A Conversation with Prof. Chad Mirkin: Nanomaterials Architect

Image Courtesy of Jim Ziv

Prof. Chad Mirkin of Northwestern University.

I met with Chad Mirkin in my office during his visit to deliver the Priestley Lectures in the chemistry department at The Pennsylvania State University.

PSW: When you started your career, where did you get your advice and inspiration?

Chad Mirkin: From many sources; I got much of it from my advisor at Penn State, Greg Geoffroy, my Ph.D. advisor. Also, from my postdoc advisor at MIT, Mark Wrighton. At MIT, a lot of the postdocs were interviewing for jobs, going out and testing the waters, and bringing back experiences, both good and bad, on the interview trail. I incorporated a lot of that in developing my approach to getting a job and ultimately to doing the work that we do. I took elements that I thought were successful and incorporated them into my own style.

PSW: You changed direction quite substantially once you got to Northwestern. Was that deliberate, or was there some path that began with your Ph.D. and postdoc that led you into that?

Chad Mirkin: I wouldn't say that I changed direction; it was more of an evolution in the sense that I started out as an inorganic/organic/organometallic chemist interested in coordination chemistry and structural diversity, and figuring out what was possible. "What are some of the crazy reactions that are possible on metals?" That was [my motivation] as a Ph.D. student. Then, I moved to MIT and learned a lot of electrochemistry, surface science, and materials chemistry. I moved to Northwestern with some ideas that came primarily out of my postdoctoral work that were enabled through the synthetic skills I had from my graduate work.

I realized as a postdoc that if you could make molecules you could ask and answer physical questions and materials-based questions that a lot of folks had a difficult time addressing because they were stuck with what I call "Aldrich chemistry." They had to take what was available to them, and then apply their really neat, new techniques to ask and to answer questions, whereas I could pick a system and make it and try to design what I thought was the perfect molecular system, or materials-based system, for asking and answering key questions in materials science.

At the same time, there were new technologies coming on board for miniaturization and studying miniaturized systems. In particular, the advent of commercially available scanning probe microscopes was really starting, and these were proliferating throughout the world. We had these instruments at Northwestern. I began to use them and to study how they work—what we could do with them first from a characterization standpoint, then from a synthesis and fabrication standpoint. What I learned was that you could do a lot of neat things with these high-sensitivity, high-resolution analytical tools, and I began to incorporate them in the way we thought about studying materials and characterizing structures and ultimately building materials.

PSW: I visited your lab as you first observed deposition from an AFM [atomic force microscopy] tip.[1−5] Richard Piner had the data that you showed me in your office. Can you take us through the evolution of dip-pen nanolithography since then?

Chad Mirkin: Dip-pen [nanolithography] is an interesting story because it evolved from a study of something very different. We were looking at the process of water transport from a tip to a surface. First, looking at the effects of the meniscus or the capillary effect, the effect that water will

To hear Prof. Mirkin's advice to young scientists, please visit us at the audio page of http://www.acsnano.org/.

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collect at the point of contact between tip and surface.

I had a postdoc, Richard Piner, who was a physicist, and he was fascinated with water transport. He was also a pipe smoker. One of the things he did was put the tip in contact with the surface, went out and smoked a pipe, came back, and did a survey scan of the surface and saw what appeared to be a little droplet of water. We didn't know what it was, but we assumed it was a droplet of water. We said, "Let's follow that!"

We followed our noses and looked at how that process works. What we found was that it was a dynamic process and one of two things happened. Either water moved up the tip from the surface creating recessed areas or down the tip creating raised areas. There were metastable structures that could be made in the form of nanoscale patterns. That was interesting because it was one of the first examples of imaging and understanding water transport and the capillary effect in a dynamic fashion.

I suggested that we think about building structures. Water is interesting, but from a chemistry standpoint, it's more interesting to be able to pattern or to deposit molecules that form *stable* structures, not metastable structures. The idea became, "Let's use ligands that can react with an underlying substrate." Alkanethiols on gold were the first to come to mind. We tried those, and sure enough it works and works remarkably well. We began to study the whole process of building structures on surfaces and thinking of this as one of the first, in fact *the* first, direct-write tool. I think that differentiates dip-pen and created the evolution and the fast development of the technique from a serial tool to a massively parallel one that has millions of pens working in parallel over square centimeter areas [Figure 1].[5] [This enabled] the routine fabrication of nanostructures consisting of anything from small molecules to inorganic materials to oligonucleotides and proteins.

PSW: What do you see as the most important uses of dip-pen nanolithography and what are the challenges to making those happen?

Chad Mirkin: I think you can talk about the past, the present, and the future. It's already clear that dip-pen is at the very least a powerful research tool, one that allows you to take a wide range of materials, pattern them on surfaces, and to control the formation of nanostructures where you can control the size, shape, and composition on the nanoscale. Anybody that does nanoscience knows that everything is different when miniaturized, and the ability to make these kinds of structures rapidly and interrogate their properties is a very valuable tool. Lots of people, including us, use it for that.

It's also a tool that can be used to study anything ranging from templated surfaces, to controlled catalysis, to controlled crystallization; to understand, for example, how biomolecules crystallize. [It is] a tool that can be used for making miniaturized patterns, that can store information, codes, so you can begin to think about brand protection and [anti-] counterfeiting applications. A tool that can be used to repair integrated circuits, to build photomasks, to repair photomasks that are important in the semiconductor industry. Ultimately, [it is] a tool that can be used to create integrated circuits to one that can be used for making gene chips and protein arrays on a scale that cannot be addressed with conventional technology.

In fact, I think it is going to open up the field of nanoarrays. One of the interesting things about nanoarrays is that you can not only create more features per unit area but you can begin to print on the scale of biology itself. The patterned features are as small as the entity you would like to manipulate—an individual protein, a virus. [We can] build an array of different materials underneath a single cell, using that capability to control important cell-surface

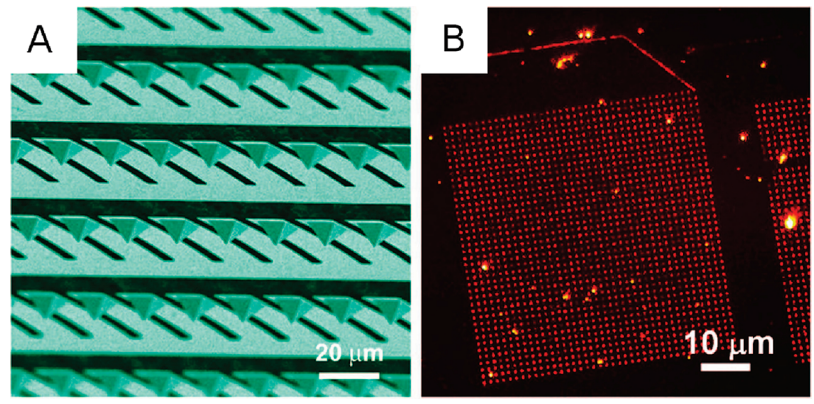

Figure 1. (A) Scanning electron micrograph of a two-dimensional array of 55 000 pens. (B) Dark-field light scattering image of Au nanoparticles hybridized with DNA created with a passive one-dimensional array of 26 pens. Reproduced from ref 5. Copyright 2007 American Chemical Society.

We developed a whole series of chip-based assays that took advantage of the particles as probes to create high-sensitivity and high-selectivity assays for different types of DNA strands.

interactions like adhesion, growth, differentiation (if you are talking about stem cells), and apoptosis or motility. All of these are important in terms of understanding important processes like how cancer works and ultimately how you can develop new therapeutics that inhibit those types of processes.

PSW: What do you see as the most important applications of DNA–nanoparticle conjugates, and what are the challenges associated with those?

Chad Mirkin: In 1996, there was a key paper in *Nature* that reported the chemistry for interfacing oligonucleotides with gold nanoparticles.[6] That was a very competitive time because, while we were trying to develop that capability, Paul Alivisatos and Peter Schultz were [also] trying to develop that capability at Berkeley.[7] We had very different goals. The Berkeley group was trying to build particles that could be aligned on DNA templates. We were trying to create multivalent particles, particles that had many strands of DNA that could then be polymerized to build extended materials where we could program the formation of hierarchical architectures. The idea was that you could sprinkle in the right types of particles, the right type of DNA, you could add in linker strands, and then you could assemble a bulk material that had properties that were designed based on the placement of the particles, their periodicity, and their arrangement in three-dimensional space, controlled by the DNA interconnects.[8]

What we discovered was that, when you worked with gold, you could not only do that (and we've learned how to build lots of crystal structures since) but you can create systems that yield really fantastic property changes as a function of the DNA that assembles these particles.[9–16] You can begin to think about these particles not as materials synthesis tools but actually as probes. That opened up a whole new era of chemistry that focused on using these types of structures as labels in biodetection. In fact, that work predated all of the work dealing with nanoparticles, including quantum dots, as labels in biodetection. What it pointed to was a simple way of doing biodetection, and in particular, what we discovered was that when you used gold particles and the DNA triggered the assembly you could get colorimetric changes [Figure 2].[9] You get very simple, almost litmus-like tests for DNA, and in fact, the binary color change was from red to blue! It's just like litmus paper.

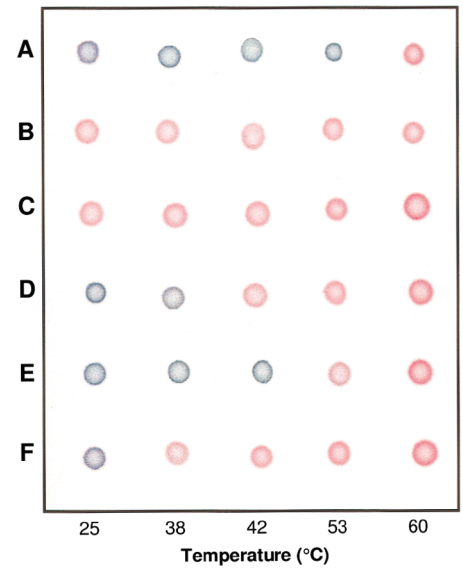

Figure 2. Colorimetric detection of DNA hybridization using nanoparticle aggregation: (A) complementary DNA to 30 base pair probe; (B) no target DNA; (C) only one of two target sequences with attached nanoparticle (and thus no nanoparticle aggregation); (D) 6 base pair deletion from the complete complementary target sequence; (E) 1 base pair mismatch from the complete complementary target sequence; (F) 2 base pair mismatch from the complete complementary target sequence. Reproduced with permission from ref 9. Copyright 1997 AAAS.

What that challenged us to do was to take that system and to probe it and to figure out how we could use it to develop useful assays. One thing led to another, and over the course of the next 10 years, we developed a whole series of chip-based assays that took advantage of the particles as probes to create high-sensitivity and high-selectivity assays for different types of DNA strands. Also, most recently, different types of protein targets.

The offshoot of that is the development of technology that can begin to challenge the community to move diagnostic tests from centralized labs to the point-of-care. One of the questions you might ask is, "Why in the 21st century do we still go to a doctor's office, give a sample of blood, saliva, or urine, that then is sent to a remote lab, processed for a couple of days, and the results are sent back for umpteen types of life-threatening diseases? Why can't that test be done at the point-of-care?" The reason is very simple: the technology.[17] Much of the technology that's used is *big*, large-scale technology, with very low throughput. It does not allow the type of work that we're talking about at the point-of-care. These types of tests enable that capability. What we're finding is that these types of [DNA–nanoparticle conjugate] systems can be commercialized; there are now FDA-approved tests based upon them, and people are using them in hospitals, and hopefully one day [they will be used in] emergency rooms and, ultimately, maybe the doctor's office and perhaps even the home.

This is an example of where understanding how you can use nanoparticles for one unusual application (in this case, materials synthesis) can lead to an understanding of new properties and new systems that can have a big impact in the area of diagnostics.

There are now FDA-approved tests for the genes associated with thrombosis, so you can identify the people who have a genetic predisposition to blood clotting. Also, for Warfarin metabolism,

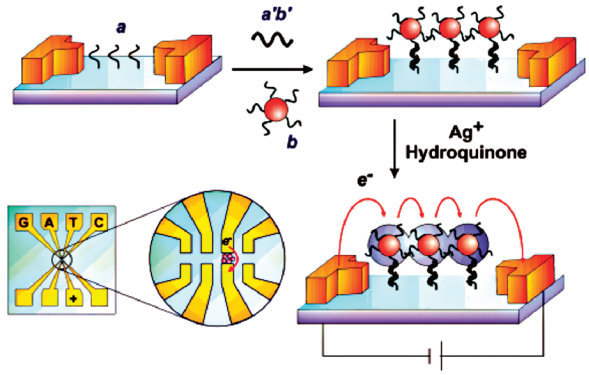

Figure 3. If target DNA is present, a target/probe sandwich is created that catalyzes the reduction of silver.[12,16] The silver can then be detected electronically (shown here) or optically (see text). Reproduced from ref 16. Copyright 2005 American Chemical Society.

for infectious diseases, for cystic fibrosis, and for a whole series of other genetic ailments.

PSW: Are these the beginnings of personalized medicine?[17]

Chad Mirkin: I think so. It depends on how you define "personalized medicine." It's certainly the beginning of decentralizing the medical diagnostics industry. When you think about "nano" and tangible benefits or outputs, it's probably one of the best examples because this type of technology did not exist before the nano revolution. It was understanding how you synthesize these polyvalent DNA conjugates, understanding their optical properties, their catalytic properties, and their hybridization properties that led to the development of high-sensitivity assays. To me, it's kind of an exclamation point on the development of a subset of the field.

PSW: How are these diagnostics put on chips?

Chad Mirkin: The way it works is you take a normal spotted array of DNA on a glass slide. Each one of those spots is encoded to recognize a particular target of interest. If the target is present in an unknown sample, the target binds and then a nanoparticle that has a region that's complementary to another portion of the target is introduced. It binds, creating a sandwich structure, and then we take advantage of the fact that nano-gold will promote the reduction of Ag^+ in the presence of hydroquinone (which is a fancy way of saying it will develop in photographic developing solution) [Figure 3], and we use that as a catalytic step to raise the signal intensity that can then be read by bringing light in through the microscope slide and measuring the scattered light off of the silver spots that are generated. The intensity tells you that you have a positive, and the magnitude tells you how much of that particular target you have present.

PSW: Is that done in an automated way?

Chad Mirkin: That is now done in an almost completely automated way. The sample handling is completely automated on a chip. We didn't do this, a company we started called Nanosphere, Inc. did this (which I should disclose that I am a board member of and I have a financial interest in). They completely automated the sample handling component and also the delivery and development of the assay with respect to silver. The only thing the user has to do is transfer the developed chip to a reader. A light is brought up to the side of the microscope slide with the silver spots, scattered light is measured with a CCD [charge-coupled device], and the rest is history.

PSW: In your Priestley Lecture at Penn State today, you discussed nanoparticle shape as an important property. Why is that?

Chad Mirkin: Well, you're controlling the "box" electrons move around in on the nanoscale. You're also controlling the chemical reactivity based upon whether you have sharp points, edges, or faces, all of which change as a function of different types of polyhedral particles that you make. I think that's one of the really interesting things about nanostructures in general—surface atoms become so significant and the way you arrange them in nanoscopic dimensions can have huge perturbations not just on optical properties, which are related to how electrons move, but chemical reactivity, which affects anything from stoichiometric to catalytic reactions.

PSW: Is some of that chemistry worked out sufficiently to exploit it?

Chad Mirkin: I think the ability to predict optical properties of noble-metal nanostructures, and probably semiconductors structures, is now well worked out. This is a real triumph in theory and modeling. A person like George Schatz at Northwestern, if I give him a particular structure, or draw the dimensions on a board, and tell him the element it's made of (in the case of a noble-metal, silver or gold, for example), [he] can tell me exactly what the spectrum will be, the color of the material, effectively, all the different transitions.[18] If I go make that, you can bet that the experimental spectrum will look very similar to the theoretically predicted one. So, there's a beautiful example of where you can use Mie theory and predict a lot of these optical properties even before you make these types of structures, which is nice! There is a nice tool to go back and forth.

We developed a whole series of methods now—in the case of silver and gold—for controlling size and shape over the 30 nm to a couple-hundred-nanometer length scale [Figure 4]. These types of particles are going to have a lot of applications, ranging from the development of new biological labels to spectroscopic enhancers, in the context of things such as surface-enhanced Raman spectroscopy, the development of new catalysts, in the case of silver to bactericides, to things like solid-state dyes, structures that can be used to modulate the optical properties of other materials where they're simple additives to those structures.

PSW: You mentioned that George Schatz was able to point out imperfections in your nanoparticles after you first showed him a sketch of the structure and then showed him a spectrum.

Chad Mirkin: Right! I would turn that around: I would say that I was able to point out some of the imperfections in his theory. Theoreticians model perfect structures. In nanoscience, although I can make a mole of molecules where every molecule is identical, I can't make a mole of particles (or any two particles) that are identical. So, when you model and try to understand the properties of a colloid, for example, which consists of many particles, you have to take into account that there's dispersity. In the case of a spectrum, you are looking at a measurement that takes into account all of those subtle differences in one composite measurement. When we went back and refined and took those [differences] into account, then of course the theory correlates *even better* with the experiment.[18]

PSW: What more can you tell us about valency in nanoparticles?

Chad Mirkin: I think valency in nanoparticles is one of the remaining grand challenges. We've made some inroads; other folks around the world have as well. I look at nanoparticles and as a coordination chemist I kind of think of them as atoms. That begs the question, "Can I begin to build molecules or extended materials?" That's one of the primary motives of using DNA as an assembler, to build extended structures. But as a coordination chemist, one of the luxuries is the idea that you can have metals with different coordination environments. You can create a coordination sphere that controls a lot of the properties of the molecules that you make from those metals. One of the things that we'd like to do, in an analogous manner, is to take particles and build valency into them. One of the questions is, "If I make a triangular prism, how do I build a coordination environment that resembles a trigonal planar coordination environment?" A trigonal bipyramidal one? How do I put different ligands, for example, different types of DNA on the different faces, on the different vertices, on the different edges of those type of structures? Does that give me a directionality that I can take advantage of in terms of building more and more sophisticated molecular analogues and extended materials analogues?

The answer is that you can begin to do this and you can do it in a variety of ways: first, by taking advantage of the difference in reactivities between the edges and the faces, so you can do ligand substitution in a kinetically controlled manner. We've done some of that. You can use masking procedures, where you put these flat structures on a surface, only modify one face, then flip them around and modify the other. In the case of template syntheses, we can make nanorods and use the template as a type of masking agent. What portions of the rod are available for surface functionalization? You can expose [the active areas] by dissolution of the template or modify other portions. We're slowly getting to greater and greater capabilities in this regard, but there is still a challenge to learn how to do this in a very broad way, so that we can dial in different types of coordination environments, and also in a way that is relatively fast and high-throughput, where we can get macroscopic quantities of these, so that we can use them to build interesting structures.[20]

I think valency in nanoparticles is one of the remaining grand challenges.

Sharon Glotzer atUniversity of Michigan and Chris Keating [at Penn State] have done some work in this area, but it's really very early in this whole game.[21,22] We have a few papers; we've learned how to make linear coordination environments where we take a spherical particle, for example, and one hemisphere can be modified with one type of DNA, the other hemisphere can be modified with another. We can use masking procedures to do that.

PSW: Dip-pen to nanoparticle assemblies to... What's the next term in the series?

Chad Mirkin: On-wire lithography![23] We've spent the last decade developing dip-pen. Dip-pen is a workhorse tool and is going to be around for awhile and used for a lot of different purposes. It's really designed for controlling nanoarchitectures on flat surfaces. From a chemistry perspective, you'd like to be able to do lithography on anything.[24,25] So, one of the questions we have is, "Can we take nanostructures themselves (or microstructures) and do lithography on them?" Free-standing structures, for example, a one-dimensional wire? Can I control the compositional space along the long axis? Can I control the diameter? Can I control the length? Can I introduce into

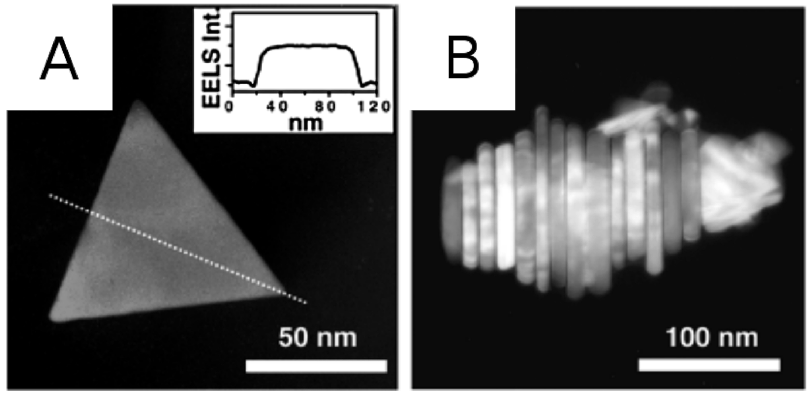

Figure 4. Silver nanoprisms imaged with scanning electron microscopy. (A) Electron energy loss spectroscopic (EELS) map of a single Ag nanoprism. The inset shows the EELS map over the line indicated; the prisms are flat. (B) An assembled stack of Ag nanoprisms on a carbon-film-coated Cu grid. Reproduced with permission from ref 19. Copyright 2001 AAAS.

that structure different architectural features, both positive and negative [relief]? Discs, for example, and recessed areas, called gaps.

We've developed a technique called "on-wire lithography" that begins to address that issue.[21] You might ask, "Why do you want to do that?" Going back to the original premise, architecture makes a difference on this length scale. You can control that architecture in a way that you could never realize with conventional synthetic methods. You can begin to realize a whole series of structures that have unique properties that can be used for all sorts of things ranging from catalysis to gaps that can be used in molecular electronics,[24] to labels that can be used in bio- and chemical detection and unique tagging types of applications to systems (for example, spectrographic enhancers) that can be used for energy conversion. As a chemist, you want to build a suite of tools and capabilities that allows you to control architecture on surfaces, in the context of three-dimensional free-standing architectures, in the context of nanostructures that are highly dispersible. If you have those capabilities, good things will follow.

PSW: With these inventions, how do you decide what to push commercially, and do you have a specific strategy for doing that?

Chad Mirkin: For a lot of this, you go by feel. If you develop something that you think is good, and that could really impact others and could be mass-produced without heroic effort and several hundred million dollars, then you have a candidate for commercialization, provided that you've also identified a big market for them because most people won't make the investment unless there's a huge market at the end of the day to tap into.

In the bio area, in diagnostics and therapeutics, it's pretty obvious. If you create things that change analytical benchmarks, if you create a system that increases sensitivity by orders of magnitude, that increases selectivity or ability to differentiate targets by orders of magnitude, that in the case of drug delivery that carry things "in" better than anything else out there with low toxicity and very high efficacy, those are candidates that could make a big difference.

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The world does not need *another* way of doing things. It needs another, *better* way of doing things. I think that's what a lot of scientists miss. You open up many journals and you can read about the development of literally hundreds of detection systems over the course of a year. But the world doesn't need a new detector; it needs a better detector. It needs a system that's going to make a difference. And one that's not just sensitive for the sake of being sensitive, but one that offers new capabilities, new applications, things that are going to change, for example, medical diagnosis. If you get that, you have a good candidate for commercialization.

PSW: What are you most excited about in the lab now?

Chad Mirkin: That's like asking me to tell you which child I love the most!

I would say that it goes back and forth. It all depends on the day, but from a broad, public impact standpoint, the intracellular gene regulation projects are extremely exciting. When you have a chance to make a difference in a disease like cancer in the way we diagnose and treat the disease, that is something that is incredibly rewarding, something that really drives you in terms of trying to make an advance rapidly, and makes you very excited about finding out what the latest and greatest results are. We're finding that the materials we have, based upon these polyvalent gold-nanoparticle conjugates, are some of the best materials out there, if not the best, for getting into cells and turning on and off genes and doing so without activating an immune response. That type of system has not been seen before and points towards (at the very least) powerful new research tools that will help us understand the disease. New candidates for therapies will allow us to treat and, hopefully one day, to cure the disease.

PSW: These are based on siRNA [small interfering RNA] and nanoparticles?

Chad Mirkin: They're based upon DNA and nanoparticles and also siRNA and nanoparticles. The interesting thing is that the particles, when you have very dense loading of DNA on their surface, are extremely resistant to nuclease degradation. Originally, the thought was that was because nucleases are sterically limited from getting to the surface of the particle, but it turns out that the big reason is that the charge density is so high the salt concentration [immediately surrounding the nanoparticle] is high. It deactivates nuclease activity, we think by denaturing the nucleases that approach the surface. As a result, the particles have kind of a stealth capability to get "in". They last a lot longer than, for example, DNA carried "in" with polymers. In addition, they don't activate the immune response, we think for the same reason. The enzymes that are designed to go

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"in" and tell the cell that a foreign entity is there are deactivated, so that pathway is shut down. As a result, you can get a lot of these particles "in". They do not cause a violent immune response, so there are no major toxic side effects, at least based on the preliminary studies we've done. They are phenomenal at affecting knockdown either *via* the antisense or siRNA pathways.

PSW: Is there a way to test that molecular mechanism?

Chad Mirkin: We have tested it. Everything points to that right now. In fact, we've tested it by using nucleases that are salt dependent and ones that are salt independent. Sure enough, if you use ones that are salt independent—which you can buy, but are not very common naturally—they do not show this retardation. The sterics are the same. That allows you to separate the steric factor from the salt-based factor. It looks like that is the primary consideration. In addition, if you decrease the loading of the oligonucleotides on the surface of the particle, you see the nucleus activity and the immune response shoot up.

PSW: How do you choose people for you lab, your companies, and your collaborations?

Chad Mirkin: We choose the best! For the lab, Northwestern attracts some of the best people in the world. Fortunately, a lot of the best people are interested in the group once they come to Northwestern; the group has a reputation of having an incredibly rigorous work ethic, an excitement, a passion for science. It's an infectious environment and people want to join. Some people think that I go to great lengths reviewing candidates and sorting through résumés, but often times people come who are not up to the challenge; they self-select themselves out of the process. We go through an interview process that involves a day's visit and a grilling by me; many postdocs and grad students are involved, and we collectively come together as a group and decide if we want that person as part of the team. If we do, we go forward; if not, we don't.

It's worked well. Every year that I've been at Northwestern, the students and the postdocs have gotten better in the group. It used to be that I would drive them, and now I'd say they drive me. I certainly learn as much from them as they learn from me.

PSW: How about for your companies?

Chad Mirkin: From the company standpoint, you have to have an idea. I typically work with the Kellogg School of Management [at Northwestern University]. We first try to identify a business strategy and a business plan for developing a new technology. Then, we go out; I have a lot of contacts in the business community. We try to find a couple of people on the business side and further develop the business plan and the ideas, and to begin to hire the first set of students and postdocs. The natural place to look is my own group; usually, the first couple of employees come from the group but then pretty soon you have lots of people that are interested in working in these areas. They apply and the company begins to become an independent entity and hires that staff on its own.

I try to separate myself from the companies as much as possible. I like to be the technology input in the early stages of the company. I like to help develop the company, the directions, and the whole team up until 10 or so employees. After that, we bring in a professional management crew. They have obviously raised a substantial amount of money to develop the ideas from that point on: the companies now have collectively raised over $330 million (and counting) in venture capital and investment.

PSW: What training do you recommend for those who want to have impact in nanoscience?

Chad Mirkin: There's always a question of, "Do I go to a nanoscience program and get trained in that, or do I get trained in one of the conventional disciplines?" I always say to train in a conventional discipline! Become good at something; become good at chemistry, biology, medicine, whatever it is you think you really want to do. Then, learn nanoscience; that's the way I got into this. You don't want to become a mile wide and an inch deep. You do want to become very proficient in a particular area and become aware of how your skills in that area can impact broadly in the area of nanoscience and nanotechnology.

You can come into nanoscience from any of those core discipline areas and make an impact. You can get involved with a group that is not so narrow that they only work on one particular technique or one particular material. You have to be comfortable about stepping out a little bit on thin ice and learning some things that you didn't initially learn as a grad student or as a postdoc (or, if you are talking about being a grad student, as an undergrad) and being in an environment where you're being exposed to many different topics, so you can see how your skills can impact that particular kind of nanoscience.

PSW: What are your ultimate goals in your scientific career?

Chad Mirkin: To keep asking and answering major unanswered questions, developing techniques that enable the fabrication, the synthesis of molecules and materials with control over architectural parameters on the 1−100 nm length scale, to be able to design systems that have complexity that goes beyond conventional small-molecule systems that have the flexibility and capabilities that exceed those that we typically associate with macroscopic materials. We've done that in the context of detection systems. A big part of what we're going to do over the next decade is to work in the area of therapeutics and to continue to push the bridge between chemistry and materials science and biology and medicine, asking, "Can we create new types of materials that can be used, for example, for new intracellular gene regulation? [Can we] create new capabilities in the context of siRNA delivery, and antisense knockdown? [Can we] begin to create materials that perhaps can have a very significant impact on cancer research,

and ultimately the development of new therapeutics for treating many types of debilitating diseases, especially in the area of cancer?"

PSW: What advice do you have for young scientists?

Chad Mirkin: My advice is to pick an area based upon interest and passion. Don't pick an area based upon what you think will lead to a great job, or something that is perceived by others as being sexy. Pick an area that really turns you on, and pursue it as aggressively as possible. Good things will follow!

[Literature citations and figures were added after our conversation to assist and to direct the reader to relevant publications.]

— Paul S. Weiss

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REFERENCES AND NOTES

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