see that I can help the people around me succeed. Frankly, you hear that from a few faculty candidates. They usually are looking at a different pathway of setting up their own lab first. What you want to then elicit, is that meant to be my lab, one my one postdoc, my one student and my one project for life, or I'm going to do that but the second half of what I want to do once that is established is to be part of a team that is going to make a difference. And so you're looking for people who are interactive, collaborative by nature.

[00:26:51]

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Tacey Ann Rosolowski, PhD

[00:26:52]

Did you play team sports?

[00:25:54]

Gordon B. Mills, MD, PhD

[00:26:54]

Yes.

[00:26:54]

Tacey Ann Rosolowski, PhD

[00:26:55]

What did you play? Where did you get these skills in other words.

[00:26:58]

Gordon B. Mills, MD, PhD

[00:26:59]

Football, rugby, hockey, baseball, I played team sports.

[00:27:03]

Tacey Ann Rosolowski, PhD

[00:27:04]

Yes you did.

[00:27:04]

Gordon B. Mills, MD, PhD

[00:27:05]

Basketball. If it was a team sport, I played it, usually at an intramural college level, although I did play rugby at a much higher level. Again, team sport concept of working with the people around you and understanding where their strengths and weaknesses are is a key point.

[00:27:28]

Tacey Ann Rosolowski, PhD

[00:27:29]

When you said you played rugby at a higher level, what did you mean by that?

[00:27:31]

Gordon B. Mills, MD, PhD

[00:27:31]

I played rugby at a city side, I played against international teams.

[00:27:35]

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Tacey Ann Rosolowski, PhD

[00:27:35]

Wow.

[00:27:36]

Gordon B. Mills, MD, PhD

[00:27:37]

So, yes.

[00:27:37]

Tacey Ann Rosolowski, PhD

[00:27:38]

Yeah. So you didn't want to brag on yourself, but that's cool, that's very cool. So obviously, a big learning experience, going through all of that.

[00:27:48]

Gordon B. Mills, MD, PhD

[00:27:50]

I think that really has been part of what I have done for my career. Indeed, I think you would have a great difficulty in finding anyone who has more collaborations, more collaborative papers, who has done constantly, the concept of developing technologies and ideas to share with others and move things forward, and that has very much been something that has worked for me throughout my career. I think I can actually give you the number. I believe that I now have papers with over fifty thousand different individuals. Now, let me check and make sure it's not five thousand, but it's still a massive number.

[00:28:42]

Tacey Ann Rosolowski, PhD

[00:28:42]

It's still a jaw-dropper.

[00:28:43]

Gordon B. Mills, MD, PhD

[00:28:45]

I would guess and I'm not going to guarantee, but we can look, that it's five thousand. We can look this up online here at MD Anderson, and I'm quite certain that that network is broader than any other individual in the institution, but it's what has worked for me. I'm not going to argue that it's right or wrong, it's the way it has worked for me, yeah. I don't know that I can get it any more. It's fifty-five thousand citations on my papers and -- it no longer gives us that number --

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over five thousand colleagues, on papers.

[00:29:21]

Tacey Ann Rosolowski, PhD

[00:29:22]

Wow.

[00:29:22]

Gordon B. Mills, MD, PhD

[00:29:24]

So it's something that I do and as I said, not everyone works in that environment but it does work for me.

[00:29:34]

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Chapter 03

A: Professional Path;

Developing a Researcher's Approach; Observations on the Current Job Market and Team Science

Codes

A: Professional Path;
A: Inspirations to Practice Science/Medicine;
A: The Researcher;
D: Understanding Cancer, the History of Science, Cancer Research;
A: Influences from People and Life Experiences;
C: Professional Practice;
C: The Professional at Work;
C: Mentoring; D: On Mentoring;
B: Education; D: On Education;
C: Leadership; D: On Leadership;
D: On Research and Researchers;
D: Business of Research;

Tacey Ann Rosolowski, PhD

[00:29:34]

Absolutely. Well tell me about -- so, we've talked about medical school and you did your PhD at the same time, so tell me about, a little bit more about the evolution of your research interest, evolving from this immunology perspective on fetus and mother.

[00:29:55]

Gordon B. Mills, MD, PhD

[00:29:56]

When I moved from Edmonton to Toronto, having been an obstetrician and gynecologist, I actually moved to the Hospital for Sick Children in Toronto, which is a bit of a challenge because the pediatricians and obstetricians sometimes are in conflict over who did or did not cause problems with babies, but it worked and this really was an immunology program and very much a basic immunology program. As I moved from there to my own laboratory, I became much more interested in the interaction between the immune environment and the tumor.

[00:30:41]

Tacey Ann Rosolowski, PhD

[00:30:45]

Now are we -- we're missing a little thing here, because you were in Australia for a couple of years.

[00:30:52]

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Gordon B. Mills, MD, PhD

[00:30:53]

No, I was only in Australia for about six months.

[00:30:55]

Tacey Ann Rosolowski, PhD

[00:30:55]

Oh, okay.

[00:30:56]

Gordon B. Mills, MD, PhD

[00:30:57]

That came about as I had developed a new technology, when I was in medical school doing research, and the immunology group, one of the best in the world, with Warren Jones, was in Adelaide, and he invited me to come and do a training program with him.

[00:31:25]

Tacey Ann Rosolowski, PhD

[00:31:26]

And the institution, just for the record?

[00:31:27]

Gordon B. Mills, MD, PhD

[00:31:28]

Flinders University, which had just opened, and it actually was a wonderful experience in sort of two ways. The first is, is seeing a totally different attitude towards trainees, and probably one that I have followed. Trainees in Australia are apprentices, they're doctors in training. In contrast, in the Canadian system and the American system to a degree, there is not the sort of understanding that you are, you will be a physician, and I respect your opinion. Instead here, it's I want to challenge everything you are and think, and I want to mold you in my design and manner. And so it was absolutely wild for me, for people to ask questions and actually want to know how I answered them, rather than what I was used to, see if I can find something to pick apart in your answer. That again, was a much more interactive, collegial, collaborative environment that I was not used to.

[00:32:40]

Tacey Ann Rosolowski, PhD

[00:32:40]

And treating people like a professional from the word go.

[00:32:41]

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Gordon B. Mills, MD, PhD

[00:32:43]

Well, and there were a lot of little things that were absolutely wild. I mean, there was beer and wine in the training room. If you had a glass of beer while you were on call fine, but if you went over the limit you were fired instantaneously. You were expected to behave as an adult and within reason, and it was just a totally different environment.

[00:33:08]

Tacey Ann Rosolowski, PhD

[00:33:10]

What was the research you were doing there?

[00:33:11]

Gordon B. Mills, MD, PhD

[00:33:11]

At that time I developed a new approach to measure B-cell immune responses in patients. The assay was sufficiently tricky and difficult, that while I could make it work, it was never broadly adapted. It was far too complex to be a practical assay, and so other approaches were developed that bypassed what I had put in place at that time.

[00:33:41]

Tacey Ann Rosolowski, PhD

[00:33:42]

What did you learn from that experience?

[00:33:44]

Gordon B. Mills, MD, PhD

[00:33:46]

Again, I think that the biggest piece of learning was that the way in which we trained physicians and people in the American system, really was perhaps not the best approach, and that this is the way I did it, and I got beat up by my attending and I'm going to now pass that on to the others. Education is by attack and challenge, rather than by respect, working with a colleague, building a team, and all of the pieces that I've been talking about. I think that was one of the big pieces.

[00:34:25]

Tacey Ann Rosolowski, PhD

[00:34:25]

I guess I was referring specifically to, was there something that you learned, through the course of that research, even though it didn't pan out as you might have wished.

[00:34:36]

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Gordon B. Mills, MD, PhD

[00:34:37]

It was part of my overall research program and so it really had to do with the concepts, and I've mentioned them a few times. One of the things that I do is to set up new approaches and new techniques, and then share and disseminate and make them available to others in a broad basis. To me, that has been an intriguing process and it's clear, as I look at my own CV, that that statement is true, but I consider myself one of the most technology adverse people I've ever met. But, when I look at my colleagues around me, I am perhaps not as adverse as most, and I guess it's just been a series of processes where we do what we need to, and again, it's what I described earlier. By being willing to do anything, we gain breadth, but as I said, I doubt that we do anything the best in the world. We are a group that integrates across technologies and approaches.

[00:35:44]

Tacey Ann Rosolowski, PhD

[00:35:46]

So, I kind of derailed you by going to the Adelaide experience, because it just looked like an interesting moment in your -- and how was it to go so far away, too? I mean, you said --well, you chose to go to Edmonton, University of Alberta, because it was home, and then you go to Australia. What was that like, experiencing being in another country?

[00:36:10]

Gordon B. Mills, MD, PhD

[00:36:11]

Well, I can say that it was an experience. There are cases where I did things that were very silly, from not being used to the different environment. It was a great learning experience, to see how a completely different approach to medicine worked. The Canadian system is a single payer system, the federal government covers all patient care. In Australia, they had a two tier system, with everybody getting basic medical care, but you could then pay if you wished, for additional care. Intriguing, that the patients who got the best care were not those that paid for a specialist. Those were the ones that went to the hospital, to the people who were seeing more patients and seeing numbers, which mattered, and so it was a very important learning experience, to see a completely different system.

[00:37:13]

Tacey Ann Rosolowski, PhD

[00:37:13]

A different medical system, yeah. Well, let's go back to your experience in Toronto. Tell me more about that and the evolution of your research.

[00:37:22]

Gordon B. Mills, MD, PhD

[00:37:23]

Well, there are maybe two or three different parts of this that turned out, I think to be very important in where I am now conceptually. The first one is, is that I worked in a very good group, and I have attempted to rebuild, in my own group, the interactions with the different postdocs in the group and with the supervisors, and really have been unable to build an environment that is anywhere near as exciting. It is truly exciting to be a postdoc and have no restrictions on what you do, where you go. You're not worried about grants, that's your boss's problem, and so it really was an incredible opportunity. There were two really, I think important pieces, and one is, is that my boss, Erwin Gelfand, had a very good view of what science was about, about the challenges, the opportunities and how to work within that environment, but perhaps even more importantly, there were two people there. One, Sergio Grinstein, that we collaborated with, and another, Brian Williams, who just was in the lab down the road, that helped me when there was no reason for them to do so, and that really became a point of saying well, you've got to pay forward.

[00:39:00]

That, I think has led to a lot of what I talked about, about building teams, about sharing, about putting technologies in place, making them available to others. I have won, I think almost every mentoring award that the institution offers. I'm not sure I consider myself a good mentor, but it really is paying attention to how you could help others, without it having to be something that benefits you directly. That was something that Brian Williams taught me. I handed him a grant of mine to look at and he said, "This is horrible, now here's what you do." I think that's the other part of mentoring. Mentoring isn't being nice. Mentoring can be tough love, and that's a little hard for people to understand. It's much easier to just be a cheerleader, but that doesn't really accomplish as much as you do saying you know hey, here's something you need to work on, this is a problem. Here are some things that are great, you have to keep them going and excited, but it is really the part of saying, I'm going to do the tough things and if somebody hates me for it that's fine, it has to be done.

[00:40:18]

Tacey Ann Rosolowski, PhD

[00:40:22]

Tell me more about that environment, because you said it was just so exciting and you've been unable, despite effort to recreate it.

[00:40:29]

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Gordon B. Mills, MD, PhD

[00:40:29]

I think that part of it is my fault. It was an environment where everybody interacted freely with each other. We criticized aggressively. I think that we had a run of over twenty papers in a row, that were accepted without substantial change, because if it got out of our Friday morning lab meeting it was at a state where it was mature and had been beat up, and we had gone over every possible weakness. Unfortunately, it has been hard to recreate that with the trainees that I have had. Most of them are not as aggressive and willing to speak up, and part of it may well be the fact that they wait for me to speak, and that's something that I've not been able to get around and build. So, I tried many times, and to a degree have decided that a different approach works now. I think it was a different time, all of the people in the lab were Canadian or American, and had come in with a very different attitude towards how you would move things forward. We now have a lot of foreign graduates who are sufficiently nervous with their language, that they just don't speak up in the same way, and also culturally, you don't question the professor. I can say that my exit interviews with visiting scientists have frequently been ones that I've gone into with dread, because I bring them in infrequently, will just let them go and do things, and I'm worried that they say well, I didn't get enough of your attention and all the rest.

[00:42:26]

But they have universally said, you taught me one thing and one thing that is important; science needs to come from bottom up, not top down. The European and even more so, the Asian system, is the professor tells you what to do. They may come in and say you will do exactly this today, without any understanding of why, and that system does not use the incredible power of these young trainees, to take their creativity, to help and direct, but not to instruct. I think that has been one of the rewarding points out of saying boy, did I do the job that I wanted, rather yes, there's an environment here that says I need to build my own project, I need to figure out how to make it work, and if I fail it's my responsibility, not my boss's. I think it's an approach that has worked for me. It doesn't work for everyone, doesn't work for all of my trainees. I've had a few that said this is just not the right environment for me, and I've helped them find positions elsewhere, but it's one that has worked. I have a very successful group of trainees, and so it's been, I think a very good approach for those where it's appropriate.

[00:43:54]

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Chapter 04

A: Overview;

The Challenging Job Market for Researchers and for Team Scientists

Codes

D: Understanding Cancer, the History of Science, Cancer Research;
C: Professional Practice;
C: The Professional at Work;
C: Mentoring; D: On Mentoring;
B: Education; D: On Education;
C: Leadership; D: On Leadership;
D: On Research and Researchers;
D: Business of Research;

Tacey Ann Rosolowski, PhD

[00:43:55]

That theme, of the fellows and trainees having an energy that they bring to an environment, that's something that's come up in other interviews. Other people have observed too, that that energy is really important for the senior researcher, because it keeps them moving, energizes them.

You're nodding, so I guess you've had that experience.

[00:44:17]

Gordon B. Mills, MD, PhD

[00:44:18]

The most exciting thing about being a department chair at MD Anderson, and anywhere indeed, is the ability to bring in not just trainees, but junior scientists, and watch them mature into the potential that they have. That excitement, I think is what keeps most of us going, but the system right now, with very few positions being available and the over-training, or training too many individuals, and having troubles finding positions where they can use the skills that they acquired during their PhD and their postdoc, has become painful. I, unfortunately, spend far too much of my time and effort with people from other labs, and to a degree from my own lab, saying that the career you envisioned, of moving through the ranks, from assistant to associate to full professor to department chair, is something that, in the current environment, is not going to happen for you. Sometimes, it's not having the right type of skills. Science is a very weird combination of thinking broadly, working narrowly, of being obsessive compulsive and creative, and indeed, in a number of the psychological testing programs, most scientists are in the very narrowest group of individuals, and also intrinsically conflicted. They're not necessarily the most well adapted people in a social environment, because it is a unique set of contradictions that one has to have. But the other part right now is you also have to be lucky, and not just being good enough to know that you were lucky, but you have to be lucky in picking a project that works, that will succeed, that is topical, and will help you get a position. I can tell you that it's not just MD

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Anderson. I have a number of grants where I mentor at a distance, meaning that I work with a number of people, usually at Harvard, and they're having trouble finding jobs, with beautiful CVs. But if you have a two-body problem, two academically oriented people or two professionals, it can be almost impossible to find an outstanding job. Or if you're geographically restricted because of your spouse, it is very difficult. One of the brightest, most striking young scientists that I've met, at Harvard, has been looking for a job for over two years, a beautiful CV, beautiful productivity, and has only had four or five interviews. He finally has a job and it's a great job, but it's taking an incredible amount of time to get there and many people are moving into career paths that are not what they had expected or fully utilizing the skillsets that we try to give them, to become a successful scientist.

[00:47:49]

Tacey Ann Rosolowski, PhD

[00:47:50]

Now is it that the jobs are so niched, in other words, they're looking for such specific qualifications or research interests? What's the cause?

[00:48:01]

Gordon B. Mills, MD, PhD

[00:48:02]

I think there are many. The first one is, is that this is a unique time when both industry and academia are contracting. The funding that drives academic research is the National Cancer Institute, the National Institutes of Health, and they have in essence, had a flat budget, which means with the rate of inflation in science, it's a decreased available funds to move forward. Further, there was a massive expansion in the doubling of the budget and the era effort, where many new scientists were brought onboard. And so there really are not a lot of available positions. I think the other problem that has happened is that the length of working time for most people has been extended, and so instead of turnover and opening up positions for bright young scientists, there are a lot more people working into their late sixties, seventies and even eighties, at this point, than there were ten and twenty years ago. And if you look, science went through another expansion about twenty years ago, thirty years ago, and those individuals are still in the system. And so I think that right now, we are training far more people than there are going to be available positions for qualified individuals, over the next ten to fifteen years. That's not just my opinion. I think that's a very broad opinion.

[00:49:43]

I'm not clear what we should do about it. We have, in the past, been able to direct people to industry, to patent law, to other areas, but those are now no longer expanding at the same rate. It's just a bad time, when many different things have come together to make it very hard to find jobs. One of those is, is that much of what we do has coalesced. I think there are thirty departments at MD Anderson with the name molecular in their title, which means all of them use

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molecular biologies, molecular genetics, technologies that are very similar, and there's not an enormous amount to distinguish different individuals in terms of looking for positions. So, people from our group, who can do the mathematics behind systems biology, big data, and do wet bench work to validate that, are finding positions. People who can cross between bioinformatics and wet bench work are finding positions. So it's really being a little bit different but not too different, that gives you a unique opportunity to find a position. And then the best, and there's no question, the best and the lucky, and those two do need to go together, are finding positions. It's not that there are none. It's just that we are training more people than there are positions for, in academia today.

[00:51:21]

Tacey Ann Rosolowski, PhD

[00:51:24]

This actually, you picked up a lot of themes that other people have talked about. When I interviewed Robert Bast [oral history interview], he talked a lot about training too many individuals. On the one side it's very sad for fields that are obviously exploding, and these individuals are making huge progress, and then on the individual level, how painful for these folks not to be able to use their training, use their passion.

[00:51:52]

Gordon B. Mills, MD, PhD

[00:51:52]

Well, and I think one of the challenges that we have is in this concept of team science. So, how does a member of a team establish that they deserve to be an independent investigator and build their own teams, or as importantly, how do you recognize the person who is in the midst of thirty people in a paper, who was an absolute critical component of making that paper happen, but it isn't obvious. This has worked in physics, where you will have an average paper with 150 to 200 authors, and they are frequently alphabetical order, and you have no idea, by looking at the paper, who did what. Instead, it is a community where recommendations and interactions are far more important than publications, whereas in the biological sciences over the last twenty years, it has been your publication list that matters, much more so than the interactions you have with others in finding positions. And so I think that we are in a time where we just don't have a good model, and that model, I think has to change.

[00:53:14]

Tacey Ann Rosolowski, PhD

[00:53:19]

Would you like to go back to Toronto?

[00:53:20]

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Gordon B. Mills, MD, PhD

[00:53:20]

Sure.

[00:53:21]

Tacey Ann Rosolowski, PhD

[00:53:22]

And all of these digressions, by the way, are fabulous.

[00:53:25]

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Chapter 05

A: Professional Path;

From Immunology to Targeted Therapy; More Observations about Team Science; Research on Interleukin-2

Codes

A: The Researcher;
A: The Administrator;
C: Leadership; D: On Leadership;
C: Mentoring; D: On Mentoring;
D: On Research and Researchers;
D: Business of Research;
D: Understanding Cancer, the History of Science, Cancer Research;
A: Overview;
C: Discovery and Success;

Gordon B. Mills, MD, PhD

[00:53:27]

In Toronto, a number of things happened. As I mentioned, I did my postdoctoral fellowship with a wonderful group of people at the Hospital for Sick Children. I then accepted a position at the University of Western Ontario, to continue my interest in the fetuses and allograft, in a Department of Obstetrics and Gynecology, but that position never happened.

[00:53:57]

Tacey Ann Rosolowski, PhD

[00:53:57]

Oh, okay.

[00:53:58]

Gordon B. Mills, MD, PhD

[00:54:00]

The department chair came to me one day and said, "I need to come see you," which was a ninety mile trip for him, and that can never be good. He came in and he said, "The lab that I promised you will not be available for two years. You can do whatever you want, we'll pay you, you can do a sabbatical, but you're not going to be able to take up your position now. We still want you." So all of that was good, but in reality, one cannot take two years off, and that meant that I needed to look for a position, and I found a very nice position across the street, at the University of Toronto Hospital or University of Toronto and the Toronto Hospital, and that ended up leading much more to my interests in signal transduction as a therapeutic target and was really the beginning of a move from a strictly immunology lab, into a combined

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immunology, targeted therapy program.

[00:55:08]

Tacey Ann Rosolowski, PhD

[00:55:09]

And so this was, the year was 1989?

[00:55:14]

Gordon B. Mills, MD, PhD

[00:55:15]

No.

[00:55:15]

Tacey Ann Rosolowski, PhD

[00:55:15]

No, 1985.

[00:55:17]

Gordon B. Mills, MD, PhD

[00:55:16]

Eighty-four, eighty-five, in that area. And a couple of things happened in that process that also became very important for learning how to lead a group and manage people. Two things happened. The first one is, is that the group that I worked in had a completely open laboratory system, meaning that we shared everything, and I was the only essentially full-time researcher. I actually did not see a patient for seven years, in order to get my research laboratory up and running at the level that I wanted it to be, and that meant that I became very much the de facto coordinator of how one would make an open lab team science approach work. During that time, my boss came to me and said, let's make this formal, and so I became the Head of Oncology Research at the Toronto Hospital very early on in my career, and basically had a group of nine hematologists working for me.

[00:56:42]

Tacey Ann Rosolowski, PhD

[00:56:42]

That was 1990. Yeah, I noticed that.

[00:56:46]

Gordon B. Mills, MD, PhD

[00:56:47]

That's fairly early.

[00:56:48]

Tacey Ann Rosolowski, PhD

[00:56:48]

Yeah. No, I did notice that, yeah.

[00:56:50]

Gordon B. Mills, MD, PhD

[00:56:51]

That very much continued to push my direction from pure immunology, into translational aspects of immunology, and a signal transduction program. One of the other things that happened during that time is that Lou Siminovitch, who was the head of the research institute across the street and to a degree had been the main competitor for my postdoctoral supervisor, who ended up moving out of town, took an interest and spent a lot of time talking about how to manage people, manage departments, manage groups, and I think probably did more to help me understand how one works to evaluate and build and maintain a team. He had no reason to do so. I did collaborate with his daughter, who was one of the scientists at the time, but this just became a very, I think powerful and great relationship. We met for breakfast, I would say once a month, and every time I go back to Toronto now, I still meet with him, usually for breakfast but sometimes for lunch or dinner. It just really added another level of here is why you would do things, what you would do, and again, the idea of paying forward. There was no reason for him to do anything to help me, none whatsoever. I was in a competing institution, I did not work with him, and so it was again, a very powerful learning experience.

[00:58:51]

Tacey Ann Rosolowski, PhD

[00:58:52]

Now, let me ask you, because I mean this is quite a while ago. I imagine, you know, as team science is becoming more and more -- people are recognizing that this is the way that certain research has to happen, but I imagine there was also kind of a lack of formal information about how you make it happen. So these breakfasts and drinks in the bar and lunches, where people shared this information, was kind of the way people were figuring out how to do it. What was the state of team science at the time?

[00:59:30]

Gordon B. Mills, MD, PhD

[00:59:32]

Very simple, there was none.

[00:59:34]

Tacey Ann Rosolowski, PhD

[00:59:34]

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There was none.
[00:59:34]

Gordon B. Mills, MD, PhD

[00:59:34]

Everybody was recognized for what they did in their lab as a group and really, the concept of doing more and going beyond that, was something that really was not happening at that time. It just was not something in the biological sciences that was really even being discussed at all. However, there was a component in the Canadian system that is important, and that is, is that the grants and the amount of money that was available is much less than that in the American system, and that meant in order to bring projects to completion, you had to interact and collaborate with others. There were no labs with fifty and sixty people, which I saw almost in shock, when I came to the American system, and further that again with spreading money around, which is how the Canadian system worked, forced collaborations and interactions. We weren't calling them team science, we were calling them collaborations. To a degree, it was a variant on team science, but not really quite there. It's a transition where you would have two or three labs work together, that would change, and you might alternate who was last author or first author, but it was not really a formal building of teams that would cross boundaries. I think that started in my career, through interactions with Joe Gray, after I moved to the MD Anderson Cancer Center.

[1:01:16]

I would say that he is probably even more of a proponent for the concept of team science than I have been, but this is someone whom I collaborated with when he was in San Francisco, Berkeley, and now in Portland. It didn't matter that he wasn't here physically. We built a collaboration where we would alternate papers, where we would share concepts, postdocs, ideas, and started the concept that you really do need to have broad teams to make progress as efficiently as we can in the current environment. I think the team science concepts are much more driven by translational research and patient care, where you are trying to say my goal is to make a difference for patients and patient outcome, in the near future. That really does require a much more team orientation than, I'm trying to improve basic science knowledge, which can really be done in a different environment. And I do not want to imply that one is better than the other. The individual who builds that knowledge base by deep, consistent study of a specific area, is what the team science builds on. These are not diametrically opposed, it's not that one is better than the other; it is that certain people are ideally suited to one, certain people to the other, but that translational area, I think really demands the team science concepts much more broadly than some of the basic science areas.

[01:02:58]

Tacey Ann Rosolowski, PhD

[01:03:00]

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Just for the record, how do you define translational science or translational research, because I've gotten a lot of answers to that question.

[01:03:11]

Gordon B. Mills, MD, PhD

[01:03:14]

People have asked me, how do you define systems biology, and I will say that it's a little bit like one of our Supreme Court judges, "I don't know how to define pornography, but I know it when I see it." And I think that that is very much where we are in a definition of translational science. I think it really is a concept that says the direct goal, not the long-term goal, of the program, is to change patient outcomes. So, a basic science program that discovers a new area such as the identification of CRISPR as a new tool, is not designed to directly impact patient outcomes, but is going to have an incredible impact on how we do that. That's the type of research where you say curiosity research eventually could have an incredible impact, but it's not directly aimed at altering patient outcomes. Translational research says the goal of this project is, within a reasonable period of time, to change how we manage patients.

[01:04:35]

Tacey Ann Rosolowski, PhD

[01:04:36]

I like that. So, Toronto Hospital, and the evolution of your research with signal transduction.

[01:04:49]

Gordon B. Mills, MD, PhD

[01:04:50]

My interest, as an obstetrician and gynecologist, in cancer, had always been ovarian cancer. It became clear, during some of that process, that ovarian cancer and breast cancer were related, and that by studying one and comparing to the other, you could learn a lot more. And so I became more and more at that interface and further, with my interest in immunology and being head of what in essence here, would be a department of hematology, that continued my interest in liquid tumors and in the immune aspects. But it came to the point where we were doing more and more around ovarian cancer, the immune system and ovarian cancer, and how those worked together to result in what was happening to patients.

[01:05:54]

Tacey Ann Rosolowski, PhD

[01:05:55]

What kinds of studies and what were the impacts on patients?

[01:05:57]

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Gordon B. Mills, MD, PhD

[01:05:58]

Well, so one of the things that I did very early in my career was to identify interleukin-2, LAKs, and TILs, which very much, through development by others, became a method of management of melanoma, renal cell carcinoma, and is still beginning to see its major application in terms of tumor immunology and immunotherapy.

[01:06:38]

Tacey Ann Rosolowski, PhD

[01:06:39]

You mentioned two terms there. You said identifying interleukin-w, LAKs and TILs.

[00:06:45]

Gordon B. Mills, MD, PhD

[01:06:45]

L-A-K-s, and T-I-L-s.

[01:06:48]

Tacey Ann Rosolowski, PhD

[01:06:50]

And just, can you give me the layperson's definitions of those?

[01:06:51]

Gordon B. Mills, MD, PhD

[01:06:52]

These are tumor infiltration lymphocytes and lymphokine activated killer cells, which is where the interleukin-2 came from. There were many people involved in this and in no way would my name be attributed to that, other than by a few in the field, but it was something that we had done.

[01:07:14]

Tacey Ann Rosolowski, PhD

[01:-07:15]

What was the piece that you contributed to this work?

[00:07:17]

Gordon B. Mills, MD, PhD

[01:07:21]

We worked on what became one of the key regulators in the immune system interleukin-2, before it was even called interleukin-2, and identified, along with others, its ability to activate and promulgate the growth of lymphocytes, and that it was a key regulator. There are now many

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other interleukins, but the fact that this was number two meant it was very early on in the process. That was when I was a graduate student, and continued to characterize how interleukin-2 worked, how it stimulated the T-cells and how they perceive their environment, and to a degree that continues to be used in how we now are attempting to trick the immune system into attacking tumor cells. And then the other aspects of what I did was identification of a novel series of growth factors that play a major role in progression and growth of tumor cells, and those have now led to criminal trials, targeting those pathways both in cancer and in acute macular degeneration, which is a related disease, because both require angiogenesis and new blood vessels. Those trials are still ongoing and that, I think linking all of that to ovarian cancer came to the point of where I was recruited here.

[01:09:02]

Tacey Ann Rosolowski, PhD

[01:09:03]

Tell me about that.

[01:09:04]

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Chapter 06

A: Overview;

Recruited to MD Anderson; A History of Translational Research at MD Anderson

Codes

A: Personal Background;
A: Joining MD Anderson;
A: Critical Perspectives;
B: MD Anderson History;
B: MD Anderson Culture;
C: Healing, Hope, and the Promise of Research;
C: Leadership; D: On Leadership;
D: On the Nature of Institutions;
C: Patients; C: Patients, Treatment, Survivors;
B: Growth and/or Change;

Gordon B. Mills, MD, PhD

[01:09:04]

Well, I got a call. Bob Bast and I had been to multiple different meetings together. He had attempted to recruit me to Duke twice and it just did not work out. Then I got a call one day saying I'm going to MD Anderson, we want you to come and set up the best ovarian cancer research program in the world, we have the resources to do so, and I said well, you know, "Don't I need to come down and interview?" He said, "No, the job is yours." How do you say no?
[01:09:39]

Tacey Ann Rosolowski, PhD

[01:09:40]

Yeah, no kidding.

[01:09:41]

Gordon B. Mills, MD, PhD

[01:09:42]

And so, that resulted in me moving and to a degree, even more of a switch from my immune aspects of what I was doing, through really focusing on tumor biology, tumor molecular genetics.

[01:09:59]

Tacey Ann Rosolowski, PhD

[01:10:00]

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You said, How can you say no but well, you could have. What did the job offer you? Why were you ready to leave where you were, you know what was the decision about?

[01:10:10]

Gordon B. Mills, MD, PhD

[01:10:11]

There were two pushes and one pull, and I think that always happens in any recruitment. My wife is American, she was born in California.

[01:10:21]

Tacey Ann Rosolowski, PhD

[01:10:21]

Her name?

[01:10:22]

Gordon B. Mills, MD, PhD

[01:10:23]

Kris, K-R-I-S-T-I-N, and absolutely interested, at that time, in coming back to the U.S. There were aspects of living in Canada and I think that being interested in moving to the U.S. was part of it. The second piece was that many of the things I wanted to do in terms of taking the laboratory and translational research we were doing, to clinical trials and patients, was difficult at that time in Toronto. And I think the statement I made when I came, and I continue to make; there is no place in the world with a greater potential to make a difference for patient outcome than the MD Anderson Cancer Center. Now, I want to emphasize the term potential. That potential, I think really has not been achieved at the level many of us would like. We've done incredible things, but we are still talking about potential.

[01:11:35]

Tacey Ann Rosolowski, PhD

[01:11:36]

Why is that?

[01:11:36]

Gordon B. Mills, MD, PhD

[01:11:38]

I think there are many reasons for why is that, but they are ones that are evolving and changing, and it is difficult to change and improve patient outcomes, and so that process I think that many of us thought was going to be much more rapid than it is, is really just a demonstration that this is a very, very tough process.

[00:12:04]

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Tacey Ann Rosolowski, PhD

[01:12:06]

So it has more to do with the actual difficulty or complexity of the subject matter? I mean, are there certain structural or systemic things going on?

[01:12:16]

Gordon B. Mills, MD, PhD

[01:12:17]

There are many structural or systemic things going on at the MD Anderson Cancer Center and I think that there have been many changes. One of the challenges that was here when I came was the reputation, and I think appropriately so, that MD Anderson was led in the translational area, by a bunch of cowboys who were going to do what they did.

[01:12:42]

Tacey Ann Rosolowski, PhD

[01:12:45]

And you're talking about the '70s.

[01:12:46]

Gordon B. Mills, MD, PhD

[01:12:46]

Mm-hmm. That the MD Anderson way was different and not necessarily integrated into this concept of sharing and team science that I've been talking about, and I think that that clearly was true. I think that potentially, because of where MD Anderson is, it had been very difficult to recruit and retain an incredible cadre of basic scientists that could drive that process, and that to a degree, I don't think the institution really had decided what it was. Was it a research university, was it a cancer center? Was it really dedicated solely to making improved outcomes for patients, and what were its strengths, weaknesses and advantages. Indeed, shortly after I came, we I think put together one of many visions for the future, that we have gone through, and I think that it was a time of evolution. There was an evolution in science in general, but MD Anderson really was a unique institution that really didn't integrate well with the rest of the community at that time.

[01:14:14]

Tacey Ann Rosolowski, PhD

[01:14:13]

You mean the surrounding community.

[01:14:16]

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Gordon B. Mills, MD, PhD

[01:14:18]

Well, no, national and international.

[01:14:18]

Tacey Ann Rosolowski, PhD

[01:14:18]

International as well, yeah.

[01:14:19]

Gordon B. Mills, MD, PhD

[01:14:19]

We were cowboys, gunslingers.

[01:14:21]

Tacey Ann Rosolowski, PhD

[01:14:21]

And had that had reputation, absolutely, absolutely. No, that's very interesting, and I'm also just kind of clicking in a little late in the day, because you came to the institution in '94.

[01:14:33]

Gordon B. Mills, MD, PhD

[01:14:33]

With "Mickey" LeMaistre.

[01:14:34]

Tacey Ann Rosolowski, PhD

[01:14:34]

With Mickey LeMaistre, or Charles LeMaistre, right, for the record, yeah, exactly. So this was before John Mendelsohn came, and John Mendelsohn being much more known as someone who had gone bench to bedside, right?

[01:14:46]

Gordon B. Mills, MD, PhD

[01:14:47]

Dr. LeMaistre was a cardiologist and really had done a very good job of managing MD Anderson, and of moving it forward at an important time. For reasons that I cannot really completely understand, we became very good friends and colleagues. If I give a talk anywhere near where he is, he and his wife will attend, if they have questions, they pick up the phone and call me. I was in his office for some very difficult discussions and concepts and listening to him struggling with the transition of leading the institution, to passing it on to a new leader and

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whether he should have rebuilt many of the systems to make it easier for the new leader, or as the regents asked, just leave it alone, let the new leader build it in the way he wanted to do. So it was a very interesting interaction for me.

[01:15:50]

Tacey Ann Rosolowski, PhD

[01:15:52]

Yeah. Did you kind of glean any lessons from that, I mean, kind of observing someone think about organization at such a high level.

[01:15:59]

Gordon B. Mills, MD, PhD

[01:16:[00]

I think there is a real question of what the outgoing president should do in terms of setting up systems for the incoming president. There were significant structural problems at MD Anderson at that time and actually, some of them still remain.

[01:16:18]

Tacey Ann Rosolowski, PhD

[01:16:18]

Can you kind of itemize?

[01:16:20]

Gordon B. Mills, MD, PhD

[01:16:20]

Yeah, I'll give you a couple that are polite. For example, our divisions and departments are backwards and that makes great difficulty outside, and to a degree internally, for people to understand what their roles are. So, is a department chair really a department chair, or are they a division head in any other institution? So the structures that were put in place at MD Anderson, to a degree were, I think unnecessarily complex and not really following an easily understood process. Some of the others, we had had a vice president for research who had very much separated the clinical and basic sciences and translational sciences, and left behind a very difficult legacy to deal with and to harmonize across the institution. That really was one of the challenges that John Mendelsohn [oral history interview] inherited, with Fred Becker [oral history interview] having been in place. I think that when Fred came to MD Anderson, that probably was a necessary process in that the basic sciences really needed to be built almost from scratch, but by the time I came, I think this had become a major problem. There were concepts of a research institute separate from the clinical aspects that really, I think was a challenge that needed to be resolved and changed. I think the vestiges of this are still there.

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[1:18:17]

There are still people who do not see MD Anderson as a translational engine, that being our renewable, competitive advantage that we should build on, versus those that still believe we should have a pure curiosity research program within MD Anderson, because that could lead to things that are exciting, and how to cross those boundaries and make them the most efficient and profitable. And again, with my basis around translational science and helping patients, I think that we have very much more so embraced the concept that we really are a driver of change in patient management, and that is our renewable competitive advantage. The number of patients we see, the unbelievably dedicated doctors and staff in a freestanding cancer center --and that is an interesting process and there aren't many of them-- but basically that's what we are and what we do. We are not a university that has a cancer center sort of as an adjunct or an important aspect of it. That is our whole basis to exist and it has a big advantage.

[01:19:49]

Tacey Ann Rosolowski, PhD

[01:19:52]

You were talking about some of those -- your conversation with Charles LeMaistre and some of the kind of lessons you learned from watching someone kind of process.

[01:20:02]

Gordon B. Mills, MD, PhD

[01:20:03]

I think that one of the things that leaders need to do is to be change agents and to a major degree, put in place the processes that will allow success. That means that they have to be the drivers of harmonizing the system, decreasing the bureaucracy, orienting every person in the institution for success, rather than protecting their job and their butt, and if I ever hear another person say, Well, the regents or system won't let me do this, when it's really an excuse not to do something, that really has to come from president down. Even though you would love to see it being an organic growth up, that's the one thing that the people down can't influence, and it really needs to be sort of a senior leadership saying that we will put everything in place to let the people that are going to make a difference, make a difference.

[01:21:21]

Tacey Ann Rosolowski, PhD

[01:21:27]

You were talking about being recruited here.

[01:21:30]

Gordon B. Mills, MD, PhD

[01:21:31]

I was recruited here and I think the comment to make is that Mickey LeMaistre [oral history

interview] had one management style. John Mendelsohn let the institution grow organically. His job, in his mind, was to bring in the resources, to put the buildings in place, to bring in new faculty, to give them an opportunity to flourish. In his mind, every single individual we recruited would be successful if we gave them the appropriate support, mentoring, and resources. I'm not sure that I necessarily agree with that. You do make mistakes and you need to deal with those, but his belief really was in an organic growth and very much bottom up. He put the resources in place, the others were to make it happen, and there really wasn't a lot of planning that led to setting of priorities. It really was planning of, Here are interesting opportunities to move forward and we can make everything move concurrently. We have a new president who, I think has almost exactly the opposite point of view, but again, both of those can work in the right environment. There are ends of spectrums of management and it's not one is right or one is wrong, but rather, what Dr. DePinho [oral history interview] came in with, is the concept of saying it is time to ask the question of whether making major progress in translational research is an engineering and implementation question, or is this still a case where we lack the basic knowledge to do so? And so he brought in a much more focused, driven program, to say can we make a difference in a short period of time? Both are right, both work, both have strengths and weaknesses, and one of the challenges that we are seeing now is still five years out, the transition from one model to another model, that in each case can make a difference.

[01:24:00]

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Chapter 07

A: The Administrator;

Major Roles Building Translational Research

Codes

B: Building/Transforming the Institution;
B: Growth and/or Change;
B: Obstacles, Challenges;
B: Critical Perspectives on MD Anderson;
D: On the Nature of Institutions;
C: Leadership; D: On Leadership;

Tacey Ann Rosolowski, PhD

[01:24:05]

I'd like to return to this question about the leadership a little bit later, maybe after we've talked about some of your roles, but I wanted to talk a little bit about what happened when you first got here, you know how you began to fit into the institution, what you saw, how you proceeded, because this was a new role for you. What were your goals?

[01:24:32]

Gordon B. Mills, MD, PhD

[01:24:33]

I had two major, or I guess three major roles, when I came to the institution. One was to take what had been a very long-term department and rebuild it, and indeed, of all of the people that were in the department when I came, none of them are in the department now. That process happened fairly quickly, with one exception, and that is the ex-department chair of the department did stay in the department, which is already an administrative challenge that worked. Most of the people with a lot of work and evaluation, we helped find positions that were much better suited for their skillsets, usually elsewhere.

[01:25:26]

Tacey Ann Rosolowski, PhD

[01:25:27]

Now what was the issue there? What were the skillsets? How were the skillsets defining the department and how did you want the department to change?

[01:25:37]

Gordon B. Mills, MD, PhD

[01:25:37]

To a degree it was one of excellence. I think that because the department chair had been in place for a long period of time, that some of the turnover that needs to happen. The recruitment of

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bright, new faculty, I tend to call them kids, I shouldn't, but bright new faculty who will drive a much more active vision of the future, had not happened in that department, and I think to a degree had not happened across MD Anderson. I also think it was a time when we were switching from, as I mentioned, this idea of an insular basic research program, into a translational research program that would make a difference, and very much my vision and I think the vision of many people in the institution, of the future at that time. That meant that we needed to help people who really didn't fit into that model find positions at more classic universities, where they did fit into the model. And so it was very much a transition time.
[01:26:55]

Tacey Ann Rosolowski, PhD

[01:26:55]

Who was the department chair?

[01:26:58]

Gordon B. Mills, MD, PhD

[01:26:58]

Jordan Gutterman [oral history interview], and he's still here as a retired professor and I still work with him, and I will meet with him again this afternoon.

[01:27:06]

Tacey Ann Rosolowski, PhD

[01:27:06]

Well, say hello to him for me. I interviewed him a few years ago.

[01:27:10]

Gordon B. Mills, MD, PhD

[01:27:10]

He did some incredible things, but it was time for a new chair. Actually, I think this is one of the problems at MD Anderson. Many of the departments, on the research side in particular, are cults of personality, driven by a very dominant department chair. Actually, I shouldn't say that, that's across the institution. And we see, as many of these department chairs are stepping down, great challenges in trying to rebuild the departments around a new leader. And so the strong leadership, the cowboy attitude, the cults of personality, are very much there. And do we need a Department of Cancer Systems Biology if I wasn't here, would clearly be a question that I would expect to be asked. It's one that my vision and the vision of the people I've recruited have driven. Is it an institutional vision? Not as clear. And I think that applies to every single department that we have. The way in which they are molded and directed has been very much dependent on the department chairs.

[01:28:27]

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Tacey Ann Rosolowski, PhD

[01:28:27]

Well and also, to be fair, dependent on department chairs who are reacting to a particular moment in history, in their fields and at the institution.

[01:28:36]

Gordon B. Mills, MD, PhD

[01:28:37]

And also as part of retention. These are incredible people that we are trying to retain, because they really do make a difference, and so part of that, in many cases, is building a department around them. So, all of those statements are true, but I think it really has become clearer, as a number of our department chairs have stepped down recently, just how powerful the leaders of a number of departments have been in setting vision and managing people, and how much of a challenge that can be after they leave. We really don't do a very good job of recruiting our successors, recruiting, retaining and growing them. Now, one of those is, is that most of them get recruited elsewhere, and it actually is good if your best people are not being offered jobs that are unbelievably good elsewhere, you're not doing a good job. I recently had a faculty member who came to me with a job offer and said well, aren't you going to retain me? And I said well, there are two reasons; one, you've already signed. If you wanted me to retain you, you would have had to come to me before you did. I will not let you renege, because that is not going to look good in your career. Second; this is an unbelievable offer, go. I mean, you're going from being an assistant professor, to being head of an institute and being deputy director of research in the hospital. Go. I mean, this is what I want to see. But, that means he's not going to be here as a successor, but again, that's a wonderful choice and chance, and we do have many of our best people being recruited away, but if you don't, you're in much worse shape. The challenge is, is then what do you do with the ones who don't get the job offers, and that was a little bit of what I talked about in the turnover that was necessary in the department or at least the part of the department that I inherited.

[01:30:45]

Tacey Ann Rosolowski, PhD

[01:30:47]

Now you were listing a few things, a few roles that you had. One was rebuilding the department. What were some of the other tasks you took on?

[01:30:53]

Gordon B. Mills, MD, PhD

[01:30:53]

The second role that I had was deputy head of the Division for Research, and my goal was to really help to evaluate, grow, and improve research, the translational research aspects, across the division, and I think that was one of those that worked. I think that we probably could have done

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a better job of it, but it was a time when that was difficult.

[01:31:28]

Tacey Ann Rosolowski, PhD

[01:31:28]

Tell me about that process and tell me about the success and then the well, we could have done this better, just to get a portrait of what was going on at the time.

[01:31:36]

Gordon B. Mills, MD, PhD

[01:31:36]

This was a time, again, of change. The whole concept was not so much whether team science should be the driver, but where was translational science within a clinical division and what degree of basic science should you have. Where should they live, who could you recruit to bring in bright, new blood into the system? That, as I said, needed change. Who would be willing to move to MD Anderson at that time, with its reputation, which was not one of having strong science and supporting strong science? It wasn't one where it was clear that its potential could really be fulfilled. And then, finally, in terms of recruiting family, this is not the first people think of, of moving to, and much more so when I came here, where the city was simply not as vibrant. I mean it closed down at nine o'clock, there was nothing downtown. Now there's lots of neat things going on. So, it was a very difficult environment to recruit to. And so all of those pieces were together, and at that time, it was a buyer's market. There were more good positions than there were good people, and so there were lots of people recruiting everywhere.

[1:33:05]

Part of our job was to recruit and I don't think we managed to land many of the people that we should have. And indeed, I mean I'm excited in one way, sort of the first ten people we interviewed are all leaders in institutions, many of them now cancer directors. We did a great job of identifying some incredible people that would have made a difference but landing them was hard, and so that's the strength and weakness of it. The other that I inherited shortly after I came was our Clinical Cancer Genetics Program. This was just as the opportunity to deal with BRCA-1 and 2, in terms of cancer risk and genetic counseling was coming to the fore, and I was asked to build that program. I had done some of that in Toronto, for five or six years, and then headed that program here for seven years, helped write the Texas Genetic Confidentiality Bill, which was signed there, which protects patients from discrimination based on their genetic background. All of those things were part of what I was building at that time. I was also asked to help build our breast cancer program here, which was not nearly as strong as it needed to be on a translational level. We had already built an incredible ovarian cancer program, which continues, and so those are sort of the early things that I was asked to take on, in addition.

[01:34:56]

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Tacey Ann Rosolowski, PhD

[01:34:57]

Now what was your personal vision, you know, what did you want to accomplish when you came here?

[01:35:04]

Gordon B. Mills, MD, PhD

[01:35:04]

You know, one of the things of having a computer is that every once in a while, you come up with old files when you're looking for something else, and one of the things that I was asked to do when I came, was to put together a vision for the future. That vision for the future is very much what I am doing now. It really was to take our absolutely rapidly burgeoning knowledge of why cancer was occurring, and build programs that would implement that into patient care. So, that sort of evolution came with my being requested to head the Kleberg Center for Molecular Markers, or actually more specifically, building it based on a donation that we arranged from the Kleberg family, of that eventually becoming the Khalifa Institute for Personalized Cancer Therapy, and then evolving a little bit further.

[01:36:10]

Tacey Ann Rosolowski, PhD

[01:36:10]

Oh, okay.

[01:36:10]

Gordon B. Mills, MD, PhD

[01:36:11]

But really, these were sort of step-by-step programs of going from identification of what was happening in tumors, the basic biology and genetics of cancer, through to molecular markers, which was the Kleberg Center, through to implementation in patient care, which is the Institute for Personalized Cancer Therapy.

[01:36:35]

Tacey Ann Rosolowski, PhD

[01:36:35]

Wow, interesting. Well, we're almost at eleven o'clock, and this sounds like a preview of coming attractions to me. Would it be okay if we sit another session?

[01:36:45]

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Gordon B. Mills, MD, PhD

[01:36:45]

Sure. I'm not sure I'm the right person but I'm glad to do this.

[01:36:48]

Tacey Ann Rosolowski, PhD

[01:36:49]

Listen. I would just say all of this is gold, from my perspective, so if you're willing, I'd be --

[01:36:56]

Gordon B. Mills, MD, PhD

[01:36:56]

Sure.

[01:36:57]

Tacey Ann Rosolowski, PhD

[01:36:57]

That would be great. Well, thank you very much for your time this morning and I'm going to be turning off the recorder now, at about ten fifty-four.

[01:37:07]

[End of Session]

Gordon B. Mills, MD, PhD

Interview Session Two: July 1, 2016

Chapter 00B

Interview Identifier

Tacey Ann Rosolowski, PhD

[00:00:02]

Today is July 1, 2016, and I'm Tacey Ann Rosolowski, and today -- let's see, it's about two minutes of two in the afternoon, and today I'm in the Zayed Building for my second session with Dr. Gordon Mills. Thanks for taking time today before the holiday weekend.

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Chapter 08

B: Building the Institution;

Department Names Reflect Shifts in an Institution and in Cancer Medicine

Codes

B: MD Anderson History;
B: Building/Transforming the Institution;
B: Growth and/or Change;
A: Joining MD Anderson;
D: Understanding Cancer, the History of Science, Cancer Research;
D: Technology and R&D;
D: On the Nature of Institutions;
C: Research, Care, and Education;

Tacey Ann Rosolowski, PhD

[00:00:02]+

You said that you wanted to kind of talk about, bring me up to date on the department. I'm interested in all of this from a pretty broad perspective. You came in 1994, as section chief for Molecular Therapeutics, and I'm real interested in kind of the crucible of things that was at work for the transformation of the Department of Systems Biology.

[00:00:51]

Gordon B. Mills, MD, PhD

[00:00:54]

Dr. Robert Bast was being recruited to the MD Anderson Cancer Center, to be the head of the Division of Cancer Medicine. He had attempted to recruit me to Duke University, where he had been several times, and that just simply did not work out for a variety of reasons. When he was pretty sure that he was coming to the MD Anderson Cancer Center, he called me and asked whether I would be interested in coming to the MD Anderson Cancer Center, and having the resources available to build the preeminent ovarian cancer research program in the United States and indeed, across the world. The initial recruitment was to head the section of molecular therapeutics, but with the clear plan that as soon as it was approved by the institution and the regents, to have me head the Department of Molecular Oncology. The term molecular oncology was chosen really, to leave the opportunities for in the directions that that department would go, almost completely open, so that molecular oncology really covers almost all aspects of cancer research that are being done today, and one of the key emphasis was to be on ovarian cancer, but it was not to be restricted to ovarian cancer. So with that title and positions and resources, we recruited a number of individuals into the department and continued to build the Molecular Oncology Department.

[00:02:56]

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Tacey Ann Rosolowski, PhD

[00:02:57]

Can I ask when was that department formally established?

[00:03:00]

Gordon B. Mills, MD, PhD

[00:03:00]

That year.

[00:03:01]

Tacey Ann Rosolowski, PhD

[00:03:01]

That year, so 1994.

[00:03:02]

Gordon B. Mills, MD, PhD

[00:03:02]

Just later in that year. It might have been '95 by the time the paperwork was done.

[00:03:07]

Tacey Ann Rosolowski, PhD

[00:03:09]

Let me ask you one other question, which may be obvious, but why was Dr. Bast so interested in posing that question to you?

[00:03:18]

Gordon B. Mills, MD, PhD

[00:03:21]

Well, I think that the idea that MD Anderson had the opportunity to become the world leader in his area of interest, by bringing together what he was doing, what I was doing, and adding additional opportunities to recruit and build, and really with the concept that you want to be the best at whatever it is you do, and it is probably far better to be the best at a smaller area than mediocre at everything. So this was part of an idea of saying that focusing in on ovarian cancer and building that program would be an incredible opportunity.

[00:04:05]

Tacey Ann Rosolowski, PhD

[00:04:06]

I was remembering too, how much of our conversation last time was about collaboration and a mentality of collaboration, and I'm wondering if that factored into it as well.

[01:04:17]

Gordon B. Mills, MD, PhD

[01:04:18]

Bob Bast and I actually shared a lab physically when I came, and so clearly, there was a strong collaboration. We had collaborated both conceptually and in publications, and so I think that a very big part of his interest was knowing that I was collaborative and would build a collaborative program. The Department of Molecular Oncology thrived, did well, and then -- and I can get the year for you, I don't have it at my fingertips, -- Mien-Chie Hung [oral history interview] was being recruited to Wisconsin and as part of his retention package, he was offered to be the department chair of a department, and he wanted to designate that department cellular and molecular oncology. That was obviously too close in name to the Department of Molecular Oncology. But with consultation, it became clear that retaining Mien-Chie as an outstanding scientist was sufficient, that we would change the name of the department to Molecular Therapeutics, which we felt would be as flexible and as open. That turned out not to be correct, and so Molecular Therapeutics really, to a degree, was restrictive. It was felt that the department, both perception and internally and externally, and with external advisory board reviews, needed to be focused on therapeutics, and really, the department was much broader in interest than just the implementation of therapeutics. When Garth Powis was recruited to the MD Anderson Cancer Center, to head the Department of Experimental Therapeutics, it became very clear that we needed to revisit the title of the department and the goal of the department, in such a way as to give it a distinct identity and make it clear that we had a role that was different from other departments in the institution.

[00:06:44]

Tacey Ann Rosolowski, PhD

[00:06:44]

Can I ask you just a quick question here, because it's like there's proliferation of all of these departments that are doing these things. What is that reflecting, [in] what is going on in science?

[00:06:58]

Gordon B. Mills, MD, PhD

[00:06:58]

You were actually a sentence ahead of me, so I was going to answer that question. Part of this had to do with the fact that there, at that time, were a large number, and there's now a larger number of departments with the name molecular in their title and indeed, if you look across the departments at the MD Anderson Cancer Center, both the clinical departments and the research departments, in many cases it is extremely difficult to differentiate those departments on goals, missions and vision. This happened really, because of a convergence of both concepts and technology, and development of new technology to where the opportunity to characterize tumors at a breadth and depth in terms of molecular characteristics, DNA mutations, RNA levels, protein changes, became available, and indeed, most major shifts in science are driven by new

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technology, not by necessarily new concepts. The technology allows those concepts to happen and to occur. For example, the ability to sequence DNA at a relatively inexpensive level, to characterize what's happening at RNA, were technological changes that then allowed a massive change in the way in which we approached cancer. So, those came together to really, a great convergence of approach across departments.

[00:08:43]

Tacey Ann Rosolowski, PhD

[00:08:44]

And that was happening consistently across institutions in the U.S.?

[00:08:48]

Gordon B. Mills, MD, PhD

[00:08:48]

Oh yeah, the whole world. Now there's a difference with MD Anderson as compared to a university. University teachers and with a teaching program, you will have a program or a teaching program in biochemistry, organic chemistry, in physiology, in anatomy; things that you don't have here at the MD Anderson Cancer Center. You have to maintain the ability to teach across those boundaries, and so you have to have people who specifically do pharmacology, physiology, cell biology, because of the educational need for a major university that teaches at the undergrad level. The departments at MD Anderson have sort of two roles. One is to be an academic organizational principal of a reasonable size to deal with, and so that most of the departments have a strong leader, some of them, as in the case of Molecular and Cellular Oncology that I mentioned a few moments ago, were created because of an outstanding person that we wanted to retain and give the opportunity to build, but they're really not driven by a need to teach across different boundaries. So as technologies arose and approaches arose, the actions and the activities and the people in those departments became more and more convergent.

[00:10:26]

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Chapter 09

B: Building the Institution;

The World's First Cancer-Directed Department of Systems Biology Emerges from a Shift in Approach to Cancer

Codes

A: Overview;
B: MD Anderson History;
D: On Research and Researchers;
B: Building/Transforming the Institution;
B: Growth and/or Change;
D: Understanding Cancer, the History of Science, Cancer Research;
D: Technology and R&D;
D: On the Nature of Institutions;
C: Research, Care, and Education;
B: Research;

Tacey Ann Rosolowski, PhD

[00:10:27]

Does that make -- I don't know how to ask this question. I've been struck by how rapidly fields change. I mean as I talk to folks like you, involved so deeply in research and you know, I've been struck with the need for people to remain kind of very mentally flexible or be passed by. Is that true? How does that have an impact on departments? You kind of understand the area I'm trying to get into here.

[00:10:59]

Gordon B. Mills, MD, PhD

[00:11:00]

One of the things that you see across academia is that you have fairly rigid boundaries between different areas, and those are really detriments. So, someone who trained as an immunologist may be stuck doing immunology, even if their interests change, because they're in a department of immunology, where you have to teach immunology and you're seen as an immunologist. Similarly, molecular biology and the rest, and that can be restrictive. The MD Anderson Cancer Center, to a degree, because we don't teach undergraduate education and have to retain those particular boundaries, there is a much greater opportunity for flexibility. That flexibility on the basic science side is really quite striking. It can be a little more problematic on the clinical side, where someone for example, is in a department of breast medical oncology and their interests and concepts then change to where studying brain cancer would be most appropriate for what they're doing. You then have an intrinsic stress of where they are located, who they are working with, the potential lack of critical mass that would help them move forward, and so we have a bit of a mixture of both.

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[00:12:32]

The flexibility and the ability to change is critically important. Indeed, my career has changed massively. I started off as an immunologist in biochemistry and trained and worked on tumor immunology, which has now come to the fore, but that was over forty years ago now. I then evolved because of a move to Toronto, and where things were going into a joint program on the tumor biology of ovarian cancer and tumor immunology, or immunology in general. I moved here and became very much more of a molecular biologist, focused on initially, ovarian cancer, but at the request of Mickey LeMaistre saying that our ovarian cancer program has grown and matured to the degree where we had a SPORE, a P01, multiple R01s, top level investigators in the area. He asked if I could help build two different programs. One was our clinical cancer genetics program, which needed additional support and work, and the other was to help take our breast cancer program to the same level that the ovarian cancer program was, and indeed, we then took the breast cancer program to where we had a DoD program project grant, an NIH program project grant, and a SPORE grant. Again, all of those cases, in all of those cases, I was not the leader of any of those grants. My job was to help them happen, the concept of collaboration and support.

[00:14:22]

Tacey Ann Rosolowski, PhD

[00:14:24]

What was your strategy? I don't know if you want to talk about one of those programs of if you want to go back.

[00:14:29]

Gordon B. Mills, MD, PhD

[00:14:30]

Well why don't we finish off the department evolution first, and then we can go back.

[00:14:33]

Tacey Ann Rosolowski, PhD

[00:14:33]

Sure.

[00:14:34]

Gordon B. Mills, MD, PhD

[00:14:36]

So, at the time that Garth Powis arrived, the confusion that had arisen over a department of experimental therapeutics and molecular therapeutics, and how they were different, had really come to the fore. Indeed, this is a problem in many cases across MD Anderson, or a challenge perhaps. When we had a Department of Biochemistry and Genetics, if you were to ask

individuals, they couldn't tell you why they were in which department. Both of them were focused primarily on genes and development, and there really wasn't much of a distinction and indeed even today, if you were to go through all of the faculty at MD Anderson, from the outside, and say why, with the work they do, are they in this department versus that department. Not are they appropriate for this department, but why specifically that department. You would have great difficulty answering that question; it's the convergence of so many different approaches. So at that time, it had become very clear that the approaches that we were using, basically reductionistic approaches of studying molecules one at a time, in depth, was not going to be sufficient to help us understand the true complexity of what was going on in cancer, and that we needed a much more integrative program.

[00:16:11]

We looked aggressively across all of the different areas and groups and really decided that we needed to develop an integrative biology or a systems biology department, to capture that unique opportunity of linking an integration of information across many different areas. A mathematical model building part that comes to be integrative, or systems biology. Now, at the MD Anderson Cancer Center, integrative biology or integrative care, has really been used quite extensively to refer to alternative therapeutic approaches. Things like medicines that have come out of China, and we needed to have a title that clearly separated us from that particular area. So, of that point, it became clear that systems biology or cancer systems biology was the appropriate terminology, and so we decided again, to make sure that it was separate from some of the other groups and had a clear identity, on the term and name Systems Biology. This was the first cancer specific or cancer directed Systems Biology Department in the United States, and as far as we can tell, in the world. This really was built very much around the concept that we needed to go beyond the reductionistic, one molecule at a time, to make progress. Now, I want to emphasize systems biology builds on that reductionistic approach. It's not that that's bad. It's a great and necessary step. This is to add a layer on top of that and stand on sort of the shoulders of the incredible work that has been done elsewhere and is still being done here. And so that's what we built and I think it has been highly successful. It is recognized nationally and internationally as the first and one of the best, cancer systems biology departments.

[00:18:49]

Tacey Ann Rosolowski, PhD

[00:18:50]

Can you give me a window into that process, because I mean, so you're looking around and what are you seeing in terms of the landscape? Is it a mixture of people taking a more reductive approach and people experimenting with other things? How did you begin to bring together this new approach?

[00:19:08]

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Gordon B. Mills, MD, PhD

[00:19:09]

So, if we were to perhaps give you a little flow to this, I had spent years and as many of my colleagues had spent years, what we call drawing arrows. Molecule A affects molecule B, molecule C is affected by both A and B. That is necessary and it's critical, but it becomes clear, when you start adding three or four of these, that you simply can't understand that by drawing arrows. Linear arrows are not how biology works. Biology works by some key pathways, no question, but with massive amounts of modifiers, feed forward, feedback regulatory loops that allow the cell to perceive its environment, and then to process an incredibly complex amount of information and give the appropriate functional outcome. That integrative process of all of these things coming in, really was not understood and when I started basically --and I use this slide still when I teach this to students-- we had this idea that cells perceive their environment and they had an outcome of what they would do. We simply, at that point in time, drew what was called a black box in the middle. That black box was clearly perception, integration output, but we had no idea what went on in that box. For many times we thought, in again a reductionistic manner, that it was one or two key events. Whether it was calcium changes, which I studied for years, protein kinase-C, that was thought to be the key integrative molecule of this process, and clearly, that's too simplistic. No one thing can allow interpretation of a complex environment. And about that time, we developed the pathways and the processes that integrate that information, but when you draw them, there are so many arrows and diagrams that it's again, back to being a black box, because it is incomprehensible.

[00:21:38]

There's just too many things that the human mind cannot deal with all of them at once, and how that integrates. So, about that time, we decided we needed to do something different, and the goal is, is can you then build mathematical models of those processes that allow you to understand how that information is integrated into the appropriate response. The piece behind that is, if I can understand that, and I can understand how it went wrong in cancer, we have the potential then, to target the processes in a much better way of saying I love this molecule because I've studied it for my whole life, it must be the target that is critically important, and maybe it's not because it's not the key integration point or it's not rate limiting. So the idea was to get away from our favorite molecule, to a process oriented concept. There's another way to describe systems biology. What we do most of the time in reductionist science could be alluded to as studying the brick, a brick in great detail. Is it red, is it heavy, is it light, is it porous, and understanding every possible aspect of a brick. But by understanding that, how do you understand what a house looks like, and even more importantly, how a house is a house or whether a house is a home. Take this a little further along and perhaps even the better way of dealing with this, where it is very challenging, is to say well, go to a Roman ruin, when you have a pile of rubble, and that's our understanding of how the cell is and what it works. So we've got this pile of rubble. Now how do you take that and put it back together to get a building? This is what Schliemann tried to do and in some of the things he built, where they were just completely

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wrong. It is absolutely clear now that what came out of this had nothing to do with what was there. But the real challenge is, is not to reconstruct the building, but from that pile of rubble, figure out what the culture was, and that's what we're trying to do in systems biology. By having enough information on the pieces, those little blocks and bricks, to start to understand not just how they come together physically, but how they interact conceptually to go from the bad illusion here, a house to a home, which is a totally different process, but that's where as good a description as I can come up of, of what systems biology is.

[00:24:33]

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Chapter 10

B: Building the Institution;

A Controversial Department Evolves: On Recruitment, Flexibility, and the Value of Failure

Codes

A: Overview;
C: Discovery and Success;
D: On Research and Researchers;
B: Building/Transforming the Institution;
B: Growth and/or Change;
D: Understanding Cancer, the History of Science, Cancer Research;
C: Professional Practice;
C: The Professional at Work;
C: Collaborations;
C: Leadership; D: On Leadership;
D: On the Nature of Institutions;
B: Research;

Tacey Ann Rosolowski, PhD

[00:24:34]

How did the department evolve from this idea that this had to happen, to something that's now recognized as being so important?

[00:24:42]

Gordon B. Mills, MD, PhD

[00:24:43]

Some of the things that happened is evolution of people, so I took a lot of what we were doing and started to move it in that direction. Now, I have an outstanding team that can drive processes of that level, but we also were allowed to recruit, by the institution. I had had a number of positions that were promised in my recruitment package, but for various reasons were put on hold for a period of time, and those were released, and we specifically went out to recruit people who could cross those boundaries. Some of the people we were recruiting were more reductionist oriented, with an understanding that the systems approach were important. Others were very much mathematically oriented but understood that the biology was important. So my goal was to bring in people that had the different skillsets, put them in physical proximity, and give them the support to begin to build such a program.

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Tacey Ann Rosolowski, PhD

[00:25:50]

Who were some of these folks?

[00:25:51]

Gordon B. Mills, MD, PhD

[00:25:52]

Well, my department members. Prahlad Ram is one of the few individuals who does a really good job of both the math and the laboratory wet bench work. We have brought in Ju-Seog Lee, who integrates information across human, mouse, and genomics. Phoebus Lin, who has done a similar job of trying to understand not how molecules are involved in DNA damage repair, but rather understand DNA damage repair somewhat agnostic to which molecules are involved. The idea here is to understand concepts and focus on concepts, rather than I studied P-53.

[00:26:45]

Tacey Ann Rosolowski, PhD

[00:26:46]

Interesting.

[00:26:47]

Gordon B. Mills, MD, PhD

[00:26:47]

Now, we need people who study P-53 or we can't build those concepts. This is not an either/or, it's not a good or bad, it's a level that needs to happen on top of everything else if we're going to integrate what some outstanding scientists like Gigi Lozano are doing with P-53, into what's happening in terms of alterations in signaling, and putting those together. That's what the systems biology is. It's an integration of all of that information or at least an attempt to do so in a manner that allows it to become comprehensible. There's also a precept that if we build models, you will learn two or three things. One is, is if your model works, great, you know a lot of what you need to know, but if you build a model, you're going to find many of the times it doesn't work, which means you are missing something. And so the idea that a model will tell you that the pieces you thought worked don't fit. The other is that sometimes in building a model, there are new concepts that arise, that are not immediately obvious from other approaches, so these types of new knowledge that come out of a mathematical process, that can't be picked up by other approaches are also important.

[00:28:19]

Tacey Ann Rosolowski, PhD

[00:28:20]

Can you give me an example?

[00:28:21]

Gordon B. Mills, MD, PhD

[00:28:22]

Well, if I was to give you an example, I guess here, a pretty good one I guess. So we draw one of the pathways that we work on, a nice vertical model. And so we've looked at that and we've built the math around that, and we've done that in great detail in a number of cell lines and a number of cell systems, and as soon as we move from one to another it doesn't work. Now that says that even though we think of this as an irreducible, canonical pathway that works this way in every cell, that's wrong, because if it did, if I built a model in one cell it would work in others. The answer is, is these pathways are very different in almost cell lineage, and normal cells and potentially in almost every cancer, and that the different pieces interact differently, sometimes subtly, sometimes quite massively. The other is, is when we built this, there were things we just couldn't explain, no matter how hard we put every piece together, and what it turns out is that there are other pathways out there that impinge very strongly on the PI-3 kinase pathway, and we simply hadn't been paying attention to them. And finally, what we thought in terms of the output of the PI-3 kinase pathway, down at the bottom, from many animal models and other studies, as being the key part and the PI-3 kinase being the key regulator, it turns out that that's not true, that although the PI-3 kinase pathway regulates that output, there are other pathways that are just, and actually more important in that process, in the epithelial cells we study for cancers, epithelial cancer, as compared to the fibroblasts, where those models were developed. So, the fact that you build a mathematical model and it doesn't work, or it does work, you learn things that you can't learn otherwise. Those are called emergent properties, things that emerge that you could not have predicted by approaches you were using otherwise.

[00:30:47]

Tacey Ann Rosolowski, PhD

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I'm smiling because it's so often there are conversations about how failures are not made public, but failures are kind of the way people learn.

[00:31:00]

Gordon B. Mills, MD, PhD

[00:31:01]

Now you're going totally off topic. One of the most challenging lectures that I ever gave was a colloquia at Rice University. Rice University assigns a topic across the whole institution, this is not just biology or cancer, it's to be very broad, and one year the topic was failure. Now they asked me to give a talk and I'm going, Is this supposed to be a message, have I failed, or is it that they want me to talk about cancer as a failure of biology, which I think is probably what they wanted. But what I decided instead to present was the fact that we are not allowed to fail, and that if we are not failing most of the time, we're not doing high enough risk studies. The whole way in which this field, and the institution operates, is that failure is considered a problem, a major problem, and in many cases a fatal problem, where in contrast, if you don't fail most of the

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time you're not trying hard enough to do something different. And so I think that as I said, this took a lot of work, to try and put this together in a way that made sense and would be an acceptable and broadly interesting lecture across all of the different fields; across engineering, across the biology, across music. And so the challenge of this being a very broad audience, and I think a critically important target that we haven't dealt with. If you go to NIH for a grant, if you basically haven't done it all already and know what the answer is, you're not going to get funded. What is funded right now, where funding is tight, is in general so low risk, as to be not worth doing. Now that doesn't mean that good things aren't done with the money that is given out to the investigators, but if there's even the slightest potential problem, it will be destroyed by a study section. I have an example that I love, which is a colleague of mine had put a grant in and it was being reviewed, and it had nine parts to it, and one of the reviewers says, I'm really worried about this part, and went on for thirty minutes or so, describing one part of the grant that was a problem. I'm a very young investigator and finally I stopped them I said, you know, let me ask you a question.

[00:34:01]

Tell me about the problems or strengths of the other eight-ninths of this grant, and they said oh, this is the most spectacular things I've ever read and I said well, do you know you are in the process of killing this grant because it has one part that you don't like? Would it matter if they never did that one-ninth? No, of course not, the rest of it is incredible. Then why are you telling me about that? Why aren't you telling me about what's great about the rest? But that's where we are now. We are so conservative, that if there's a little problem somewhere, we'll focus in on that and use it as a reason to say well, you know, we shouldn't fund this because it has one little flaw. Contrast. That flaw says this guy or this person is trying to do something a little more challenging and risky, and you need to have that, and so you shouldn't expect everything to succeed. If you do it's boring, it's predictable. And so I think we've gotten into a place where things are far too safe. I must admit that perhaps setting up the Department of Systems Biology, which was not safe, was not necessarily supported broadly.

[00:35:21]

Tacey Ann Rosolowski, PhD

[00:35:21]

I was going to ask about that.

[00:35:22]

Gordon B. Mills, MD, PhD

[00:35:22]

Because people didn't understand what it was or why. It was a very interesting and challenging step.

[00:35:30]

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Tacey Ann Rosolowski, PhD

[00:35:31]

I was going to ask if it was a controversial move.

[00:35:34]

Gordon B. Mills, MD, PhD

[00:35:35]

Vastly so.

[00:35:36]

Tacey Ann Rosolowski, PhD

[00:35:37]

Yeah. And what were the comments that people made?

[00:35:39]

Gordon B. Mills, MD, PhD

[00:35:40]

Well, some people said that this is just an aspect of everything else, there's nothing independent about it to warrant there being a department. Others said we've never seen anything like this, it's different so therefore it can't be good.

[00:35:54]

Tacey Ann Rosolowski, PhD

[00:35:55]

Can't be good. Change is hard.

[00:35:59]

Gordon B. Mills, MD, PhD

[00:36:[00]

That's right. Finally, the other was, is well it's risky, why would you do something risky, let's stick to what we know. We don't see how this will necessarily help us understand what is happening in cancer. We also had an external review board come in and one of the people on the review board says well, I have somebody in my lab that does that, I can't see why you would want to do this broadly, it shouldn't be independent. And I had investigators, very senior investigators in the institution, come and tell me I should resign because I had made a bad mistake, it wasn't a great idea. So you do get that type of response whenever you publicly say, I want change. Now you can frequently make change happen just by doing it quietly, but this was very public. Because it was a new name, it had to go to the regents, it was a new direction, it had to go through multiple different committees. But in the end, there was a clear understanding that if this worked, if we made this process better than it was, it would be very worthwhile.

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[00:37:10]

Now, this has gotten to the point where the National Cancer Institute, the Library of Congress, actually have grants specifically related to this area. There is a variant of systems biology called computational biology. The difference to a degree is a computational biologist generally doesn't do wet bench work. They really just do the math, whereas a wet bench biologist doesn't do the math, and you sometimes get them to work together. Our goal is to have people who can work with, or at least across both sides, and make this happen in a better way, but even the computational biology is now one of the areas of emphasis of CPRIT, saying we need the ability to take this incredible trove of information we're generating, the amount of information we're generating, and find ways to begin to make sense out of it so that you can then test this experimentally. What we do is try and do both of those. Now, one of the other things that we have done is bring in collaboratively, a fairly large number of computational biologists or bioinformaticians in this case, in to close and strong collaborations with the department, where we will provide data, resources, ability to test hypotheses, to the computational biology group and vice versa. If they come up with something neat, a concept that we will test those hypotheses, if possible, experimentally, for them, and that back and forth has been, I think very important for the success, not just of department members, but of many across the institution.

[00:39:13]

Tacey Ann Rosolowski, PhD

[00:39:13]

The department was founded in 2006.

[00:39:16]

Gordon B. Mills, MD, PhD

[00:39:17]

Yeah.

[00:39:18]

Tacey Ann Rosolowski, PhD

[00:39:19]

And I mean it's ten years later. So what was the arc of acceptance, you know the profile of the department within the institution?

[00:39:29]

Gordon B. Mills, MD, PhD

[00:39:30]

I'm not sure I'm the right person to answer that question.

[00:39:31]

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Tacey Ann Rosolowski, PhD

[00:39:32]

Well, you know, it's your perspective.

[00:39:33]

Gordon B. Mills, MD, PhD

[00:39:34]

Yeah, I guess it's my perspective. I think conceptually, it is extremely well accepted within the institution, and I think there are two reasons for that. One is, it is a group of very good scientists and we've maintained that level and that bar by bringing in new people, turning over people, helping people find new career positions. Some of them have gone on to be from assistant professors in my group, to be co-directors of research institutes. So, it's been very productive for those that have stayed and for those that have left. But I think within the other part that I've emphasized, the group is collaborative and that means we help a lot of other people do more than they could do otherwise. Further, we've done a massive job of setting up technologies and supporting those technologies and making them available to others in the institution, nationally and internationally. One of the platforms we've developed, which is our protein array platform, which is necessary for this type of a process, to develop information on a large number of proteins in perturbed systems, has now had over a hundred and twenty thousand samples sent for analysis, with about half of those from outside of MD Anderson and from all around the world. And so that type of data generation support of others, because we need it for ourselves, but them immediately make it available to others, I think has resulted in the department being highly accepted. And then I put a lot of effort as a representative of the department, into trying to make MD Anderson a more successful institution. So I think it's come across very well.

[00:41:43]

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Chapter 11

B: Overview;

The Cancer Genome Atlas and the Positive Side of Serving as Department Chair

Codes

C: Discovery and Success;
B: MD Anderson Impact; C: MD Anderson Impact;
B: Research;
C: Leadership; D: On Leadership;
C: Mentoring; D: On Mentoring;

Tacey Ann Rosolowski, PhD

[00:41:44]

And it sounds as though the department has had an impact in the sense that it's making new things possible. Can you give me an example of an outside department that was able to do something new?

[00:41:59]

Gordon B. Mills, MD, PhD

[00:42:00]

Well, probably the biggest impact of what we have done is on the cancer genome atlas. The Cancer Genome Atlas that was originally constituted, was to look at DNA and RNA only, and through pushing very hard and covering much of the costs from my own flexible sources, we have now run the majority of the samples from the Cancer Genome Atlas, providing a DNA, RNA, and protein data source that can now be integrated, not just here at MD Anderson but around the world. That has led to well over a hundred papers just looking at that one aspect of DNA, RNA, and protein integration, and at least in terms of the collaboration with the Cancer Genome Atlas, that's more than thirty papers, in *Nature*, *Cell Science*, *New England Journal of Medicine* or equivalents, where this information has contributed markedly to the construction of those documents. So it has been very powerful.

[00:43:19]

Tacey Ann Rosolowski, PhD

[00:43:20]

So, is there anything outside of what you've already sketched, that you feel has been achieved over these ten years?

[00:43:29]

Gordon B. Mills, MD, PhD

[00:43:30]

We have accomplished one of the key things that I think is why one wants to be a department

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chair. There are sort of two major areas of being a department chair on the positive side. The negative side is that comes with a massive administrative load that one needs to do, so you can do the fun things. The two pieces are to support, mentor, and allow junior faculty to develop, and I mentioned one of those in terms of faculty who have now going elsewhere and are having major impact. The other is exactly the same concept around trainees. And so we have had many trainees come through the department, who are now in many places around the world, providing related impact to what we are doing and bringing out the concepts that we bring forward with in terms of collaboration of systems biology, technology development, and sharing. And so those are the two biggest things that we have accomplished.

[00:44:50]

Tacey Ann Rosolowski, PhD

[00:44:51]

Is the field different now than it was ten years ago?

[00:44:55]

Gordon B. Mills, MD, PhD

[00:44:56]

The field of systems biology or cancer research?

[00:44:58]

Tacey Ann Rosolowski, PhD

[00:44:59]

I'd say cancer research, given the emergence or the coalescence, if you will, of systems bio.

[00:45:07]

Gordon B. Mills, MD, PhD

[00:45:08]

Well, so if I use here, a broader term perhaps, for a while, of integrative biology, which is saying that systems biology and integrative biology, computational biology, are all absolutely necessary components of the process of dealing with the high quality, massive datasets that we are now available -- sorry, able to develop in terms of patients, animal models, cell lines, all of the other pieces that you're looking at, with thousands of DNA sequences available across patients here. Nineteen thousand is a point right now. RNA analysis in thousands, protein analysis in the thousands, and how you now integrate that information in a way you couldn't do before, but even more than that, that you even think that you could do this. I mean, if I talk about some of the things we're doing today in the Institute for Personalized Cancer Therapy and in the department, and if I had talked about those ten years ago, I would have been laughed out of the room, saying you'll never be able to do that, it's a physical impossibility, not doable. So yes, we've totally changed because of the new technologies that have come out, to look at DNA, RNA, at a massive level, and to a degree, the maturation of technologies that let you look at protein, and

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then manipulate those through things like SIRNA, SHRNA, and CRISPR technologies, our ability to analyze, assess, perceive, manipulate, perturb, repeat the process around the cycle, to develop and test hypotheses, is just happening at a scale that couldn't be conceived of ten years ago. It's also mind boggling and frightening, because I can't do much of the math and the analysis that my colleagues do. I can't go to a computer and solve a partial differential equation, it's just not within my skillset any more, and so seeing that those areas have matured massively and that by bringing in the right people and the right technologies and what we do, providing the data that they need to move it forward and see it moving, is both very rewarding and again, something that couldn't have happened ten years ago.

[00:47:50]

Tacey Ann Rosolowski, PhD

[00:47:51]

There are a number of other roles that you served, in addition to shepherding all of this, and I'm not meaning to make a radical subject change here, because I have a feeling they're all interrelated. Should I give you a break here?

[00:48:06]

Gordon B. Mills, MD, PhD

[00:48:07]

No, that's okay.

[00:48:07]

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Chapter 12

The Kleberg Center for Molecular Markers

B: Building the Institution;

Codes

B: MD Anderson Culture;
C: Leadership;
B: MD Anderson History;
B: Building the Institution;
A: Overview;
D: Ethics;
A: Definitions, Explanations, Translations;
C: Discovery and Success;
C: Donations, Gifts, Contributions;
C: Discovery, Creativity and Innovation;
D: The History of Health Care, Patient Care;
D: Politics and Cancer/Science/Care;
D: Technology and R&D;

Tacey Ann Rosolowski, PhD

[00:48:08]

Okay. I wanted to maybe go back, because when we were talking, kind of doing the identifier for the last session we had together, you know, you made sure to mention that you were head of the Kleberg Center for Molecular Markers in 2004, and you're still serving a role over there. Do you want to talk about that and kind of show how it maybe was working in parallel with some of these developments? Oh, dear.

[00:48:37]

Gordon B. Mills, MD, PhD

[00:48:38]

No, no, no. I want to say this in a way that doesn't come across wrong.

[00:48:42]

Tacey Ann Rosolowski, PhD

[00:48:43]

Okay, sure, yeah.

[00:48:43]

Gordon B. Mills, MD, PhD

[00:48:44]

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One of the things that I've been asked to do many times at the MD Anderson Cancer Center is to develop an area, to support an area, and then get out of the way and let somebody else move in and take it over. That's not an easy thing to do because most of the time, when you start doing something to that depth, you want to own it. So, one of the things that perhaps is one of my greater strengths or weaknesses, is a variant of adult attention deficit syndrome. I get bored real easy and want to move on to the next challenge. And so, shortly after I arrived here, I was asked to develop, as I mentioned, the ovarian cancer program, breast cancer program --we haven't talked about the clinical cancer genetics program-- all of which we built. And then my goal was then to get out of the way and let others take it over. I think that that process and showing that they were successful, resulted in the institution having confidence and perhaps trust, in what I did. So nothing predicts future success any better than current success. My boss, who loves -- my postdoc boss, who loves aphorisms, says, "A plow horse is never going to win the Kentucky Derby." You know, what you're going to be or how someone is going to behave by what they did in the last five years, predicting the next five. And so with that, I was asked to put in a proposal to the Kleberg Foundation, to build a molecular markers program and we did that. It was not required by the Kleberg Foundation, that we call it a center, or use their name in the center, but given the significant, or at least what I thought was very significant, investment, that was part of what we did, and they've supported us quite extensively over time.
[00:51:03]

Tacey Ann Rosolowski, PhD

[00:51:04]

So this was philanthropic support.

[00:51:06]

Gordon B. Mills, MD, PhD

[00:51:07]

Oh, absolutely.

[00:51:07]

Tacey Ann Rosolowski, PhD

[00:51:08]

I was going to actually ask you, I'm not meaning to shift gears here, but I was going to ask you, when we had the NIH discussion, who was funding more innovative research, and is this an instance of a philanthropical source taking that kind of risky step.

[00:51:26]

Gordon B. Mills, MD, PhD

[00:51:27]

One of the ways to describe this is we have three types of funding that are available right now; that from the major funding agencies, which in general are extremely conservative and in general

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very, I guess sort of cap out. Once you've got a set amount of money, it's very hard to get any more, and to try and use those funds for truly risky projects is hard. Every penny that comes in from philanthropy, into our group, we estimate that we leverage sevenfold, give or take, with NIH grants, other foundations, industry, and use, to a very major degree, the philanthropic funds, to do high risk, high yield, exploratory projects that are going to fail most of the time or much of the time, and use that to build the information that you can then get funding from the more conservative agencies. Now, the Kleberg Foundation support --
[00:51:48]

Tacey Ann Rosolowski, PhD

[00:51:49]

I'm sorry, can I just ask you one question?

[00:51:49]

Gordon B. Mills, MD, PhD

[00:52:50]

Sure.

[00:51:51]

Tacey Ann Rosolowski, PhD

[00:51:51]

Because you said there were three funding sources, and I think I missed --

[00:51:52]

Gordon B. Mills, MD, PhD

[00:51:52]

Industry.

[00:51:52]

Tacey Ann Rosolowski, PhD

[00:51:53]

Oh, industry, okay.

[00:51:54]

Gordon B. Mills, MD, PhD

[00:51:54]

I did mention industry.

[00:51:55]

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Tacey Ann Rosolowski, PhD

[00:52:55]

Okay, yeah, you did.

[00:52:56]

Gordon B. Mills, MD, PhD

[00:52:57]

So what you have is a very conservative, very important, critically important funding source from the major agencies. And note, when funding is tight, they become more conservative. When funding is a more reasonable level, they can be just as innovative, just as supportive of new ideas and concepts, and indeed, the NIH pushes those but not through its standard approach. It's through U-grants and other more innovative programs, so they do try very hard, but the reviewers become quite conservative because money is so tight and we're so nervous. It's us, we're the problem, we're the reviewers. Industry provides funds, but most of those are for fairly targeted areas, to look at how you would develop this particular drug or this particular target. Those can be very high risk, high yield, but they're targeted and they're not going to say, Well just go ahead and follow your nose. Philanthropy, again sort of fits with both of those, to allow in many cases, truly high risk, high yield projects. And indeed, what we built, through the funds from the Kleberg Foundation, very much became the basis for the Institute for Personalized Cancer Therapy, that I now co-head with John Mendelsohn, with the idea that many of the things that we put in place, we expanded upon and really leveraged what we had, to go way further than what we were doing.

[00:54:43]

Tacey Ann Rosolowski, PhD

[00:54:44]

What were some of the first projects you undertook through the Kleberg money?

[00:54:48]

Gordon B. Mills, MD, PhD

[00:54:49]

Our big project in the Kleberg, that they funded, is something that we call T-9, which was to characterize ten thousand tumors, across ten thousand patients, to really, nine times by the time you go through all of this, to really begin to understand what was going on in cancer, something we didn't know at that time. That was leveraged, or not leveraged. That supported many of the efforts we put into the Cancer Genome Atlas. Then on a more patient oriented basis, what we did in the Institute for Personalized Cancer Therapy. We've now gone beyond the ten thousand we promised and we've done almost twenty thousand. The idea here is really, to get an idea not just of the baseline events that are happening in tumors, that was coming out of the Cancer Genome Atlas, albeit at that time that wasn't even started, to ask what's happening in our cancer patients, who are usually heavily pretreated, very difficult diseases to manage, a very different

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spectrum of patients from what was being characterized in the Cancer Genome Atlas. And so that really was what the process was and those two led together, to this program.

[00:56:04]

Tacey Ann Rosolowski, PhD

[00:56:05]

What were the kinds of things you were looking at, just so I have kind of a more concrete -- I mean these were genetic profiles of cancer tumors?

[00:56:24]

Gordon B. Mills, MD, PhD

[00:56:25]

Our initial emphasis was on DNA, and the reason it was on DNA goes back to what I talked about, the technology to do that had become sufficiently mature, that it was something that we could develop and implement. Indeed, the first technology we used to do this hadn't even been dreamed to be used for this reason. It was called a Sequenom platform, where we were able to measure mutations on a massive scale. The platform had been developed by a company, to look at what was happening in the fetus, by looking at what was going on in maternal blood, and hearing a seminar from them, I said well, if you can do this in maternal blood, just think of what I could do with a patient's tumor. We actually built this as a platform to characterize what was happening and we built it sufficiently well and robustly, that it was adopted by our CLIA laboratory, as their standard platform for measuring what was happening clinically in patients' tumors. Since then, they've moved away from this platform, to genome ones.

[00:57:23]

Tacey Ann Rosolowski, PhD

[00:57:24]

So this was your brainchild?

[00:57:26]

Gordon B. Mills, MD, PhD

[00:57:26]

Yeah

[00:47:26]

Tacey Ann Rosolowski, PhD

[00:57:27]

Okay, well, I didn't know.

[00:57:28]

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Gordon B. Mills, MD, PhD

[00:57:29]

You don't have to know.

[00:57:29]

Tacey Ann Rosolowski, PhD

[00:57:30]

I'm glad you told me.

[00:57:31]

Gordon B. Mills, MD, PhD

[00:57:32]

There's no reason to know.

[00:57:32]

Tacey Ann Rosolowski, PhD

[00:57:33]

No, but that's key, and I think also, really indicative of the sort of open territory that this is. You know idea, oh, that could be useful, adopt, put it in a new context, let's find a way to implement. What was the company that built?

[00:57:51]

Gordon B. Mills, MD, PhD

[00:57:52]

Sequenom is the name of the company.

[00:57:52]

Tacey Ann Rosolowski, PhD

[00:57:53]

Is the company, okay.

[00:57:54]

Gordon B. Mills, MD, PhD

[00:57:54]

Actually, it was one of those wonderful coincidences, in that I got a call from the development office, about ten minutes after I walked out of that seminar, saying someone wants to donate money to the institution, this is the amount, they want to buy a piece of equipment, their name would be on it, and I said well, I have got an idea for you. So, it was a very nice piece coming together. Now, we negotiated sufficiently, this company, the donor said well, you know, we're giving you the money, why haven't you spent it? I said look, be patient, give me another month or two, I'm going to get them to give me this machine. We'll use your funds then, to buy

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materials and make it run, but by having that money in my hand and saying I'm serious, to the company, I was able to more than double what we got back from the company, actually with another company and John Mendelsohn and a very similar type of sequencing process. I went to him and said look, I need you to back up a philanthropic check of X number of dollars. I will virtually guarantee that I am going to return it to you and get the equipment for free, but if I went to the company saying just give it to me, rather than saying I believe in this enough that I can pay for it but it's going to be to your advantage to give it to me, because we're going to do this, this, and this. I handed the full check back and John Mendelsohn said, "This is the first time anybody has ever done this, given me money back." I said look I didn't ask you for the money to spend. I asked you to let us leverage this in a way that happens. And I think we perhaps don't do that as much as we should. We have incredible power here, to leverage what we're doing, and it's not used, I think as well as we could. It takes time. You have to be patient, you have to do a lot of things around it, but it does really come back and accomplish much more.

[01:00:00]

Tacey Ann Rosolowski, PhD

[01:00:01]

As they say, money makes money.

[01:00:02]

Gordon B. Mills, MD, PhD

[01:00:03]

That's right.

[01:00:04]

Tacey Ann Rosolowski, PhD

[01:00:04]

Yeah. Well, I derailed you a little bit with the question about funding. Are we good?

[01:00:05]

Gordon B. Mills, MD, PhD

[01:00:14]

Mm-hmm.

[01:00:15]

Tacey Ann Rosolowski, PhD

[01:00:16]

I'm just reviewing where we were, because I had asked you for an example of a study that was done, that fed into the Institute for Personalized Cancer Therapy. Have we finished the story about the Kleberg Institute [Center], or do we need to talk about it before it segues?

[01:00:36]

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Gordon B. Mills, MD, PhD

[01:00:37]

No, the Kleberg Institute continues, and so one of the things that has come out of this -- or the Kleberg Center, sorry, it's not an institute. That's what you wrote down before. Once the Institute for Personalized Cancer Therapy was developed, we went back to the Kleberg Institute and said okay, what's the difference? Or Kleberg Center. And the first piece was, is that the Institute for Personalized Cancer Therapy is very much an implementation arm, to take technology and approaches that have been developed in other areas and implement them at a scale that you couldn't do otherwise, and to facilitate, working with pathology and lab medicine, implementation into patient care. And so the Kleberg Center focused, for quite a while, on the discovery pieces that led into and supported the implementation, and the two worked together beautifully. We, about two years ago now, took a look at where we were in the Kleberg Center, and with funds that we had left, and said maybe it's time to look at something a little bit different, still focusing on identification of markets, but in a little different approach than we had been doing. One of the things that the Cancer Genome Atlas taught us is that most of the cancers that they looked at, big diseases, are driven by fairly diverse events across those diseases. There will be ten, twenty different types of mutations that will happen broadly across the tumors, but what was coming out in a few other studies is when you looked at what were rare cancers, things that were truly different, they fell into two classes. One of those, where you look just like the common tumors; the breast cancers, the lung, the cancers of aging, where you had this diverse pattern of mutations, and you could learn from the Cancer Genome Atlas, what was going on in those.

[1:03:03]

In contrast, some of these rare tumors had a single gene mutated in almost all, and to a degree, we believe for some of them, it is all. In the cases where we can't find that is a misdiagnosis, a separate disease. An example is a very rare tumor called small cell cancer of the ovary, maybe a hundred cases in the U.S., that is caused by a point mutation in a single gene, and in almost all cases, exactly the same nucleate change, one single event. What that does is provides an absolutely smoking gun, if not more than a smoking gun, that this is a critically important gene to understand. That information can drive a lot of studying. So we have taken the Kleberg Center and now use it to focus on rare cancers, and rare here in our definition is any cancer that hasn't been studied in depth by anybody else, and using the strength of our size and number of patients at MD Anderson, to say that things that are so rare, you can't do elsewhere, we can do here. And so we have processes on really, truly unusual and rare cancers, that just couldn't be studied without a major consortia elsewhere. And by the way, we're completely willing to bring in samples from elsewhere. This is not a, we just work on our own processes, but we've used this to build a rare cancer program and find these new types of events.

[01:05:01]

Tacey Ann Rosolowski, PhD

[01:05:02]

When was that decision made? You said a couple of years ago?

[01:05:05]

Gordon B. Mills, MD, PhD

[01:05:06]

I think formalized, I would guess three years ago, two years ago, in that area, and we went back to the Kleberg Foundation and told them we were doing that and that we were reorganizing the funds that we had left. We weren't asking for new funds, simply for permission to change the direction in which we were going, and given that the Kleberg family had brought their money together based on cattle breeding and cattle genetics, this was something that they were very pleased to hear, to say okay, we get it, understanding the genetics here is important, you told us you were going to do this T-9 project, you've already told us you've done more than you had proposed and you have money left over, of course we would like to see you do more. And so that's really where that has evolved.

[01:06:03]

Tacey Ann Rosolowski, PhD

[01:06:04]

Now, what kind of -- I mean, I'm sure it's hard to say, but obviously this is not only interested in addressing these rare cancers, but this is an engine for producing new knowledge. What kind of possibilities does that new knowledge create?

[01:06:23]

Gordon B. Mills, MD, PhD

[01:06:24]

I'll give you an example again, around this small cell cancer of the ovary, this extremely rare disease. Had a particular mutation in a single gene and it is mutated across cancers, and so now instead of trying to figure out whether this was a driver or a passenger, important, not important, it's absolutely clear that this is a very important gene to study and understand not just what it does normally, but why is it abnormal in cancer. In terms of the other piece is we had been studying its closest relative in cancer, so one of these is called SMRK-4, the one we had studied is ARID-1A, and it doesn't really matter what their specific names are, but just really close family members. And because of the information coming out of the small cell ovarian cancer, we went back and redoubled our efforts to try and understand what both of these are doing, and again, in collaborative studies, some directly from my lab, some with a group in Holland, some with another group here at the MD Anderson Cancer Center, some with a group in British Columbia. We've gone in and it looks like the function of these genes in cancer may be multifactorial, again to this systems biology concept, but part of it completely unrelated to what we thought these genes did previously. They were thought to play a role and a particular

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functional complex and a particular function in DNA replication, and it looks like they do that, but in addition, do something completely different, that may be why they're involved in cancer, and we're using that to develop new therapy approaches and indeed, one of them has gone from discovery through to the clinic.

[01:08:30]

Tacey Ann Rosolowski, PhD

[01:08:31]

What is that approach?

[01:08:31]

Gordon B. Mills, MD, PhD

[01:08:31]

It turns out that we think that these particular abnormalities will sensitize tumors to a new drug that has come out and is looking very impressive, which are called PARP inhibitors.

[01:08:48]

Tacey Ann Rosolowski, PhD

[01:08:49]

I'm sorry, PARP?

[01:05:49]

Gordon B. Mills, MD, PhD

[01:08:50]

PARP, P-A-R-P, inhibitors, which were thought to be important as providing synthetic lethality, that is killing cells only if they had abnormalities in BRCA-1 and BRCA-2, the two breast cancer genes, and ovarian cancer genes, and it turns out that there may be many other things that these drugs work with. These two genes I was talking about look like their other ones in that family, and so there are clinical trials where if you have abnormalities in these genes, you can receive PARP inhibitors and we'll see if it works.

[01:09:31]

Tacey Ann Rosolowski, PhD

[01:09:32]

When did those trials start?

[01:09:33]

Gordon B. Mills, MD, PhD

[01:09:34]

Oh, about a year ago.

[01:09:34]

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Tacey Ann Rosolowski, PhD

[01:09:35]

About a year ago, yeah.

[01:09:36]

Gordon B. Mills, MD, PhD

[01:09:37]

Yeah, we think that that's not going to be enough. Single agents are not going to cure cancer. Cancer, epithelia cancers, they're far too complicated for one agent to work. We need combination therapy, that's very much what Frei [Dr. Emil Frei] and Freireich [J Freireich; oral history interview] taught us, that's what chemotherapy has taught us. Single agents aren't enough, you need combinations and you need combinations that work, and so we have a major program around how to find those, how to develop those, and we have a number of processes where we use those two abnormalities I told you about, as a base to ask what combination therapies would I use for Mrs. Green, who has an abnormality in one of those two genes.

[01:10:27]

Tacey Ann Rosolowski, PhD

[01:10:28]

Well, I'm smiling because there was an interview I did with someone who had been hired many, many, many years ago, and was working with combinations, and I said you know, how did you put these combinations together, and he said well, we would sit down and I'd say, "What have you got?" And they would write them down on a napkin. It's a different world now.

[01:10:48]

Gordon B. Mills, MD, PhD

[01:10:49]

To a degree, we only had a napkin. No. There are now a thousand drugs, give or take, that are in or about to be in clinical trials, and if you were just to think of all of the two-by-two combinations, and then layer that on top of the DNA, RNA, and protein abnormalities, to say which patients you would like to treat, you come up with a completely impossible matrix to do. We have tried a lot of hypothesis driven research, and that's been very good, it's gotten us to where we are in many cases. What we do, as our major driver of this, is to look at one type of resistance to therapy called adaptive resistance, and try and build a platform that allows us to see that adaptive resistance efficiently. That platform is our protein array platform that I mentioned earlier, and what we do simply is say treat a cell with a drug. It can be any drug, it can be any cell, most cases it's many drugs and many cells, to get an idea of what's happening broadly, and say how does the cell adapt. What changes does it make to stay alive in the presence of that stressful drug? If I now target those changes, do I see those two drugs working together in a logical manner? And with some exceptions, that has been extremely informative and has led to

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multiple combinations that make sense, and to others that we would never have come across without doing this type of an analysis. Several of them are entering or in some cases supported by this result, not necessarily driven by this project, in trial. Some of the ones that are entering trials would never have come up without this study.

[00:13:01]

Tacey Ann Rosolowski, PhD

[01:13:02]

Wow, interesting. Do you call that evidence based research?

[01:13:09]

Gordon B. Mills, MD, PhD

[01:13:10]

I call that rational combination therapy. The rational is probably what you're talking about in terms of evidence.

[01:13:16]

Tacey Ann Rosolowski, PhD

[01:13:17]

I was just asking, because you know, that is obviously a term that's used a lot, but was just curious what your term would be.

[01:13:23]

Gordon B. Mills, MD, PhD

[01:13:24]

Well, I think evidence based care is the term, patient care is where it's usually used. We try and think of hypothesis driven research, rational combinations, as compared to say, some companies that have gone out and taken all thousand drugs and done every possible two-by-two combinations on cell lines and said okay, do we find anything here that we can move forward. So far, that brute force approach has proven to be not very efficient or effective.

[01:14:01]

Tacey Ann Rosolowski, PhD

[01:14:02]

I was wondering if it's, I was going to say ethical. Is it more ethical to use the approach that you're using?

[01:14:08]

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Gordon B. Mills, MD, PhD

[01:14:09]

I don't think it's ethical in either way. I think in anything that leads you to something that can benefit patients is ethical. If you're saying is it a good use of resources, the two-by-two combinations were done primarily by companies, the random ones, and if they had the money to do that, that's their prerogative and actually goal. We didn't know if this would work. It was a test of the hypothesis that just doing enough of those would give you useful information and it's not proven to be as predictive as we would have liked.

[01:14:54]

Tacey Ann Rosolowski, PhD

[01:14:55]

Are we good with Kleberg?

[01:14:56]

Gordon B. Mills, MD, PhD

[01:14:57]

Yeah.

[01:14:57]

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Chapter 13

B: Building the Institution;

The Zayed Institute for Personalized Cancer Therapy, Part I

Codes

B: Building the Institution;
B: MD Anderson History;
B: Research;
A: The Administrator;
C: Leadership;
C: Donations, Gifts, Contributions;
B: Building/Transforming the Institution;
B: Obstacles, Challenges;
B: The Business of MD Anderson;

Tacey Ann Rosolowski, PhD

[01:14:58]

Do you want to go on to the Institute for Personalized Care?

[01:14:59]

Gordon B. Mills, MD, PhD

[01:15:00]

Sure, why not?

[01:15:03]

Tacey Ann Rosolowski, PhD

[01:15:04]

Were you in the ground floor of getting that all...?

[01:15:07]

Gordon B. Mills, MD, PhD

[01:15:08]

No, I wasn't.

[01:15:08]

Tacey Ann Rosolowski, PhD

[01:15:09]

So tell me about when you came in and why.

[01:15:10]

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Gordon B. Mills, MD, PhD

[01:15:11]

The Institute for Personalized Cancer Therapy had been developed by John Mendelsohn, with a clear understanding that this was an important area to move forward, that at that time, it looked like our greatest opportunity to have a major impact on patients and patient outcomes; matching the therapies to the underlying genomic aberrations that were present in the tumor.

[01:15:36]

Tacey Ann Rosolowski, PhD

[01:15:37]

Now, your involvement came in 2010, but remind me, when was the institute actually started?

[01:15:43]

Gordon B. Mills, MD, PhD

[01:15:44]

Probably 2006 to 2007, was the inception and implementation, and in that time period, they had initially asked Dr. Stan Hamilton and Dr. Waun Ki Hong, to manage the program. Their approach was very much to use pilot funding support to say can people build and develop, with small amounts of funds, a program that would then lead to improved outcomes based on these precepts.

[01:16:24]

Tacey Ann Rosolowski, PhD

[01:16:25]

These were philanthropic funds at the time?

[01:16:26]

Gordon B. Mills, MD, PhD

[01:16:27]

These were philanthropic funds. It's been driven primarily by philanthropic funds, at least initially. After a few years, it became clear that that perhaps was not the most efficient way to move the program forward, that the idea of a more top down, broad development program, would make sense. The institution then went out and started a search process, to find somebody who would potentially run the program, interviewed a lot of people, both internally and externally, and I think because the direction of the program was not clearly articulated and indeed, I think that Dr. Mendelsohn and a number of people hoped that the person they would recruit would articulate that direction, but if it's not articulated, do you recruit the right person, was this circular problem. They decided to again, to disband the committee and look at additional candidates, and one of the candidates that they brought in said to John Mendelsohn,

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"Why are you talking to me? You've got the right person here already." And so Dr. Mendelsohn came to me and said, "Would you consider this?" How do you say no?

[01:18:04]

Tacey Ann Rosolowski, PhD

[01:18:05]

Well you can but you didn't, so why didn't you?

[01:18:05]

Gordon B. Mills, MD, PhD

[01:18:05]

That's the story. In general, with my Canadian background, if you are asked by your boss to do something, you do it, and unless you feel that you are absolutely the wrong person and not able to do it, you would do it. It's not really a question, it's an order.

[01:18:34]

Tacey Ann Rosolowski, PhD

[01:18:35]

So in 2010, you took on that role. Did you shed some other roles in the process?

[01:18:38]

Gordon B. Mills, MD, PhD

[01:18:39]

Should have. No, not really. So there's a little more to the story. At that point in time, I was asked, by Dr. Ray DuBois and Dr. John Mendelsohn, to put together a program that would take what we had been doing in the Kleberg Center, which they were modeling this on, the fact that we'd been successful in that process, and take this another level. And so I was putting that together when, one day I got a call to come and see Dr. DuBois and Dr. Mendelsohn, to talk about this, which was fine. They wanted me there at eight in the morning, that was no problem, and then at the end of that discussion, Dr. Mendelsohn said, "I need to talk to you." Okay, when? I was on my way out of town on a trip and he says, "Today." Okay. When do you have time here? Okay, I will change my flights, I'll be there, and I come in and he says, "What do you think about me stepping down as president of the institution and running the institute with you?" So, that was kept very quiet for a number of reasons, because there was potential conflict of interest, he could not play any role in anything to do with this if he was going to play a role as co-head later on. So, it took a lot of work, a lot of time and a lot of planning and process, to where he stepped down, and we have been co-directors of the institute since.

[01:20:10]

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Tacey Ann Rosolowski, PhD

[01:20:11]

How did you go about collaborating to develop that? What did you want to achieve?

[01:20:38]

Gordon B. Mills, MD, PhD

[01:20:39]

There are two ways to move an area forward. One of the things, at that time, is there really was a very strong philanthropic support for the institution, and a pretty significant bankroll to make this happen. We looked at this and said, instead of asking for RFAs and small projects, let's take on some big questions, bring together an advisory board, but very much in the way that I like to see things happen. Get a small group of people together, build a plan, put that plan in place, and then ask others to say how should we modify this, is this something that makes sense? And took that book to internal advisory boards, external advisory boards, and said here is what we want to do, but we're going to do this big. That led to much more of a centralized planning group, but once that general process and concept was in place, we had Dr. Mendelsohn, myself, we recruited Kenna Shaw, who had been running the Cancer Genome Atlas, which I talked about, because of its scale and scope and outstanding scientific administrator who is not just an administrator, she is an active player. And then, in order to implement on the clinical side, we brought in Funda Meric-Bernstam, who was a surgeon, to help as medical director of the program, with the idea that I had worked with her and there was no one that I knew who was more able to deliver on making things happen, and we needed to do that.

[01:22:43]

Tacey Ann Rosolowski, PhD

[01:22:44]

Could you repeat her name please?

[01:22:45]

Gordon B. Mills, MD, PhD

[01:22:46]

Funda, F-U-N-D-A. Meric, M-E-R-I-C, dash, Bernstam, B-E-R-N-S-T-A-M.

[01:22:57]

Tacey Ann Rosolowski, PhD

[01:22:58]

Thanks.

[01:22:58]

Gordon B. Mills, MD, PhD

[01:22:59]

She is now also, in addition to being medical director of the institute, the chair of our phase one program, and that actually came very much out of her success in the institute, as showing that she could deliver in this area. So, it's been, I think very useful for her career development also, but very much so, the direction was driven by the four of us sitting and planning, and putting processes together and then checking, improving, checking, improving, rather than necessarily, a process of whole group in the middle, people in a room and brainstorming. We felt that putting together a plan first, and then using that to have people organize and improve, would be the way to go, and that's how we've worked the program ever since. We get lots of input from EABs and IABs and advisors, but it's been much more of a use of funds at a, to do things big that you can't do as individuals. Again, this idea of team science, collaborations, and most of what we do is support the efforts of others, but in a big manner.

[01:24:12]

Tacey Ann Rosolowski, PhD

[01:24:13]

Now, how do those collaborations work, because I remember when I was talking to Dr. Mendelsohn about this a few years ago, at that point he was talking about the need to reach out and invite people to basically make institute projects an extension of their research. So how has that process proceeded or progressed since then?

[01:24:59]

Gordon B. Mills, MD, PhD

[01:25:00]

I think that the way I would describe this is a little bit differently than Dr. Mendelsohn did. We put in place an infrastructure and resources. I mean you've sort of heard this from me before, facilitating, for example, molecular testing for cancer patients, thousands of cancer patients, that then our physicians could use that information in treating the patients, obtaining drugs, doing trials, moving things forward in their own studies. But rather than saying, You need to come and work with the institute, just go ahead and do your work, we're going to help make that happen. I think that it was much more of an infrastructure basis. Now, we also recruited some outstanding people who wanted to work in that environment and were collaborative, interactive, and used this, and we assigned or we selected or we worked with and found a representative of each of the different departments to function as a liaison who would come to our meetings, who would in theory, go out to their department members and make sure that the technologies were available, the processes were available, the information was available. So, I think rather than soliciting projects, which I think Dr. Mendelsohn would have liked to have seen, we actually instead, built an infrastructure and let others use it. It's sort of this, if you've got some big funds, do something big, rather than if you've got some big funds, do a lot of little things. I think we pushed very hard to try and do things that were big and I think that there's little question in the community,

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that the MD Anderson Cancer Center led much of what has happened, because of the IPCT. In terms of the implementation, identifying the challenges, and to some degree trying to find solutions for those challenges. Excuse me for a second.

[01:27:23]

Tacey Ann Rosolowski, PhD

[01:27:24]

Sure, let me pause.

[01:27:24]

[The recorder is paused.]

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Chapter 14

A: Overview;

On Leadership, Leading, and Dealing with Kids

Codes

C: Leadership; D: On Leadership;
A: Personal Background;
A: Character, Values, Beliefs, Talents;

Gordon B. Mills, MD, PhD

[01:27:25]

The head of the Division of Cancer Medicine, before John Mendelsohn, or sorry, before Bob Bast came and took over the division, Dr. Kriehoff used to have a book called *The Management Approaches of Attila the Hun*, that if you came into his office and that was in the middle of his desk, you knew that there was a problem. And so this was given to Bob Bast when he arrived, and there were lines like, "Happy huns are disciplined huns," and all kinds of beautiful opportunities.

[01:28:11]

Tacey Ann Rosolowski, PhD

[01:28:12]

Well, just for the record, since that's an amazing surprise, you know on the recorder, given the subject matter of our conversation before the pause, I was just noticing that there's a little pot on the bookshelf that's entitled, "ashes of problem employees."

[01:28:27]

Gordon B. Mills, MD, PhD

[01:28:28]

And so the story that goes with that is there needs to be a little bit of insecurity or fear for a senior administrator, in many cases, to be effective. If everybody thinks you're a marshmallow and that you love everyone and everything, it can decrease your ability to accomplish things. Just a little bit of edge is not a bad idea. Respect is very important and that comes with just this, I'm not quite sure what's going to happen.

[01:29:11]

Tacey Ann Rosolowski, PhD

[01:29:12]

Keeping people off kilter a little bit.

[01:29:13]

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Gordon B. Mills, MD, PhD

[01:29:14]

That's right, off balance.

[01:29:14]

Tacey Ann Rosolowski, PhD

[01:29:15]

A little bit, a little bit.

[01:29:16]

Gordon B. Mills, MD, PhD

[01:29:17]

Not too much, just a little bit.

[01:29:18]

Tacey Ann Rosolowski, PhD

[01:29:19]

When you start building fires on your chairs, turning people into ashes, then they'll know they're in real trouble.

[01:29:25]

Gordon B. Mills, MD, PhD

[01:29:26]

Yes. I think I get a lot of jobs because of that. One of the more challenging ones that I was given was the head of the Endowed Positions Committee, which I was asked to take over. That is a -- at the time, is a plum position to have, because you get to give out chairs, you give out endowed positions, and that makes people happy.

[01:29:58]

Tacey Ann Rosolowski, PhD

[01:29:59]

Except for the people that don't get them.

[01:30:[00]

Gordon B. Mills, MD, PhD

[01:30:01]

Well, even there, that's the responsibility of the committee more than the chair. The people who do get them thank the chair. But immediately after I was asked to do this, I got called into Dr. Mendelsohn's office and he said well, "You need to understand why we asked you to do this," and I said this isn't going to be good. He says, "I need a series of endowed chairs to help recruit people and retain those that I want, and that means I need a process to take the ones away from

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those people who no longer need them or deserve them. It is your responsibility to figure out how to do that." And so we now have a process that went through all of the committees, to make that happen, but in order to make it clear and stick, the first thing that I had to do was to go to Margaret Kripke and convince her that since she had become vice president for research, that her endowed chair specific to immunology was no longer appropriate and that she would have to turn that back in to the system. So this was a case where I asked if I could have a bodyguard and someone to check under my car every day for bombs. So as you point out, sometimes it comes with a bit of worry.

[01:31:28]

Tacey Ann Rosolowski, PhD

[01:31:29]

It does. But I'm remembering that story that you told. I'm not even sure if I had already turned off the recorder, about when you had that job, that summer job, and the guy asked you to -- what was it he asked you to do?

[01:31:43]

Gordon B. Mills, MD, PhD

[01:31:44]

My job was to get someone to quit within a week.

[01:31:47]

Tacey Ann Rosolowski, PhD

[01:31:48]

That's right, that's it.

[01:31:49]

Gordon B. Mills, MD, PhD

[01:31:50]

Yes, that's part of the job.

[01:31:50]

Tacey Ann Rosolowski, PhD

[01:31:51]

That's part of the job, yeah. Obviously, there's something about your aura, you're the man that can get that job done.

[01:31:59]

Gordon B. Mills, MD, PhD

[01:32:00]

Right. At least that's what people think. It's nice for people to think you're mean. I'm not but it's

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nice to have people believe that.

[01:32:08]

Tacey Ann Rosolowski, PhD

[01:32:09]

And then they're so pleasantly surprised when they have a different face of you.

[01:32:12]

Gordon B. Mills, MD, PhD

[01:32:13]

Most of them never get to see it.

[01:32:15]

Tacey Ann Rosolowski, PhD

[01:32:16]

I'm sure that's not true. Actually, I can't remember who it was that told me this, but someone said oh, you should ask him about how good he is at taking care of little babies. You look shocked, but somebody said that you've got a way with little kids.

[01:32:32]

Gordon B. Mills, MD, PhD

[01:32:33]

Oh yeah, that's a different story. I'm an obstetrician by training.

[01:32:35]

Tacey Ann Rosolowski, PhD

[01:32:36]

Oh well, okay.

[01:32:36]

Gordon B. Mills, MD, PhD

[01:32:37]

So you have to be able to deal with little kids, because when mom comes into your office for their postpartum exam, you have to keep the child entertained while you're talking to mom, so you become good at it.

[01:32:49]

Tacey Ann Rosolowski, PhD

[01:32:50]

You become good at it. So that wasn't, you know, because you took care of siblings or anything

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like that.

[01:32:53]

Gordon B. Mills, MD, PhD

[01:32:54]

No. I have taken care of a number of difficult children.

[01:32:59]

Tacey Ann Rosolowski, PhD

[01:33:00]

Your own or others?

[01:33:00]

Gordon B. Mills, MD, PhD

[01:33:02]

Others. My child, my son is great. No, and sometimes it's not -- I guess the best story is that children are manipulative, they are born knowing how to manipulate parents. I had a good friend of my wife's, who had a baby who, according to her friend had colic and she was just about ready to quit, whatever, could not deal with it anymore, and I said well why not bring the baby here and you go out. The two of you go do something, I don't care what it is, take two or three hours off, I'll be a babysitter. The baby and mom came in and basically, cried from the time that the mother arrived at the door and was picked up and carried and still cried, and you could understand why she was going crazy. Basically, because I'm an obstetrician, a crying baby is a healthy baby. When you deliver a baby and they're quiet, that's what scares you incredibly, that's something wrong. Babies make noise when they're born. And so the baby was crying and I said fine, cry, it's not going to hurt you, not a big problem. Cry. This kid cried for a good half an hour and finally realized that it wasn't going to do it any good, and it got to sit in its cradle, so what's the point of crying. And so basically, every time the mother would drop the baby off, which was about once a week, the baby would cry for ten minutes and say, Oops, not going to help here, play, have fun, no problem. We'd play together, but I wasn't picking it up and doing what it wanted. The mother would come in the door and instant baby heard mother's voice, crying again, and was picked up and handled and carried. Didn't speak a word, I mean it was two years old and it just pointed, or not two years old, but old enough, had not learned how to speak by the time it was two years old, because mom did everything for it, just on request. One day, out of probably ten times I babysat; the kid probably did have a bit of colic and did cry, but the rest of the time, no problem. There was no colic here; this was not a bad baby. This was a baby that had trained mother. And so yeah, you can do that.

[01:35:39]

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Tacey Ann Rosolowski, PhD

[01:35:40]

Don't play me, kid.

[01:35:41]

Gordon B. Mills, MD, PhD

[01:35:42]

That's right. You have to be able to deal with crying and tears. I've had people in my office in tears because of things going on in their life, and jobs. You acknowledge, you accept, but you do not melt, and that helps. So that's what I learned from the baby.

[01:36:13]

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Chapter 15

B: Building the Institution;

The Zayed Institute for Personalized Cancer Therapy, Part II

Codes

B: Building the Institution;
D: On Research and Researchers;
D: Understanding Cancer, the History of Science, Cancer Research;
C: Research, Care, and Education;
B: Research;
B: Building/Transforming the Institution;
B: Multi-disciplinary Approaches;
B: Institutional Processes;
B: Devices, Drugs, Procedures;
B: MD Anderson Culture;
B: Working Environment;

Tacey Ann Rosolowski, PhD

[01:36:14]
Shall we go back to the story of the institute?
[01:36:14]

Gordon B. Mills, MD, PhD

[01:36:15]
Sure. Yes. What story would you like about the institute?
[01:36:19]

Tacey Ann Rosolowski, PhD

[01:36:20]
Well, we were talking about kind of shepherding it, moving it through and kind of getting connections with the institution, and just wanted to ask, kind of what are the newer developments. We've got a new building.
[01:36:33]

Gordon B. Mills, MD, PhD

[01:36:34]
The building is named after the people who donated the funds. The proportion of the building that is dedicated to the institute is actually quite small.
[01:36:45]

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Tacey Ann Rosolowski, PhD

[01:36:46]

Oh really? Okay.

[01:36:47]

Gordon B. Mills, MD, PhD

[01:36:48]

The great news was, is those funds were used to build this incredible facility, and it is truly an incredible facility, and that many of the things that will happen in the building are related to the goals of the institute. But the actual institute space, physical space for people who work directly related to the institute, is quite small.

[01:37:12]

Tacey Ann Rosolowski, PhD

[01:37:13]

I didn't realize that. And just for the record, this is the Zayed Building. What's so amazing about the facility?

[01:37:20]

Gordon B. Mills, MD, PhD

[01:37:21]

There are several things. First, this is the last current, new space, available for research, in the institution. I've been here twenty-two years. This is the first time there is not a construction crane on the property in twenty-two years. This is the only new building that we're going to be able to put new researchers in, reorganize space, probably for the next five or six years. There are plans for more buildings, but it's going to take time for those to come to fruition, and so this is an incredible opportunity to bring in new people, new ideas, and also in some places, to move people to give better contingencies to others. So it's not necessarily that everyone who comes into the building will be new, but the space they release will allow us to expand and bring in new people. One of the other pieces that will happen is we have old facilities that have to be vacated, they're just no longer viable. So, built at a time when they just did not have the ability to plan this far in the future, for the flexibility that's needed, and they just need to come down and be replaced.

[01:38:37]

Tacey Ann Rosolowski, PhD

[01:38:38]

What kind of features does the building have to facilitate the kind of research that you folks need to do?

[01:38:45]

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Gordon B. Mills, MD, PhD

[01:38:46]

The building was designed with the concept of collaboration in place. Just talk about a couple of physical things first, that make it a neat place to work. The first one is, is the ceilings are a foot higher, and there is this feeling of openness that comes with that. Massive amounts of glass, again, openness that comes with that, and those are really two very important aspects. The building was also designed to, as much as possible, in an environment of research, to facilitate and encourage collaborations. So the first is, is there are four towers, but every tower is connected to the other by a large interaction room in the middle, where people going from their offices to the towers will have an opportunity to run into others and develop collaborations and interactions. There is nothing like bumping into someone, talking, and making something happen. Now, I'm not saying that that's working as well as was hoped, because people are very busy with their own things right now and the amount of information and challenge and stress with grants and the rest, has restricted some of that free time to interact and talk. The other is, is that all of the labs are open, they're glass, well they're open in two ways. There's no walls in each wing. Basically, the whole lab or the whole wing, is one open area, again designed to facilitate interactions and flexibility. Then, the walls, all of the rooms, on the outside, are glass, so people can walk by and look in and say ah, there they are, I can go talk to them, or this is what's going on there or here's a piece of equipment. The idea is again, to foster the idea of openness, sharing, collaborations, interactions. We will see how well that works over time. Right now, there's only a very small amount of the facility occupied, in what's called phase one. Phase two and phase three and supported to start very soon. The funds are available and so they will begin. There are some design processes that are being put in place, in that the fire marshal rules changed from when the building was planned, to when people have come into the building, resulting in a need to re-plan some of the ways in which different parts of the building will work to deal with the worries about flammables and explosions. That's in process now and we're excited, because we're going to get new space in that expansion.

[01:40:47]

Tacey Ann Rosolowski, PhD

[01:41:48]

Now, you said that the other occupants of the building are going to be related to the activities of the institute. What do you mean by that?

[01:41:58]

Gordon B. Mills, MD, PhD

[01:41:59]

Well, related. One of the things, the Zayed family, or the Foundation, has supported both the Institute for Personalized Cancer Therapy and pancreatic cancer research specifically related to the disease that brought them in touch with MD Anderson. So, the Pancreas Cancer Research Group is one floor below us, and we do interact with them. I'm not sure that proximity is as

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important as it was five years ago. The ability to communicate at a distance, through the Internet, through Skype, through others, I think has taken down a little bit, the need for physical proximity, although knowing people makes those distance communications easier. I have multiple Skype meetings with people around the world, but most of them I knew before we start that process, and so once you know someone it's easy to collaborate. Interacting with them will help and, you know, we share agents, we share equipment, and so those are working. The others is that most of the groups at MD Anderson have, over the last ten or fifteen years, evolved, partly because of opportunity, partly because of this convergence we talked about, and partly because the National Cancer Institute demands evidence that what you are doing can help patients. That's their jobs, since it's a national cancer institute, not the National Science Foundation, which is a little different concept. With that in mind, the translational aspects are much more prominent, I think in most people's minds here, so the people that come into the building will, in most cases, have a goal of translating things through to the patient, which is what the institute is all about.

[1:44:06]

Now, one of the major roles that the institute serves is as an advocate for different things across the institution. This institution is big and it's hard for people to have an impact with ideas and concepts, and drive directions of the institution, and so the institute has very much taken on the role of saying we are the advocates for personalized cancer therapy and all the things that go with this. What we are doing now, in one of our major programs, is to attempt to recruit and support the next generation of scientists that are going to benefit from the concepts and precepts that we have helped put in place. We don't have as many outstanding young physician scientists that are going to be the next generation as we would like to have, and so John Mendelsohn has taken a personal charge to find, recruit and support those people. Now, young here can be assistant and associate professors, not just trainees, but people who can come in and help build this program more broadly. So I think that this is one of the other legacies that will come out of the institute and its support. One of the other pieces of evolution that has happened, and I think that this was not something we thought about at all when we started this program, is that the average physician has very few tools to help them deal with the amount of information we can now generate for patients. And so the concept of what's called decision support, providing useful approaches to take all of the stuff that is being generated in pathology and lab medicine, in our group, in other groups, and say how do I take that information to Mrs. Green's particular circumstance and help her, is one of our big programs. This is headed by Funda Meric-Bernstam, again, and it's our decision to support the program.

[01:46:53]

Tacey Ann Rosolowski, PhD

[01:46:54]

How does that work? What sort of support is being put in place?

[01:46:57]

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Gordon B. Mills, MD, PhD

[01:46:58]

Well, it comes in many levels. One is, is we've developed a website, which is a user friendly website, that website is used worldwide. We make everything we can, as much as we can, we make it publicly available to all, to help all. There's an internal website that is a little more directly linked to the results that you would get from molecular testing on a patient here, and then we had a PODS program where, by email or by phone call, an individual can call and say I've got this abnormality in a patient, what do I do? Giving direct feedback to help. With that process started and built, we were able to get a CPRIT grant, we being Funda, to move that further along, and also to make it available to everyone across Texas.

[01:47:59]

Tacey Ann Rosolowski, PhD

[01:48:00]

Wow, wow. I remember Dr. Mendelsohn telling me just about the data management challenges now, and one end is for the researchers, managing -- how do you keep abreast of all the research that's coming out and understand all the data that's coming out, but then on the other hand for clinicians, how do you process and integrate so you can apply.

[01:48:34]

Gordon B. Mills, MD, PhD

[01:48:35]

So how do you take the thousands of papers that exist and distill the key points that you need. The website that we've developed goes everywhere from very superficial to this is the name of the gene, this is what you might do, down to direct links to a paper about the most minutia point about, this is a particular change in that gene and this is what you would do because of that one change. So the idea here is that the physician determines the amount of information that they want back.

[01:48:10]

Tacey Ann Rosolowski, PhD

[01:49:11]

Who designed the website?

[01:49:13]

Gordon B. Mills, MD, PhD

[01:49:14]

Funda.

[01:49:14]

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Tacey Ann Rosolowski, PhD

[01:49:15]

Okay, and did she have a team of people?

[01:49:17]

Gordon B. Mills, MD, PhD

[01:49:18]

Our PODS program. I don't know how many people she has working on this but there's a team to help her make that happen.

[01:49:26]

Tacey Ann Rosolowski, PhD

[01:49:27]

And I'm sorry, the PODS program.

[01:49:27]

Gordon B. Mills, MD, PhD

[01:49:28]

Yeah, I knew you were going to ask.

[01:49:31]

Tacey Ann Rosolowski, PhD

[01:49:32]

I've never heard of it before, so I can be excused.

[01:49:34]

Gordon B. Mills, MD, PhD

[01:49:35]

No, I can't remember. It's Physician Oncology Decision Support, I think.

[01:49:40]

Tacey Ann Rosolowski, PhD

[01:49:41]

Oh, okay.

[01:49:42]

Gordon B. Mills, MD, PhD

[01:49:43]

But let me find out for sure.

[01:49:44]

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Tacey Ann Rosolowski, PhD

[01:49:45]
I can look it up too.
[01:49:46]

Gordon B. Mills, MD, PhD

[01:49:46]
I doubt you can, because I can't.
[01:49:54]

Tacey Ann Rosolowski, PhD

[01:49:54]
Interesting.
[01:50:00]

Gordon B. Mills, MD, PhD

[01:50:01]
Here it is, I hope. I knew when I said that, I was going to regret it.
[01:50:09]

Tacey Ann Rosolowski, PhD

[01:50:10]
Well, it's actually pretty important, I mean this and --
[01:50:14]

Gordon B. Mills, MD, PhD

[01:50:15]
Precision Oncology Physician Support.
[01:50:15]

Tacey Ann Rosolowski, PhD

[01:50:16]
Precision. Great, thank you. And when was that set in place, do you remember approximately the year for that?
[01:50:23]

Gordon B. Mills, MD, PhD

[01:50:24]
The various aspects of it have been being built over the last three to four years. Becoming highly useful would be the last two years, give or take. Funda herself and her husband, Elmer Bernstam, are two of the leading medical informatics people around. Elmer is at the University

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of Texas, Houston, and medical informatics is the process around medicine. This is one aspect of that process. They have multiple grants in this area. It's a little hard to say, I'm not sure we can say, how many or how much of what we've done, based on philanthropic funding, has been necessary, integral, required, for leveraging of grants and other funding support. It's very hard to track, but these are some clear-cut examples of funding in these areas, that would never have happened without the institute.

[01:51:37]

Tacey Ann Rosolowski, PhD

[01:51:38]

Wow. So this PODS program started with philanthropic dollars?

[01:51:43]

Gordon B. Mills, MD, PhD

[01:51:44]

Oh, yes.

[01:51:44]

Tacey Ann Rosolowski, PhD

[01:51:45]

Oh wow, that's amazing. Well, it sounds really, really exciting.

[01:51:54]

Gordon B. Mills, MD, PhD

[01:51:55]

Again, like most high risk, high yield, not sure where it's going to go programs, you have to start with philanthropy, and once you get it to a stage where it's more concrete, you can bring in grant support.

[01:52:12]

Tacey Ann Rosolowski, PhD

[01:52:13]

We're almost at four. Would you like to stop for today?

[01:52:15]

Gordon B. Mills, MD, PhD

[01:52:16]

I've got to do some other work.

[01:52:17]

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Tacey Ann Rosolowski, PhD

[01:52:18]

Yes, makes sense. Okay, so I want to thank --

[01:52:19]

Gordon B. Mills, MD, PhD

[01:52:20]

And I don't want to cough in your face any more.

[01:52:23]

Tacey Ann Rosolowski, PhD

[01:52:24]

It looks like it's coming on a little stronger. I wanted to thank you for your time today.

[01:52:27]

Gordon B. Mills, MD, PhD

[01:52:28]

Good.

[01:52:29]

Tacey Ann Rosolowski, PhD

[01:52:30]

I'm turning off the recorder at about three fifty-two.

[01:52:31]

[End of Session]

Gordon B. Mills, MD, PhD

Interview Session Three: November 9, 2016

Chapter 00C

Interview Identifier

Tacey Ann Rosolowski, PhD

[00:00:02]

Okay, our counter is moving. It is nine fifty-five, on November 9, 2016, and I'm in the Zayed Building this morning, for my third session with Dr. Gordon Mills. Thank you very much, for making the time for me this morning. Did you want to just kind of launch? We had kind of strategized a bit, today's topic is research, and if you want to just start that's great.

[00:00:26]

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Interview Session: 03
Interview Date: November 9, 2016

Chapter 16

Creating Support for Team Science: The Challenges and Possible Solutions

A: Overview;

Story Codes

A: Contributions;
A: The Researcher;
B: MD Anderson Culture;
D: On Research and Researchers;
D: Understanding Cancer, the History of Science, Cancer Research;

Gordon B. Mills, MD, PhD

[00:00:27]

I'm going to perhaps lead you in a little different direction. One of the major challenges that we have today, and this will relate to many of the things that you wanted to talk about, is how to develop and implement the team science that is going to be necessary to fully capitalize on the incredible amount of information that we have generated. Throughout my career, and indeed my complete career, one of my major roles has been to facilitate the research of others around me. Indeed, if you look at my CV, I have probably the broadest group of collaborators and collaborative papers, really starting from when I began my career. One of the roles that I played and the opportunity that I was allowed, was to develop techniques, technologies and approaches, and then make them available broadly. This is becoming much more important and apparent in the community today; however, it is still met with a lot of challenges. So how do we balance the concepts of team science, of people working together in teams, in groups, where it's not entirely clear, in a publication, what the contribution of a single individual was, with the concept of career development. So I, and other people in the field, and I would say perhaps the most active person in this particular area of team science and career development has been Joe Gray, one of my long-term collaborators, have worked on how we start to put together a program wherein the contributions of individuals across different efforts and team science, are recognized.

[00:02:54]

Tacey Ann Rosolowski, PhD

[00:02:55]

What does that look like?

[00:02:59]

Gordon B. Mills, MD, PhD

[00:03:00]

It's a challenge. One of the things that we have attempted to do is to understand how this works in the area of physics, and one of the reason I know about this in fair detail is that a physicist also

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goes by G.B. Mills, and you will find his papers with fifty, sixty, a hundred authors on every paper, and most of the time in alphabetical order. And so the question is, is how do people in the physics field deal with the fact that any project is a five, ten-year project, for a single paper. The technology, the costs, are so enormous, that you have to build teams, you have to plan as a group, you have to then implement the process and yet, develop a career for those bright, young scientists who are going to be the next generation of leaders. We have not figured out how to do that in the biological sciences, but in the physics field, in part it's a smaller community, and when positions become available, you simply pick up the phone and call the leaders at the different centers and say I have a position, who is the person that we should be looking for. And I think that to a degree, we should do that a lot more in the biological sciences, because this will allow us to deal with this concept of how do you build, maintain, support, the teams that are going to be necessary to deal with the new information deluge and the new technologies that are available.

[00:04:53]

With Dr. Mendelsohn, we sat down and looked at this, when he was president, and implemented a couple of pieces, with the Promotion and Tenure Committee, with the concept that individuals would be able to indicate, on each paper, that where they had a major contribution, even if they were middle authors, and were to be given the same credit as if they were last authors, with the idea that my contribution was critical to the development of this project and the paper that arose from it, and it would not have happened or not have happened as well or quickly without me; therefore, I should get complete credit. I think that's helped a bit but only a bit. There still is a historical view to most of what we do, and the idea of the R01 driven scientist, with a lab, a postdoc, a student and a technician that will study an area in incredible depth, pervades the field. Now that type of study is absolutely critical. You cannot do the broad, translational sciences without those types of studies, so in no way am I implying that this should be either/or. But rather to build on all of those studies that have occurred over the last fifty, sixty years of support from the National Cancer Institute and other mechanisms, to really make a difference, is going to require a team effort, that it has to be structurally different than what we've had, and the challenge that that raises. The biggest challenge that that raises is how do you recognize team members and support them in their career. I have met with the president's advisory board, with multiple different groups, to have these discussions, and I think that we really are in the midst of trying to figure out how to make this work. Some areas, such as bioinformatics and informatics, I think this is working much better. They are newer fields, newer disciplines, and much more open to newer approaches.

[00:07:38]

Tacey Ann Rosolowski, PhD

[00:07:39]

What are some of the approaches used in those fields?

[00:07:40]

Gordon B. Mills, MD, PhD

[00:07:41]

I think there, it's a small enough field that you know each other.

[00:07:45]

Tacey Ann Rosolowski, PhD

[00:07:46]

So that seems to be key.

[00:07:47]

Gordon B. Mills, MD, PhD

[00:07:47]

I think that's a big part of it, and so the idea of participation in the team is important and indeed, I review grants in England, for example, or the United Kingdom, and there, pretty well everybody knows everyone else, and their participation in the community, and it's not quite the same as team science, but in the community, is a major component of how they are viewed in terms of ongoing support for their research, and it is not as tightly tied to a narrow document that is in front of you, that you use to determine who will or will not be funded, but a much broader view of the role of that individual in moving science forward, not just in their own lab, but within the community effort that is needed.

[00:08:46]

Tacey Ann Rosolowski, PhD

[00:08:47]

What are some of the activities that become important, because what you're saying is obviously, a person is more than his or her CV. So what are those, you know, activities that aren't reducible to the document, that are taken account of?

[00:09:02]

Gordon B. Mills, MD, PhD

[00:09:03]

So how much effort do you put in, to making people around you better, or making what they produce better. Can you build -- so that's one aspect of it. A separate question is can you build, maintain, and work with, a team that can do more than a small group, that can cross disciplines.

And I think that's the real key component of a team, is that you're not having just a hundred biochemists in a room. What I'm talking about is building a group where you have some biochemists, some oncologists, clinicians, surgeons, imagers, bioinformaticians, and that they work together providing much more than each can do on their own. Indeed, I think we are in an era where the scientist, physician scientist for example, who does everything, is probably not

going to be sustainable. You're going to have to build teams of a physician, a bench scientist, a bioinformatician, and use the optimal skillsets of each of them. And how to do that and how to maintain those interactions is really part of the challenge.

[00:10:40]

With the fact that scientists are taught, during their training, to be individuals, selected to be individuals because you progress by what you accomplish early in your career, finding and nurturing people who can work across those boundaries and put aside their need to be last author on every paper because of their ego, to saying am I going to make progress for our patients, is a major challenge. And frankly, if we don't figure out how to do it and do it well, I think that we will not move ahead as quickly as we can, with the new technologies, new information that we have. Now, one of the pieces that forces that is the fact that our technologies not only are evolving rapidly, but the infrastructure to make them happen is expensive. So, having your own piece of equipment in your own lab, that is used 10 percent of the time, versus having a group of people who can put together that same piece of equipment and then use it extensively across labs, without possessiveness and ownership, is part of this concept of team science. That applies not only to equipment, but also to the data that one generates, which again is very expensive to generate, and if I hold it in my own silo saying it's mine, I own it and I'm going to mine it, because then I will be last author, versus putting it out and saying you know what, I may lose something because somebody abuses it, uses it, but on the other side, the benefit from that, of moving things forward, of collaborations that occur, is where we have to find the balance.

[00:12:40]

Tacey Ann Rosolowski, PhD

[00:12:41]

To what extent... I assume, maybe wrongly, that there is some resistance to this, and you're smiling, so I guess I'm right. What's your evaluation of the source of that, I mean to what degree is it a person -- this, this is a paradigm shift, and to what extent is an individual just not getting it, they can't kind of extend their framework for understanding work and the generation of intellectual capital, into this kind of model? To what extent is it personality, and maybe other things that I'm just not even thinking of?

[00:13:22]

Gordon B. Mills, MD, PhD

[00:13:23]

Well, part of it is cultural. I can tell you, and this to me, was one of the most disappointing events that happened around recruitment in quite a long while, is that there was an open recruitment in another department, and the department chair who was running the recruitment simply said to their assistant, add up the number of first author papers, multiply that by the ISI score of the journal, and order the people from top to bottom.

[00:13:59]

Tacey Ann Rosolowski, PhD

[00:14:00]

Oh, my gosh.

[00:14:01]

Gordon B. Mills, MD, PhD

[00:14:01]

And that immediately removed any concept of whether the individual had been collaborative, interactive, all of those things where they sit in the middle of the paper, and made those around them better, was eliminated. Now, it's easy, it's straightforward and indeed, we still do this because it is easy. I can look at the first author papers and I can look and say that they made a major contribution, I can look at the journal and say this is the relative impact, but when you start saying well, when somebody is in the middle, what does it mean and what did they do, and did they actually do anything, it is much harder to determine what that process is. So, I think that part of it is ease, the other is, it's cultural. We have been taught, and this is the example of it, that you count up the first and last author papers, and that's what you pay attention to. Again, it's easy, it's straightforward, it takes no extra thought and work, and with that culture in mind, of how individuals are evaluated, promoted, and to a degree get grants, it generates a system where people say well, I'm not last author, why would I be on a paper? And indeed, one of our senior scientists, who will go unnamed, at MD Anderson, said I'm not last author, I don't play, I don't participate. It's not my role, not my job. My job is to be the senior driver of this project and if I'm not, not interested. So that shift, from the way we were trained to do things, to a different process, is very hard. The other one that I think is the one that we noted a moment ago, which is the career development aspect of it. So if you have a young trainee, and they take a look and say I'm only going to develop a career, if I'm first author or co-first author on papers, and that's the way I need to behave to get my job, to get my first grant, that then promulgates not just the behavior, but the type of person where that is their behavior. We teach it, but we also select it, and so it is, I think very hard for people to understand that that is a transient role in one part of your career, and then change this role later on; some people right from the beginning, but change that role later on in a career.

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Chapter 17

The Challenges of Big Data; Developing “Clinical Trial Grade” Data to Foster Data Use

B: Overview;

Story Codes

A: The Researcher;
B: MD Anderson Culture;
D: On Research and Researchers;
D: Understanding Cancer, the History of Science, Cancer Research;
D: Ethics
A: Definitions, Explanations, Translations;
A: Overview;
B: MD Anderson Culture;
B: MD Anderson History;
B: Research;
B: Institutional Processes;
B: Devices, Drugs, Procedures;

Gordon B. Mills, MD, PhD

[00:17:39]

Now the other question of sharing of data and information is one that is a major challenge. The amount of information that we are generating today, in terms of DNA sequencing, RNA sequence, RNA copy number, just generally masses of data across samples, across conditions, is such that probably each month, maybe each two or three months, we exceed the total amount of data that had been generated by all scientists over all time.

[00:17:39]

Tacey Ann Rosolowski, PhD

[00:17:40]

Oh my gosh.

[00:17:41]

Gordon B. Mills, MD, PhD

[00:17:42]

So this type of data --and I'm careful to use the term data, it is not information, it is not knowledge, it is just simply data-- and that requires then, a totally new way to think about how we move that forward. That data has value and indeed, there are a number of institutions that look upon the data that we generate at this level, as a potential for monetization. Can it be used with industry or with other approaches, to generate money that can then be put back into the

system, to improve what is happening, or should it simply be shared with the community broadly, under two or three sort of justifications? The first one is, is that the information comes from a very limited number of sources. One of them is, is most of it is from patient samples, and so we have a covenant with our patients who provided those samples, to help cancer research, to improve outcomes for them and for the next generation of people. It was paid for by tax dollars most of the time, frequently by philanthropy being part of it, and both of those have the goal of improving outcomes in the future. So you have this question of do I use this information to generate funds that will help accomplish that goal, the monetization concept, or do I simply put it out for the world to work on, with the assumption that that data should be shared and open? It is a major challenge. There is this two different concepts, both of which have value.

[00:19:47]

You can certainly tell, from the tone and the terms I use, that I believe this should be shared, and that this is a strong point of view. The other part that comes with this is sharing is hard, and so data has to be carefully curated, put in formats, put in ways that can be shared so that mistakes aren't made in the interpretation of it, and there is very little money available to make that happen. So it is not straightforward, of saying here is the sequence data that I've generated on a thousand patients, and just go at it. That isn't going to work, and so we need to figure out this whole concept of how you support this process, how you build the culture so that you can use the concept, and how you make it move forward. One other argument that I have been pushing and leading, along with many others, I'm not applying it's me specifically, is the idea that this incredible amount of information that we can generate has an unbelievable promise to transform how we move ahead, this idea of big data, big data sharing. However, the one great limiting factor in my mind is the fact that this data will not, or this approach, will not fulfill its promise unless it is linked to high quality clinical outcomes data, and I use the term "of clinical trial grade," meaning that imaging is taken at appropriate times, that the images are properly done and evaluated. The patient is followed throughout their career. We know what they are treated with, when and how, and all of that information is then integrated with the deluge of information that we are generating around the genomics of that tumor, et cetera. Now, the other challenge that comes up with our lack of sharing is unacceptable redundancy and cost, and a good example is that there are approximately two thousand cell lines in existence, and I would say that most research is done on three hundred of them. Those three hundred cell lines, in hundreds of different labs, have been characterized for proteomics, invasion, proliferation, for genomic sequence, and that has been done because one has to do it, but frankly, the cost of that and doing it over and over again, in different laboratories, is unacceptable. So, the failure to share just the sequence data on the cell lines, and other resources in a similar manner, results in this challenge of having to redo things in different labs, with basically funds from the public. And so there has to be a better way to figure out how to share all of this information.

[00:23:29]

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Tacey Ann Rosolowski, PhD

[00:23:30]

Now, when you're talking, when you gave that example of the sharing information about the cell lines, were you referring to individuals within MD Anderson, who are repeating that, or in general, in the community of biomedical sciences?

[00:23:44]

Gordon B. Mills, MD, PhD

[00:23:45]

Yes to both.

[00:23:45]

Tacey Ann Rosolowski, PhD

[00:23:46]

To both, yeah.

[00:23:47]

Gordon B. Mills, MD, PhD

[00:23:47]

To both. And some of this is new and emerging technologies that require things being done differently, so it's not strictly saying everything done on cell lines is redundant, but rather, some of the very hardcore, unchanging events in a cell, such as its DNA sequence, which changes a bit but very little. Its DNA sequence could be done and then released and that's it, or it could be required that it be done, released and that's it, and put in a format that the world can use. Now there are groups that are doing this and are doing a wonderful job of it. The Broad Institute has developed the Cancer Cell Line Encyclopedia. Cosmic has a similar effort. We have released an enormous amount of data, but the idea that most of the time it's not known and not coordinated and not easily found, has been a problem.

[00:24:47]

Tacey Ann Rosolowski, PhD

[00:24:48]

Are there any individuals who object to such an idea on intellectual grounds, I mean feeling that it's absolutely essential that all those activities be within a single study method?

[00:24:59]

Gordon B. Mills, MD, PhD

[00:25:00]

I think in some cases, this is required by reviewers of journals, to say did you check your variant of this cell line, and I think in some cases that's true. I think that the general information, if done properly, would be useful, but the biggest problem, if I run an experiment that I want to put into

a paper, it gets constrained, it gets done by a postdoc, and that data then sits on the postdoc's desk. For me to take that data and then make it available to the world in detail, in a rapid manner, outside of a paper, is something that is not funded and supported, and we do not have, in general, the resources to do this.

[00:25:45]

Tacey Ann Rosolowski, PhD

[00:25:46]

This may be an inappropriately specific question, so you can tell me, but I'm curious, what are the kind of activities that are required to take this raw data and curate it, is the word you used.

[00:25:02]

Gordon B. Mills, MD, PhD

[00:26:03]

There are many different steps. You start off, and let's just use cell lines as an example. The first thing is, is the cell line really what you think it is? The community now knows, from studies that have been done in many centers for two generations, that many of the cell lines that we use are mislabeled. They have been mixed up over time. They have either been mislabeled because you write the name down and you transpose two letters over time, or they've been mixed up because someone picks up one vial and another vial and mislabels it, and also because of care of use in that some cell lines grow very fast and if you get one cell into that preparation, it will outgrow. Other times, the history of the cell line is very poorly annotated and it will be labeled as an ovarian cancer cell line when it's a cervix line, or a melanoma line. So just even that step, of curating and knowing what you're working with, is massive. The second is, is as you generate data where do you put it, where does it go? How do you quality control it? An example is that I trust sequencing from some centers and I trust data from some centers, and frankly, I don't trust it from others. We do things differently. I happen to trust the way we do things, not necessarily that it's better but it's what I'm used to. We have approaches that I think we've set up to be high quality control, but we know there are errors in the data out there. Joe Gray, who I mentioned a few moments ago, and myself, have talked about writing a paper on the problems of sequence data available on cell lines, because we went in, doing a particular study, and the correlation across the major databases for even well-known, well-characterized mutations, was very low, sufficiently low, that clearly, errors had crept in from different places. Sometimes it's simply how they annotate sequence, sometimes it was mixed up cell lines as I talked about, and sometimes it's older technology that has now been superseded, and you don't know exactly what was done in another group.

[00:28:41]

So all of those have resulted in some concerns about how you manage this information. If we take the cell line question, the community, with support from NCI and other places and our own group, have now started to develop new cell lines, where we have a much better pedigree of the

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cell line, we know what patient it came from. We have better annotation and now we have technology that allows us to know whether this is the tumor that we started with, has it changed over time, things that we could not do ten, fifteen, twenty years ago. So all of these things are happening, but this is just one example of the microcosm of how you do this. Another example. There are major sequencing efforts of patient tumors across many different centers. MD Anderson has done sequencing data on twenty thousand tumors, give or take, but with different technologies, different approaches, different quality control, clear questions around how mutations were called, how they changed over time. And so if we were even just to put that data, or try and put that data, into a usable format, it is a massive effort. But even more importantly then, linking that to high quality outcomes that I mentioned earlier, again, is an effort beyond the capability of any group. It would be an institutional process, and indeed we are trying to do that, but the effort required to curate, quality control, remove bias, make sure everything is accurate, not mixed up, is massive and needs to be supported. Now, we have a major effort at MD Anderson to put this in place, and it is a critically important process for the future. I will argue that we have not put as much effort, as I mentioned earlier, into attaining the high quality clinical trial grade outcomes that are necessary, partly because we don't have the resources, partly because that's not how we manage patients, partly because we thought we could get this from the patient record, but I think more and more studies are showing that our current patient records are inadequate in the term of clinical trial grade data. So, we're having to rethink a lot of how to make this whole process valuable.

[00:31:28]

Tacey Ann Rosolowski, PhD

[00:31:29]

What's required to improve the -- to bring the grade of patient information up to what is appropriate for clinical trials?

[00:031:38]

Gordon B. Mills, MD, PhD

[00:31:39]

I think there's two things that are required. One is culture and the second is money, and will. Culture and will here, I think go together. But the culture is, is that we manage patients inside of a clinical trial in a very constrained, very rigorous, very expensive process, and that patients that we are caring for in our normal care get outstanding care. This has nothing to do with quality of care. But our annotation and our follow-up, of every step in that patient's career as a patient, or lifespan as a patient, whatever term you would like to use, is one that we don't do in the same rigorous manner. It is a time consuming and expensive process and so it would be a culture shift. And when I talk about expensive, I don't mean just dollars to do the imaging at the right time, but you're going to have to free-up physician time, nurse time, to do that extra work. It is expensive in time and dollars, to attain that type of information, but again, it is absolutely necessary if we

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are going to truly fulfill the promise of the data that we are generating.

[00:33:10]

Tacey Ann Rosolowski, PhD

[00:33:11]

Who's talking about this now?

[00:33:13]

Gordon B. Mills, MD, PhD

[00:33:14]

Lots of people. There are a number of people who talk loudly. I've been at several big data conferences, of the people who work on the big data, and have espoused that particular point of view. Many other people understand this, are putting the same thing forward. I actually recently heard a presentation from Google, which are one of the very big data analytic groups in the world, the medical branch of that is called Google X or Verily, and they have actually discussed the potential of building or buying, their own hospital, so that they can simply say, we are going to get this type of data, because we have found that the data that we get from the community does not have the depth of information, the granularity that we need to make progress. And to hear an analytics group, a pure information group, saying we know that this is the rate limiting problem, says that I think we're having an impact. I was asked recently, to participate in a debate at one of the major meetings in Europe, simply about this question of what it is that we need to do to benefit from the information that we are generating. So there is an understanding, and so please don't in any way think I'm leading this or I'm the only person.

[00:34:49]

Tacey Ann Rosolowski, PhD

[00:34:50]

Sure.

[00:34:50]

Gordon B. Mills, MD, PhD

[00:34:51]

This is a major discussion. The challenge is how are we going to pay for it.

[00:34:56]

Tacey Ann Rosolowski, PhD

[00:34:57]

How to make it happen, yeah.

[00:34:58]

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Gordon B. Mills, MD, PhD

[00:34:59]

And how are we going to cause the culture shift. This again, fits into this concept of team science and how do you fund it, how do you support it. How do you make these big efforts work?

[00:35:16]

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Chapter 18

Educating, Hiring and Retaining Team Scientists: A Challenging Time

A: Overview;

Story Codes

C: Mentoring; D: On Mentoring;
B: Education; D: On Education;
C: The Institution and Finances;

Tacey Ann Rosolowski, PhD

[00:35:17]

I was also wondering, unless you had a sense of the next direction to go in?

[00:35:20]

Gordon B. Mills, MD, PhD

[00:35:22]

We can talk about Moon Shots.

[00:35:23]

Tacey Ann Rosolowski, PhD

[00:35:24]

Okay. I also wanted to just ask you a bit about education though, because I'm thinking the types -- you were talking about how individuals are trained to be individual researchers, but then there will be a time in their career when they have to shift. What are the kinds of -- what's the kind of training that they would need, to be able to embrace that second role?

[00:35:50]

Gordon B. Mills, MD, PhD

[00:35:51]

Well the first piece of training is to have role models who have made it work, but we are trained to be individuals. In all of the processes that one gets through graduate school and as a postdoc, in most biological sciences, you are trained to be an individual, you are trained to be selfish, you are trained to be driven. Yes, there are people that are exceptions, please don't say it's everyone, but the overall direction for those individuals who are going to get a position in the current environment, in the biology side of this, is to be selfish. So that's a challenge. We do not have ongoing training in most cases, for faculty. We do, at MD Anderson, have a Faculty Leadership Academy, to teach people how to lead and how to work together and how to work in groups. It doesn't really focus on team science and the pieces that are needed to do that, although leadership

to a degree, encompasses some of those aspects. I think the biggest thing that I learned from the academy is that not everybody is like me and that the personality and cultural here --and I do not

mean ethnic culture, I mean research culture-- and what drives individuals, are totally different. That has been a very difficult thing for me to work with. I have people that I have worked with for fifteen, twenty years, and I assume that they're like me because we've done this together. But in reality, these are people who, every day, need me to come in and say, You're doing a great job. They need that every day reinforcement of their value, so they are extroverts, that means that their value comes from outside, whereas I am scored as a high introvert. I'm happy with what I'm doing and if somebody says good, great, but if not, it doesn't matter as much. And so that understanding is hard. We're not taught how to do this and we're not rewarded in many cases, for moving down this pathway, and so I think it's going to take a major culture shift. And there are people doing it, there are incredible teams and groups that do this, and indeed, many of them are attracted into environments where you can do this. It becomes a bit of a circular, or a self-fulfilling process.

[00:38:46]

The other thing about training, this is a very difficult time. My joy for the first long period of my career, or at least one of them, and particularly once I took on a leadership role, was being able to recruit, train, nurture, mentor, support and see people develop. That went from graduate students, through postdoctoral students, through junior faculty, all the way up to senior faculty. However, we are in a situation now, where we have far too many molecular biologists, as an example, laboratory-based biologists in the medical field or the biomedical field, for the number of positions that are going to be available. The AAAMC estimates that there will be ten qualified people for every position available for the next ten years, and that means that I have far too many people in my office, or on email, saying I don't know what I'm going to do next, my career is over, my goal in life is not going to be fulfilled. It's luck in many cases, it's not skill. Did you pick the right project or were you given the right project by your supervisor, were you able to find the right supervisor, and did somebody happen to do it two days before you did and publish it, all comes to a very difficult time today. People who got jobs or were able to get jobs easily five years ago, with a skillset, they're not even getting interviews. And so for me, having that problem has made at least the training and education part of what I do quite painful, and so taking away the joy of knowing that I've got a bright, young student, and we give them the support that they need, it will work, to where it's going to be almost a stochastic event. Yes, they contribute and it's part of it, but a lot of it is luck, and that is painful, and it now extends throughout people's careers. I was just told by one of my colleagues at another institution, that the last four junior recruits that they brought in will all be fired on December thirty-first, because they were unable to obtain sufficient amounts of grant funding to continue to support their research. This is a painful process and I have had discussions with people here, many of them, of I'm not able to get grants, what do I do next? How do I support a lab, there is no money available, and I can't even afford students and trainees, so then how can I get a grant? And so it is a very, very difficult time and this part of science is not good.

[00:42:18]

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Chapter 19

About the Moon Shots: Philosophy, Timelines, and Challenges

A: Overview;

Story Codes

A: Overview;

D: On Research and Researchers;

D: Understanding Cancer, the History of Science, Cancer Research;

C: Discovery and Success;

B: MD Anderson Impact; C: MD Anderson Impact;

Tacey Ann Rosolowski, PhD

[00:42:19]

Do you want to turn to the Moon Shots?

[00:42:22]

Gordon B. Mills, MD, PhD

[00:42:23]

Sure. The Moon Shot, as I embrace it and understand it, at MD Anderson, was developed to ask and answer a very important question and one that I embrace completely. And that is, Have we acquired sufficient knowledge to, if applied and adequately supported, to transform outcomes for cancer patients, to go from the 1 to 2 percent improvement in outcomes a year. Note that's pretty good, to say can we make leaps of 5s and 10s and 15s. And to really ask the question of if we can't, is this because we are not implementing that knowledge that we have, or is it that our knowledge is inadequate? Answering that question definitively, yes or no, and it does not matter what the answer is, would drive the way in which research moves for the next ten or fifteen years. And we don't know. Is the problem of improving patient outcomes at a more rapid rate due to an implementation concern? Is it the lack of sharing of data, is it structural, is it the way in which we develop drugs? All of those pieces, versus is it a lack of understanding of the basic characteristics of cancer, the pathophysiology of cancer, would really set our research agenda for a long time. I think it's easy to state that we do not know the answer, and further, that until recently, we couldn't even ask the question without the knowledge leap that we've had over the last decade. This really was a moot question and the reason it relates to the concept of a moonshot, was the idea of Kennedy and others, was going to the moon now a scientific knowledge problem or was it an implementation/engineering problem, and the answer was clear. It was an engineering problem and that an adequately funded, driven project delivered. And so it is time to ask that question and ask it definitively. Now, that's not easy to do and I'm not going to say that I'm convinced that we are at a place where we can do that, or even that the way in which we are implementing the Moon Shots today, will give that definitive answer. But certainly, asking and answering that question is sufficiently important to say that the whole

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moonshot concept, if implemented correctly, would change the way in which we think about making progress.

[00:45:54]

So for me, this is why this was an incredibly exciting opportunity. One of the questions that has come up and one that I would put on the table, although it's in retrospect. When you develop a new physics program, say the Hadron Collider and these massive facilities, nothing happens for four or five years, literally. You will say it is time for a new project, why don't five or six groups self-assemble and start to put together a plan by which you could do this. You then meet as groups and then super groups, and say okay, how could we now, as a community, come to a conclusion and say this is worthwhile? This is similar to things like the Hubble Telescope, where the amount of funding that is needed requires the community to come together and plan, and nothing happens functionally for several years. You build the concepts, you build the ideas, you build the way forward, and then the next step is you put in place, the infrastructure to make it happen, and still, you do nothing. You're putting in place, all of the pieces that are needed, that once you pull the trigger things happen quickly and efficiently. Unfortunately, I would say that while the goals and the concepts of the Moon Shots, in some ways fit that idea, with the concept of building platforms and infrastructure to make it happen, the process, because of the urgency, for many extrinsic reasons, started quickly. And I think that there has been a fair amount of struggle in figuring out how to move forward and truly answer those questions. So, I think that the idea is spectacular, I think that the concepts behind it are great, but that I think we need to really step back and say where are we in the implementation of this process.

[00:48:14]

Tacey Ann Rosolowski, PhD

[00:48:15]

Could you give me some examples, so I can visualize where some of these difficulties emerge.

[00:48:23]

Gordon B. Mills, MD, PhD

[00:48:24]

Well, I think we can do this in broad terms. I don't want to point fingers at anyone.

[00:48:28]

Tacey Ann Rosolowski, PhD

[00:48:29]

Sure, I understand.

[00:48:30]

Gordon B. Mills, MD, PhD

[00:48:31]

One of the ways in which this was planned to happen was to build a series of technological platforms, that all of the different disease oriented areas could avail themselves of, to make rapid progress. The idea that these platforms would be spectacular in their technology, their capability, their implementation, their ability to bring samples in and deliver high quality data out in a short period of time.

[00:49:03]

Tacey Ann Rosolowski, PhD

[00:49:04]

And what are some of these platforms?

[00:49:05]

Gordon B. Mills, MD, PhD

[00:49:06]

Oh, we have a cancer genomics laboratory, which is for sequencing of tumors, we have an immune monitoring platform, we have a proteomics platform. There are a number of them, and they keep changing as the needs of the program changes. In general, these platforms were not ready for the onslaught of requests that came, and failed to deliver in a timely manner, at least at the beginning. It's getting better. The other is, is that running a platform is very much the antithesis of running a research laboratory. So instead of me focusing on my research and what I want to do, I would turn around and say okay, I will set up this platform that other people are going to use, and I get no benefit from it. Again, this culture shift of saying right now, funding is so tight, that I have to focus on my own research, my own direction, so that I can get my funding in place, and saying I don't have the time, effort or drive, to run these platforms.

[00:50:32]

Tacey Ann Rosolowski, PhD

[00:50:33]

So, I guess I was assuming that someone would be hired to run a platform, but I guess that was a naïve assumption.

[00:50:39]

Gordon B. Mills, MD, PhD

[00:50:40]

Well, we did, and in many cases we hired a technical person to run the platform and that's great, but that's not enough. You need to be -- for these platforms to be cutting edge, innovative, delivering high quality work, you don't need -- sorry. You need the technical people who can do it, but you also need the people at the top or out on the edge, but they're out on the edge doing their own stuff that they have to get funded then it's pretty hard, in many cases, to put the time

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and dedication into making a platform deliver for others. It's just not part of the culture. And so yes, people were hired, and some spectacular people were hired, but again, even that says that if I want to hire those spectacular people, I shouldn't have been saying my platform was going to deliver until all of those pieces were in place, and so it was a timing issue. So it's very hard to build, from scratch, with a very tight and aggressive timeline, because you need to deliver and there's urgency, and you're promising your constituents, being philanthropy granting agencies and others, that you will deliver quickly, when in reality, time is a good way to do this. I'll give you an example of something I'm proposing, which we'll see what happens.

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Chapter 20

The “Unholy Triad Moon Shot” and the Women’s Cancer Moon Shots

A: The Researcher;

Codes

A: Definitions, Explanations, Translations;
A: The Researcher;
A: Overview;
A: Definitions, Explanations, Translations;
C: Leadership; D: On Leadership;
D: Understanding Cancer, the History of Science, Cancer Research;
B: Research;
B: MD Anderson Impact; C: MD Anderson Impact;
C: Discovery and Success;
B: Industry Partnerships;
D: Business of Research;
C: The Institution and Finances;
C: Donations, Gifts, Contributions;

Gordon B. Mills, MD, PhD

[00:50:40]+

I have been asked to make a presentation on what is called the unholy triad Moon Shot. There are three molecular events in cancer that we really do not or cannot target efficiently today, and they are the most common genetic changes across tumors. That is mutations in P-53, mutations in RAS, in amplification of MIC, and it's called the unholy triad because they are so common. They represent ugly, nasty tumors, and we can't do much about them. We have a few ideas and a few hints but barely. And indeed, we generally call these untargetable.

[00:53:04]

You know, our personalized cancer medicine program, we do not have good ways to target these, and so I've been asked to put together a proposal. This encompasses the vast majority of difficult cancers we deal with, and my plan for the first year is to do nothing, is simply to step back and pull every single paper out of the literature that has given a hint of what you might do about these, and now ask, is that information robust, generalizable, real, and are there hints already in existence, that if we just pay attention, we can pull this across what's called the valley of death, the research idea into how you would implement. You would do building during that time. You would build the technologies necessary to say if I had something, would I know? If I had a drug that would have activity in a RAS mutant tumor, would I even know I had it? Do I have models that make sense and do they really reflect what's happening in patients? These are things that again, going back to the concept that I put forward, of getting together a team of leaders, getting together people who are thinking, and then actually doing almost nothing. It's not really nothing,

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but we're not going to say here are the thirty things we're going to do, but rather, saying we don't know what we're going to do, now let's figure it out. Again, that's the antithesis of science. If I went to NCI with that idea, I'd be laughed out of the room, at least a grant application to NCI, saying all I'm going to do is figure out whether what other people have done is real, they would say you're nuts, but that's what we do need to do.

[00:55:06]

Tacey Ann Rosolowski, PhD

[00:55:07]

Yeah.

[00:55:07]

Gordon B. Mills, MD, PhD

[00:55:08]

Not real, but real in application, this implementation question.

[00:55:11]

Tacey Ann Rosolowski, PhD

[00:55:12]

That seems like an essential building block, to know the intellectual terrain in which you're going to be moving.

[00:55:19]

Gordon B. Mills, MD, PhD

[00:55:20]

But actually going in and taking the stuff from that intellectual terrain, and now asking, in a rigorous manner --much of what's done in industry, by the way-- of saying, Is this a valid target? Is this something that is worth now, investing \$100 million, which is what industry is talking about, of building a drug to take through to the clinic. Actually, that's an underestimate of what it costs. So you have a very different set of criteria that one would move for validation of concept, and I think that that rigor, that cynicism, that saying I'm talking about building a five or ten-year project, not something I'm doing this year to get a paper out so I can get a grant, but rather, five or ten years from now, how do we make this process happen, is one that we'll see if there's any traction.

[00:56:21]

Tacey Ann Rosolowski, PhD

[00:56:22]

We'll stay tuned on that one. When do you present that?

[00:56:26]

Gordon B. Mills, MD, PhD

[00:56:27]

Sometime in the next few weeks. We don't have a set date. I had actually proposed to do this for P-53 only, and the reason behind that is that in high grade serous ovarian cancer, the worst ovarian cancer, I headed the Women's Cancer Moon Shot, which is now the Breast Cancer Moon Shot and the Ovarian Cancer Moon Shot, I was a co-head. In high grade serous ovarian cancer, every patient has a mutation in P-53, or an abnormality in P-53. Indeed, if they don't, the pathologist was wrong, and that's the way I would state it. Over five hundred cases have been looked at extremely carefully, and there's maybe one where there isn't a mutation in P-53, where the pathologists agree it really is high grade serous ovarian cancer. And I would say that one out of five hundred says there's a mistake somewhere there. Was it mis-sequenced, was it missed, or is it simply not a high grade serous ovarian cancer? But that then makes this such an absolute requirement, that we have something to do about it. Now, we have some drugs that we are evaluating here at the MD Anderson Cancer Center, that may have activity, that is a little better in P-53 mutant tumors. We, my own laboratory, is attempting to identify and validate drugs that correct certain types of P-53.

[00:58:12]

I have interacted with a significant number of leaders in the field outside of MD Anderson, to say Would you be interested, would you play, would you even consider moving to MD Anderson, to lead this program, and there's been a lot of enthusiasm. I must admit, that when I bring up the concept of just simply stepping back and saying what could be moved forward, I do get sort of two answers: 'Well, I already have something that needs to go forward, my own idea is great,' and the other half is Oh yes, this is what we do need to do. And so I think it's an intriguing opportunity. My argument was --is-- that okay, MD Anderson could simply stand up and say, We are taking on the hardest of the hard problems. The National Cancer Institute has built a program around RAS, the whole National Cancer Institute and all of the United States is doing RAS. MD Anderson will do the tougher one, P-53, by itself. That would be something that we could use to drive a program, to drive fundraising. The senior people said, Well, why don't we just do this big and call it the unholy triad, and put together the concepts that cross the processes, and if we can't convince the community that this is an effort that should be supported and funded, we're not doing our work right. The important thing is, is it crosses pretty well every Moon Shot, and so this would be something that would, I think begin to bring together concepts across all of them and teams, now teams of teams, across Moon Shots. I think there's a few where these are not major players, but the vast majority of the cancers that are encompassed in the Moon Shot, are the tough, ugly cancers, and they are defined by these three aberrations.

[01:00:14]

Tacey Ann Rosolowski, PhD

[01:00:15]

Interesting. Did you want to speak in more detail, about the Breast and Ovarian Moon Shots?

[01:00:29]

Gordon B. Mills, MD, PhD

[01:00:30]

I'll talk about the Ovarian Cancer Moon Shot for a moment, or even I'll talk about both. We were asked originally, myself, Mien-Chie Hung [oral history interview], and Anil Sood, to put together a program that would integrate the breast and ovarian cancer difficult diseases. And that being the high grade serous ovarian cancer that encompasses 70 percent of ovarian cancers, and the triple negative breast cancers, including particularly, a subset of those called basal breast cancers, which encompass about 15 percent of breast cancers, but are the worst and the most aggressive, and those that we have the least opportunity outside of chemotherapy, to help today. The reason behind this is that remarkably, these two diseases have more in common in terms of their underlying processes, their pathophysiology, than does triple negative breast cancer and luminal or ER-positive breast cancer. They are different diseases, they are unrelated to each other, they do not interconvert. They can't interconvert. By learning both at a clinical level and at a basic science level, across ovary and breast, you could potentially do more with the group of scientists involved and clinicians involved, than you would do looking at each one separately.

[01:02:21]

Tacey Ann Rosolowski, PhD

[01:02:22]

I recall that you were, when you were working with the interleukin-2, you said you were working at the interface between ovarian and breast cancer. So this is really an extension of that early interest.

[01:02:34]

Gordon B. Mills, MD, PhD

[01:02:35]

I think many people have worked on both sides. These really are very related diseases and although I told you it's universal in ovarian cancer, to have P-53 mutations, it's about 80 percent of triple negative breast cancers. I'm suspicious that if one were to ask about the function of P-53 in its pathway, it would be much higher than that. The other major commonality between the two is the role of the BRCA-1 and the BRCA-2 genes. Now, they're called breast cancer 1, breast cancer 2. They are actually ovarian cancer 1, ovarian cancer 2. They have much more impact on ovarian cancer than they do on breast cancer, but breast cancer is more common, and so it came out of that direction, but those, the genetic abnormalities that lead to BRCA-1 and 2, both inherited and acquired, and the therapeutic liabilities that are engendered by those are the same across the two different tumor types. So, one of our major opportunities and one of our

major drivers across the combined Moon Shot and continuing in each one of them somewhat independently, we still work together. This is not a matter of saying you're going over here and you'll never talk together. We still work together and I'll come back to that in a moment. Is to capitalize on that abnormality and drugs that are currently available to target that abnormality, called PARP inhibitors. Both programs have major efforts around how best to use those drugs, how to combine PARP inhibitors, how to identify patients that will benefit from PARP inhibitors and indeed, we've run trials within the Women's Cancer Moon Shot, with both breast and ovary being entered on exactly the same trial. The other part is that the term I like to use is that many of these cancers are due to an inherited abnormality and the genetics of this does not respect the organization at MD Anderson, where breast cancer is here and ovarian cancer is here. These patients are at risk for both diseases almost equally, as well as many others, and that we need a program to help, not only the patient who is in front of us who may have abnormalities in BRCA-1 or BRCA-2, or related genes, where we know that even with no family history, 15 percent, give or take, of patients, with high grade serous ovarian cancer or triple negative breast cancer, will have an inherited gene, and that means their family members are at risk, and so one of the opportunities again, was to build an outreach program wherein we would offer testing to every single patient in the program, and find a way to help their family members.

[01:06:01]

One of the opportunities that is exciting is if one could do that and determine how to identify and prevent cancers in these high risk individuals, i.e. family members of people with cancer, you could potentially, with appropriate prevention technologies that are currently available, not ones that we like but that are available, have a 5 to 10 percent change in outcomes in five years, by preventing people from developing these two ugly diseases that we can't treat well once they occur. So having these together made great sense. What has happened is that there are not only commonalities, but there are differences in the diseases. And further, the initial efforts were focused around just one type of ovarian cancer and one type of breast cancer, where there are many types of each of those, and it came to the point where each of the groups said, We've done this neat stuff together, it's time for us to be able to spread that effort and process much more broadly and have a breast cancer group, an ovarian cancer group. And yes, we will continue to work together, but the breast cancer group will be able to focus on the ones that are like ovarian cancers and be able to work freely on other types of breast cancer that are important. And the same question on the ovarian cancer side, of Yes we have been focused on this high-grade serous ovarian cancer group, but patients who have other types of ovarian cancer need major efforts. There is quite limited commonality between those and breast cancer, and so we've moved a little more into two programs, adequately supported, more support for the two programs than the two together. So the institution has said that this really is a promotion, not a concern, to really give these programs the chance to move forward on a broader basis.

[01:08:34]

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Tacey Ann Rosolowski, PhD

[01:08:34]

What are some of the findings? Are there findings that are being converted into care opportunities right now?

[01:08:51]

Gordon B. Mills, MD, PhD

[01:08:52]

I'm actually going to do one or two things first. So, simply having made this commitment to making a difference, through the Moon Shot effort as I described it, has engaged parts of the community. For example, Astra Zeneca came forward and said, We want to participate in the Women's Cancer Moon Shot, albeit the funding that we have available is for ovarian cancer, but we will develop an alliance with you wherein we bring our drugs, ideas, and \$10 million to the table, no questions asked, and we will work together to do information driven clinical trials, not to try and register our drug, which is their normal role in life, but rather, to understand how our drug works, who it works for, and more importantly, what is the next combination we need to do. That would not have happened if there had not been a Moon Shot, and in part, we leveraged the Moon Shot against the Astra Zeneca funds, and vice versa. We will cover, from Moon Shot efforts, some of the translational and basic biology studies that will make their effort go further, and vice versa.

[01:10:38]

Tacey Ann Rosolowski, PhD

[01:10:39]

So obviously, I'm assuming that Astra Zeneca felt that there was, basically MD Anderson was taking over some of the research work, so they could afford to invest in this way? What made them say we don't need to use you to help register the drug?

[01:10:56]

Gordon B. Mills, MD, PhD

[01:10:57]

They have programs to register drugs elsewhere. They came to us because of the unique concept of the Moon Shot, which is to make progress over time and to have some of that flexibility and the resources to do so. So, I think it is the point of -- and I'm not saying we don't participate in registration trials. It's that this alliance was separate, with the idea of this very clear and important goal that most of the time is not the major driving effort of industry. And you understand why. Industry wants to get their drug registered so that they can get money coming in. They have investors. That's all critically important. But this was a group of people that -- because the Moon Shot was in play, and because we had said this is what we are going to do-- were quite willing to say, We'll work with you to make this happen. The Moon Shot existing helped make that occur. I can't say it wouldn't have occurred without it, but I am quite

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comfortable that it was a major part of why this happened and happened easily. And indeed, I have another company that came to us about the same time and said we want to develop a new technology with you, and we will put funds on the table to make that happen, again, because the resources of the Moon Shot will make what we can do go further, and further the ability to say we're participating in the Moon Shot. That's a nontrivial process by which they can leverage their own efforts and funds. So those consequences are really a major positive and we've used this with philanthropy, we've used it with grants, we've used it with industry, as I was just talking about. So just having this concept of saying we will answer this question one way or another, has been something that we can leverage.

[01:13:12]

Tacey Ann Rosolowski, PhD

[01:13:13]

I'm really glad you told those stories, because they really bring together, the information that you've provided earlier, about what happens or what can happen when you reorganize the way science is being done. So it's really put a nice cap on all of that, yeah. Anything else that you would like to tell about the Moon Shots at this point, or final thoughts?

[01:13:42]

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Chapter 21

The Moon Shots at a National Level

A: Overview;

Codes

A: Overview;
C: Leadership; D: On Leadership;
D: Understanding Cancer, the History of Science, Cancer Research;
B: Research;
B: MD Anderson Impact; C: MD Anderson Impact;
C: Discovery and Success;
B: Beyond the Institution;
B: MD Anderson and Government;
D: Politics and Cancer/Science/Care;

Gordon B. Mills, MD, PhD

[01:13:43]

I think one of the key questions now is how the efforts that have been seeded at the MD Anderson Cancer Center, are going to integrate with community-wide efforts. The fact that a national Moon Shot effort has been put in place, which is not an extension of our Moon Shot program. It is rather, a program that has its own set of goals that are really very similar. Conceptually, it is how can we improve, as a community, patient outcomes, in a short period of time. And again, converting this 1 to 2 percent per year improvement that we are seeing, into transformational leaps in improvements in patient outcome. This is a national community-wide effort and how we, at the MD Anderson Cancer Center, are going to work with that effort, leverage that effort, support that effort. I think is going to be the major evolution over the next year or two.

[01:15:09]

Tacey Ann Rosolowski, PhD

[01:15:10]

What's the group that's organizing this national version of the Moon Shots?

[01:15:16]

Gordon B. Mills, MD, PhD

[01:15:17]

This started out of an effort by Joe Biden. He was charged, by President Obama, in a speech in the Rose Garden, to make this happen, and Biden, with his support team, has interacted with scientists across -- scientists and physicians across the United States, actively, to attempt to understand what are the challenges and rate limiting factors, and bring the respect that Biden has and funding that had been put aside to at least seed the program. As of last night, we'll see what

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happens to the program. It may or may not continue in any major manner. But this started and gained a significant amount of momentum, to where most of the major players in the field, and here being the National Cancer Institute, the American Association for Cancer Research, ASCO, all of the different groups, got together, and started to work with his team to build a plan of how you would at least do the initial pilot studies to say what can you accomplish. The goals have changed somewhat. Part of it is, when you get lots of people together, you start to build camels. Some of it is, is that the great ideas that came out initially needed to be refined, but some of the pillars are access to care for patients, access to novel drugs for patients, sharing of data broadly, and putting together the infrastructure and teams that can deliver in a way that we haven't done before.

[01:17:27]

Tacey Ann Rosolowski, PhD

[01:17:28]

When was this? When did Obama and Joe Biden announce this?

[01:17:37]

Gordon B. Mills, MD, PhD

[01:17:38]

I think it was May, last year. It's a little over, about a year and a half ago, that this started to gain traction.

[01:17:43]

Tacey Ann Rosolowski, PhD

[01:17:44]

So we're talking late 2014 or 2015?

[01:17:47]

Gordon B. Mills, MD, PhD

[01:17:48]

Fifteen.

[01:17:48]

Tacey Ann Rosolowski, PhD

[01:17:49]

Fifteen, okay. So, what are the conversations within MD Anderson, about engaging with this broader movement?

[01:18:02]

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Gordon B. Mills, MD, PhD

[01:18:03]

Well, I think the conversations are around what is it that we are doing, that we want to hold internally and locally, versus what can we do and share broadly, and that goes from all of the things we've talked about. Clearly, MD Anderson plans, or faculty at MD Anderson, plan on participating in aspects of this; to request funding, to be parts of projects. I think all of those are clearly part of what we want to do. I think the big questions that we talked about, about team building, multicentered teams, crossing boundaries, data sharing, sharing resources, are things that are going to have to evolve over time, as we see what this program looks like. Again, there has been, at least in Congress and verbally, bipartisan support for the concept that cancer is something that the two parties can say we've worked together on, we can cross boundaries, we can cross the middle of the House and do something together. I think that that is a politically positive event for many individuals and hopefully it is something that we can leverage. Now, with a Republican controlled House, Senate and president, we will see how well and how strong this particular area resonates over the next year and a half. And I think that as with every new president that comes in, particularly when there is a shift in parties, just simply dealing with the critical first level questions is going to consume all of the time and effort probably until middle of next year, and at some point this will come to the fore and we'll see where we're going. That will be the broad support of cancer research in general, research in general, both NIH and NCI, and then the idea of, is it time to implement a different way of moving this research forward. I think that's going to be a dialogue that will take quite a while to come to a conclusion.

[01:20:42]

Tacey Ann Rosolowski, PhD

[01:20:43]

Final thoughts?

[01:20:43]

Gordon B. Mills, MD, PhD

[01:20:44]

No, those are them.

[01:20:44]

Tacey Ann Rosolowski, PhD

[01:20:45]

Those are them, okay. Well, I want to thank you for your time, I really do. It's been very interesting.

[01:20:55]

Gordon B. Mills, MD, PhD

[01:20:56]

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Okay, great.
[01:20:56]

Tacey Ann Rosolowski, PhD

[01:20:57]

All right. Well, for the record, I am turning off the recorder at quarter after eleven.

[01:20:58]

[End of Session]