Nanotechnology in Cancer Diagnostics

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Joe Balintfy: We're wrapping up our series on nanotechnology and cancer in this episode. We're talking with Dr. Chad Mirkin, director of the International Institute for Nanotechnology and professor in chemistry at Northwestern University. Before we start, I wanted to remind of a couple terms we use. One is we talk about cancer markers—those are usually proteins or DNA signatures that tell when the diseases is present or on the rise. And an assay is another word for test. So Dr. Mirkin, we're talking about diagnostics. Is nanotechnology good for cancer screening and diagnostics?

Dr. Chad Mirkin: Well, the beauty of nanotechnology is that one can begin to build structures that allow you to detect markers for cancer much earlier than what we can do so—or what we can do with conventional diagnostic tools. And so you can kind of think about it as having a more powerful radar. And that allows you then to catch cancer earlier. And most people tell you that that's really part of the game here in terms of managing or ultimately curing the disease. The earlier you catch it the better chance you have of managing it or ultimately curing cancer.

I'll give you an example. We have a new detection system based upon the technology we call a "bio-barcode assay" that allows you to fish out markers at very, very low concentrations. And so we've been using that in the context of PSA detection. And we're not trying to create—at least at this time—a better screening tool for prostate cancer. We're trying to create ways of dealing with folks that have had prostate cancer, and determining whether or not they're going to recur earlier than we can with conventional diagnostic tools. And so we made the hypothesis that everybody post-prostatectomy, which is one of the treatments for prostate cancer, has a measurable level of PSA, but they register zeroes with conventional diagnostic tools, because that concentration is lower than what you can pick up with those tools. So with these new nano assays we've proven, with now around 450 patients, that everybody has a baseline level of PSA post-prostatectomy. And you have two groups of people. Those that flat line and will never be detectable with conventional tools—those folks are effectively cured—and then we have folks that might flat line or just gradually rise with time, and those people are going to recur.

And so—you say, "What is the good of that type of tool?" Well, the first part is it in principle will allow—once it's completely validated properly—it will allow us to take half the people, roughly, and tell them, "You're not going to die from this disease." You take the weight of the world off their shoulders. For the other folks, they're going to recur. And you could say, "Well, that's not very helpful, because we don't have new therapeutics that are effective for treating recurrence in the context of prostate cancer. And that's true right now. But the first step towards a viable therapy is a good diagnostic for monitoring the disease. In particular monitoring how it responds to new therapeutics. So we're going to use these tools in prospective studies to begin to monitor how patients that are going to recur respond to experimental therapies. And hopefully lead then to very effective ways of treating the disease.

So the point here is by being able to see those markers at really low concentration, we can treat those folks earlier when they have a better chance -- a better chance for a good outcome. And we can tell whether or not the therapy is working by looking at the rises or lowering of PSA levels post-prostatectomy in conjunction with these types of experimental therapeutics.

Balintfy: Is prostate cancer just one example of a particular type of cancer that might lend itself to a nanotechnology screening compared to other cancers?

Mirkin: No, I think we're going to see this everywhere. We've tried to pick one where we're going to be able to clearly delineate the power of nanotechnology in the short time frame, as opposed to the long time frame.

Balintfy: What are some other or more recent nanotechnology breakthroughs in cancer diagnostics that you can share?

Mirkin: Well, as I said—well what's happening is we are now creating a nano-based assays that are higher in sensitivity, meaning you could fish out these disease markers at earlier times and at lower concentrations, much more accurate, so the ability to get it right without having a lot of false negatives or false positives, which is critical because you want good information. These are not only life-threatening diseases, but the therapies have both positive—potential positive and negative consequences. And then finally, the ability to do what's called multiplexing, where you can go after many markers associated with one disease, so that you get that level of assurance, so that you know a specific type of cancer. Take for example the case of prostate cancer—there are different forms of it. Some are very aggressive forms, and others are less aggressive forms. And how you ultimately recommend treatment is going to depend upon your ability to stratify the population that's affected by these diseases and put them into different buckets. And I think nanotech is going to be the answer to that because we are really opening up the ability to do point-of-care diagnostics with simple, fast, high-sensitivity, high-selectivity-based assays that allow you to sort through and identify these markers at early time points, both from a routine screening standpoint and also from a recurrence analysis standpoint.

Balintfy: Are these assays—are these tests—when do you expect these to be available in the clinic? Is this something that will be diagnosing soon? Or are already being used to diagnostic tools?

Mirkin: Well, the good news here is that many of these nanotech assays, at least that we're involved with, were initially invented back in the late '90s and early 2000. They have gone through commercial development. They are part of FDA-cleared systems now. And the challenge now is to get the cancer markers on these platforms and to, for example, in the case of PSA, looking at routine evaluation of -- not, I'm sorry -- looking at the evaluation of recurrence, validating that concept that I described. What I described was primarily a concept that is backed up now with patient data in the very early days. To do this right, we're going to have to do prospective studies and begin to measure people at very close time points to see if we can create these baselines where we understand whether they're in the cure or recurrence buckets. And then if they are in the recurrence buckets, giving those folks the chance to ultimately have therapeutic options that many clinicians would like to try and validate and use that high-sensitivity test to see

how they respond. So, we're going to see these rolled out over the next few years. And I think you're going to see a very big impact -- frankly not just in the cancer area, but in medicine at large.

Balintfy: Okay. Can you explain a little bit more of the cool science aspect of nanotechnology? How are these little tiny particles, or little micro machines, what's the job that they're doing? And how do they do it on such a small level to help with cancer diagnostics?

Mirkin: Well yeah, you might ask, "Well, why nano? Why not just some of the conventional ways of doing things?" It turns out that nano's interesting not because it's small, but because it's large compared to molecular counterparts. There's a whole field of molecular diagnostics that use things called molecular probes. Again, they go after disease markers. And they have molecules that light up when they bind those disease markers.

But it turns out with a nano particle you can add lots of different functionality. You can add things that recognize a disease markers. You can add things that provide a signal to tell you that disease marker's present. And you can also add things to it that allow you to amplify the signal, so that you get a very large response that allows you to fish out these markers at really low concentrations. So the beauty of nano structures is that they are small enough that they are, you know, invisible to the naked eye. They can be dispersed in solution. But they're large enough that you can decorate them with different functionalities. They give you many additive capabilities that you don't get with conventional molecular systems.

Balintfy: I've heard that term "decorate them" before, and I think of a Christmas tree. But these are little tubes. They're little -- what are those little things that you're decorating?

Mirkin: Well, if you want to use a Christmas tree analogy, they're little ornaments. They're balls. They're little nano clusters, in our case of gold. And we decorate the gold surface with DNA or proteins that can recognize the disease markers. And then we use the gold itself as a catalyst to generate a lot of signal. Because it turns out that if you use these as probes, for example, on a chip-based assay where you're trying -- they have a color associated with them. And when they bind to a chip that's captured disease marker, you can get a color developed in a spot, for example, that localizes the disease marker. But you can increase the sensitivity or the magnitude of the signal by flowing ordinary photographic developing solution over that chip. And the nano gold will plate out silver and increase the signal by a factor of 100,000 in less than five minutes.

Balintfy: Are these something that can be used in more than just diagnostics?

Mirkin: Absolutely. These types of structures are being used to open up a whole new area of gene therapy, for example. An area of chemotherapeutics that takes a drug that ordinarily is almost intractable in terms of delivering it and creating constructs that can be delivered very effectively to parts of the body that create a therapeutic payload that kills cancer cells selectively and does not cause a lot of the side effects of conventional chemotherapeutics along the way. And that's really exciting. And we have lots of medical doctors now that are looking at how they can use these constructs in anything ranging from glioblastoma, brain cancer, pancreatic cancer, ovarian cancer, bladder cancer, and also breast cancer and prostate cancer.

And so I think, again, for the same reasons that there are advantages in terms of nano structures for diagnostics, you have similar advantages for therapeutics. And that is the ability to take the structure that's bigger than a molecule but not so large that it can't be suspended in solution, and decorate it with lots of functionality that allow you to target a particular organ or a particular part of the body, carry a therapeutic payload, and in certain cases even provide a signal. So there's a whole new area of theranostics, where you can watch the therapy working because you have a signaling agent as the particle is delivering a therapeutic payload.

Balintfy: Well it sounds like it's not just then the diagnostic. It's all in the same package -- the diagnostics and the treatment.

Mirkin: You got it. It's a whole new frontier of nano medicine. It's an exciting frontier. I think it has a chance to have a very big impact in humanity. But we have to really learn how to use these nano structures and to use them safely and to use them well for each given disease type.

Balintfy: Terrific. Anything else that you'd care to add that I may have missed or that's worth reemphasizing?

Mirkin: I think that's probably it. I mean, I don't know if you're going to talk about the corporate side at all or not.

Because I think people need to understand that these types of technologies are not just dreamt up in the ivory towers, in a lab with a few graduate students that will never see the light of day. They are technologies that are going to see the light of day. They're going to be ultimately commercialized. And they're going to see widespread use. But it takes a long time.

If you use the diagnostic example, so after 10 years, we now have FDA cleared systems. Those are going in hospitals all over the U.S., and soon all over the world. That's a pretty exciting development. They'll end up being used in lots of different types of disease management scenarios, including cancer, which is very exciting. And this type of research that we're doing will add these types of technologies to that platform.

On the therapeutic side, we're going to see similar types of advances. And I'm convinced that—well, a decade—two decades from now, almost all therapeutics will be in part nano-enabled because of what I said. But that takes time. It takes first research, which is what the NCI is funding and developing. But then it takes entrepreneurs. And it takes a lot of hard work in engineering and work with the pharmaceutical companies to ultimately get these out the door. But it'll happen, and it'll make a big impact.

Balintfy: And I guess it also takes the part of the public to understand how this can help, and the patient's willingness to accept and try it.
Mirkin: Absolutely. I mean, in the end that's what it's going to require. I mean, the first, for example, tests that you do are toxicity tests, in terms of FDA approvals. You need patient buy-in that this is something worth doing, that this is something that might have—might not have an

immediate benefit to the first few folks that try and help out in this regard. But it will lead or blaze a path to new therapies that will save a tremendous number of lives in the process.

(THEME MUSIC)

Balintfy: Thanks to Dr. Chad Mirkin at Northwestern University. For more information on nanotechnology and cancer, visit the website nano.cancer.gov. That's it for this episode of NIH Research Radio. Please join us again on Friday, January 28 when our next edition will be available. If you have any questions or comments about this program, or have story suggestions for a future episode, please let me know. Best to reach me by email—my address is jb998w@nih.gov. I'm your host, Joe Balintfy. Thanks for listening.

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