

ACS AMA: Hi Reddit! My name is Nathan Gianneschi, a nanomaterials researcher. Ask me anything about biomedical applications of nanomaterials!

AmerChemSocietyAMA¹ and r/Science AMAs¹

¹Affiliation not available

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Abstract

ACS AMA Hi Reddit! My name is Nathan Gianneschi and I research nanomaterials at the University of California, San Diego, but I am moving my laboratory to Northwestern University; coming soon, at the beginning of July this year. Recently work in my lab was published in ACS Central Science, an open access journal, entitled “Mimicking Melanosomes: Polydopamine Nanoparticles as Artificial Microparasols” <http://pubs.acs.org/doi/full/10.1021/acscentsci.6b00230>. This work describes a nanomaterial that could be used to protect cells from UV damage. I look forward to answering your questions about this research today! More broadly, our research group takes an interdisciplinary approach to nanomaterials research with a focus on multifunctional materials with interests that include biomedical applications, programmed interactions with biomolecules and cells, and basic research into nanoscale materials design, synthesis and characterization. For this work I have been awarded the NIH Director’s New Innovator Award, the NIH Director’s Transformative Research Award and with a Presidential Early Career Award for Scientists and Engineers. My academic background started with my B.Sc. (Hons) at the University of Adelaide, Australia in 1999. In 2005 I completed my Ph.D at Northwestern University. Following a Dow Chemical postdoctoral fellowship at The Scripps Research Institute, in 2008 I began my independent career at the University of California, San Diego where I am currently Teddy Traylor Scholar and Professor of Chemistry & Biochemistry, NanoEngineering and Materials Science & Engineering. In addition to my NIH citation, I was awarded a Dreyfus Foundation Fellowship, I am a Kavli Fellow of the National Academy of Sciences, a Fellow of the Royal Society of Chemistry, and am an Alfred P. Sloan Foundation Fellow. Ask me anything about using nanomaterials for biomedical applications, including this work on melanosome mimics. I will be back at 11am EDT (10am CDT, 8am PDT, 3pm UTC) to answer your questions. I’m back to answer questions (10am CDT). Hello! Thank you to all of you for your interest and fantastic questions. I have enjoyed trying to answer as many of you as possible, and I apologize if I was too brief, or could not get to your question today. Thank you to the ACS, and the journal, ACS Central Science for setting up this AMA session. All the best with your work, studies, life and health. Signing off - 12:57pm (CDT)

[REDDIT](#)

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[ACS AMA](#)

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What do you think the most obvious change to the average citizen is when talking about Nanomaterials?

[Nehema-](#)

This is a very good question, and a difficult one to capture here. Many of the materials we think of as "nanomedicines" that have been approved for clinical use, or that are in development, have the potential to positively impact individuals with serious diseases including cancer. This of course could impact society as a whole.

June 27, 2017

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However, more broadly, nanotechnology is all around us. You find examples in electronics, including in display technologies. These are applications we all see every day.

I think, perhaps the biggest impact, has been from the kind of materials we can now make because we have instruments and techniques to visualize and image nanoscale objects and features. These tools include things like electron microscopes. These tools have ushered in an entire age of innovation enabled by the precision preparation of complex systems with nano- and microscale features. I would argue then that it is not our ability to "make" things at this length scale that has driven innovation and that impacts society, but our ability to figure out what precisely we have made!

In essence, we "see" the outcome of control at the nanometer length scale in the macroscale devices we hold in our hands. The inner workings of which are largely a "black box" when looked at with our own eyes.

That said, there are tremendous challenges before we have true control over matter at this length scale. And with tremendous challenges come incredible opportunities for science and technology.

What do you think the human toxicology situation of these materials is? Are the particles large enough that they don't partition in to the skin? I know there has been concern about nano-TiO₂ for sun care.

[nate](#)

The inherent toxicity of any material is always a concern when applied to cells or tissues, in the laboratory, or in humans in the clinic or other settings such as in cosmetics. Typically a battery of tests are applied to understand and then mitigate those effects - both short term and long term. Whether we are applying nanoscale materials, or standard small molecules, these are critical, core concerns.

For the artificial melanosomes, we see no toxicity over the concentration ranges that gave us an effect. This is the critical point. That is, the "medicine" has a window where it's active, and a concentration where it's toxic. You want the gap between those two things to be large, such that it is safe. In our case, we consider it safe. In addition, the material is very similar to naturally occurring melanin, so chemically, it's safety profile makes sense.

One concern with any new technology in medicine is overuse, as seen with mammograms, PSA tests, colonoscopies, genetic sequencing, and a myriad of other procedures/tests. The routine use of highly specific diagnostic and preventative tools is one if the reasons healthcare is so costly in the United States.

My wife was diagnosed with an invasive melanoma about 7 years ago, so any technology that can minimize the likelihood of recurrence is of major significance to her, and I sincerely thank you for doing this research. I just wonder how the medical field would react to learning of a material that could help prevent skin cancer.

My question is do you think this should be applied to the population as a whole, or just in high-risk cases?

[hnglmkrnglbry](#)

Preventative medicine can take many forms of course. This includes early and routine testing as you mention, as well as exercise.

I'm Australian, and as such, as a kid I grew up hearing the familiar refrain - Slip, slop, slap. Slip on a shirt, slop on some sunscreen and slap on a hat. Melanoma has a high prevalence in Australia relative to many other countries, and skin cancer risk receives a lot of attention as a public health concern. The

slip, slop slap, campaign is about preventative strategies. Sunscreen used regularly decreases the risk.

What we have developed has not been tested for its ability to work in humans. We have not even tested if it can indeed penetrate real skin. We just know it can shield human skin cells in a dish. So, plenty of science to go before we know if it is useful in any setting. However, what we envision is a material that would enter the skin and protect from within, as tanning does. I would imagine you would still apply standard slip, slop slap measures.

In summary, it is, as with many treatment or prevention strategies, a cooperative effort. For some, the cosmetic benefit of a material that provides a "tan" may be interesting. If that could be combined with a therapeutic effect in otherwise "at risk" people, then we will have achieved our goal to some extent.

How far do you think the application of nanomaterials in medicine could go, for example which diseases do you think you could cure/treat with nanomaterials?

[Plyarso](#)

My opinion is that systemically delivered (e.g. intravenously injectable, or orally consumable) nanomaterials will be best applied in settings that rise to the level of an acute disease, in emergency settings, and in situations such as in otherwise untreatable cancer.

My laboratory focusses on these kinds of applications. Particularly in cancer, and in heart disease, where the needs are great. We look, for example, to deliver drugs that are unsafe delivered on their own. Or, we look for diseases where there is little to no known pathway forward.

In the case of the melanosome work in the paper highlighted here, we are looking to potential topical applications, where one may expect local delivery of the material.

Do you think engineers and researchers will be able to find a way to mass produce nanomaterials like carbon nanotubes and buckyballs in the near future? How do you think this would change the usage of such nanomaterials and their accessibility to others?

[blooperie2](#)

Yes, indeed. In fact, many groups are working on scaling and importantly, purifying carbon based materials including graphene etc. (see for example the work of Mark Hersam and coworkers).

The use of complex materials like this in large scale applications such as coatings, building materials etc. of course will rely on the ability to produce large quantities.

Naturally, in the context of biological or medicinal applications, much less material is required. Scaling for these applications is not trivial, but it is within reach, and is a design concern from the outset. For these applications, one is also very concerned with purity, and the processes by which it can be made reproducibly.

When you go to the lab to design your new nanoparticle, or functionalized carbon-based system, consider how it might be reproducibly produced at scales that align with the application. This is perhaps one of the greatest challenges facing the field.

Is it really possible to rebuild lost limbs, or at least lost tissue? Or is that too far fetched for right now.

[imsickwithupdog](#)

Technologies to provide for bone regeneration and tissue healing are very much at the forefront of biomedical and bioengineering research.

This is in the context of implants capable of providing scaffolds for bone regeneration after breaks, tumor removal, or other trauma (see interesting work by Becker et al in this area). In addition, there are materials being developed for healing heart tissue, or for guiding tissue regeneration in hearts following heart attack (see the work of Christman in this area, for example).

These are in various stages of development and application. So, this is not at all far fetched. It presents an important set of materials science problems, and how materials interface with growing, or healing tissue. In addition, it tests our knowledge of how materials may be impregnated with chemical factors that aid in the healing process.

In terms of regenerating entire limbs, we are a long way from that. I would think a more realistic goal is the development of better prosthetics that interface with our intact nervous system to make that interface more and more seamless. That is likely how the future will look in that respect.

On that final note - there are other organisms as you know that do regenerate limbs, and geneticists and others have long been fascinated by what molecular (biochemical) triggers and signals are used to achieve this. Perhaps there will be a route for inducing an equivalent process in humans...

What is the tech status of using nanomaterials to target specific delivery sites within the body to allow directed delivery of hazardous materials for application in chemotherapy and imaging?

[Slammy1](#)

The idea of the "magic bullet" is a well known concept in medicinal chemistry, pharmaceutical science and of course in nanomaterials for medicine (or "nanomedicine"). However, of course, as soon as you see the word "magic" you should become highly skeptical; though not cynical.

What we are talking about is the development of strategies that make drugs (e.g. otherwise toxic chemotherapeutic, immunotherapeutic drugs) safer to inject. The safety comes from our ability to inject therapeutic doses.

Therapeutic doses are described scientifically as the amount of material a doctor might inject per kilogram, or square meter of surface area of the organism (a human like us for example). These doses are ones that might do useful things like kill tumor cells, or slow their growth, or switch on the immune response to those diseased tissues.

For traditional chemotherapeutics that window between what is therapeutic, and what is toxic is quite narrow. This means the drugs make a lot of people sick (as you know), and we often refer to the "dose limiting side-effects" of these drugs. The goal of targeted nanomedicines, and indeed any targeting strategy, is to increase the amount of drug that gets to the diseased tissue, and/or decrease the amount that goes everywhere else.

Imagine the challenge then! You inject something into someone's veins. It goes all over the body. Some often used chemo drugs have known problems like heart toxicity, so you can see the problem immediately.

The challenge is that you are trying to defy millions of years of evolution, and basic physics. You want a tiny, virus sized particle to be ignored by the immune system and the systems that vacuum up little foreign particles and get rid of them, but you want that same particle to be recognized by your tumor. It is a tremendous challenge, and one that those in the field are acutely aware of. However, we have a

long way to go.

Many materials that work in cell culture (think little dishes of cells in pristine labs), or even in animal models of disease, do not translate into larger mammals (i.e. you and I!). Our bodies, and our tumors are complex environments, that come in many different flavors. This is where developments relating to the expression of specific signals in specific organs at different times, and the presence of certain biomarkers in specific people and diseased tissues at specific times, are extremely important. These developments coupled with our ability to make AND characterize complex nanomaterials, will be the key to success in targeting.

But, remember, if you hear about "magic", turn your skeptic-meter on high alert.

programmed interactions with biomolecules and cells

I think of programming in terms of languages (C#/Java/etc etc) - how do you programme interactions for biomolecules/cells? What is the context of programming here, is there an IDE, tooling, how do you "debug"?

[iamapizza](#)

We tend to use the word "programming", or refer to "programmed materials" to refer broadly to methodologies for designing a synthetic material to respond in a defined manner. For example, a polymer may have a "programmed degradation rate". This would be a defined half-life for example under specific conditions, over which one would expect the polymer to decay. This is "chemically programmed" into the polymer when it is made. The wheels are set in motion, so to speak.

More complex examples exist in the field of DNA-nanotechnology, where information is encoded in the primary sequence of the nucleic acids, and is "read-out" by interactions with other nucleic acids encountered.

Programming an interaction with a cell: For example, cells of a specific type (let's say a breast cancer cell), may be producing proteins that catch nutrients at their surfaces. They provide hooks for those nutrients at higher concentrations than normal breast tissue. One can, in principle, design a material that mimics the nutrient, and is caught by the hook. The particle may then enter the cell (so called, Trojan horse), and be degraded by the cellular machinery that processes said nutrient. If the particle has hidden soldiers inside (cell killing drugs), they leap out and attack. This is an example of what we mean by programming interactions with cells. 1) Binds selectively (hopefully, maybe...) 2) Drugs come out at a set rate and time.

These are biochemical recognition events that are interlaced into the chemistry of the system when it is made.

I would like to know more about nanobots -

- how soon are they going to be a reality?
- if there were a nanobot outbreak like in the sci-fi novels, how can humanity save itself?

your thoughts pls

[TRIVARGA](#)

The mental image of a futuristic "nanobot" is certainly a compelling one. It has also been brought up by many in this string of questions.

A clear definition of what one means by a "nanobot" is essentially missing as a scientific concept,

which is not surprising because they exist more firmly in the realm of science fiction for now.

What I think of is a material on the nanoscale that can perform functions in an entirely autonomous fashion. There are materials that fall into this category in some limited ways. For example, materials that sense their environment (a specific chemical signal for example from a cell), and then perform some switchable process. Indeed, that kind of limited (very limited compared to the image of a "nanobot") does exist, and has been used.

As for saving humanity... Let's keep working together on that one!

Can you make some nanomaterials that are absorbed by specific kinds of cells?, that could be used to deliver antibiotics directly to bacteria, or medicine directly to the specific kind of cell that needs it

[Frigorifico](#)

Getting into a specific cell type is not necessarily a problem for a synthetic material in a laboratory setting. This is where cells are grown on a surface as a single layer. Cells can have specific receptors that we can bind to with synthetic materials and enter. This has been demonstrated many times in single layer cell culture.

The issue is how to target to real tissues in living organisms. This is far beyond a "cell targeting" problem, as different tissues are made up of many cell types, and this includes diseased tissues including tumors. For example, a particle in the blood stream "sees" the walls of the vessels of tumor, but not necessarily the nasty tumor cells inside. So, how we begin to think about crossing specific barriers, and specific times (like the walls of the vasculature), and then engaging specific cell types (immune cells, vs cancer cells, or some other system), is where the challenges remain.

Hello. I feel like a bit of a dunce because I don't understand a whole lot about what you wrote, but my sister is a physicist and my brother in law in a chemist so I love talking about science-y stuff.

I was wondering what your favourite project to work on has been? And why you found it so exciting? Maybe it's a project you haven't started working on yet! Thanks, and I appreciate you taking the time to do an AMA, what you're doing is so fucking cool.

[madmaxime](#)

Unfortunately, a lot of science, and chemistry is certainly no exception, is filled with terminology and language that can make it seem inaccessible. Especially if dunces like me give a technical answer in response to a highly technical question.

At times like this, just ask a simple question, and ask for a simple answer. These are often the most challenging for the scientist. So, just go ahead and ask.

Favorite project - I have to say, I have very much enjoyed this work on melanin and melanin mimics. The first author, Yuran Huang just defended her thesis, and is a fantastic scientist. She really worked hard and was inspirational to me and others who have worked with her. It also involved many years of collaboration with others in my group and outside my group including Prof. Yiwen Li (now a professor at Sichuan University in Chengdu, China).

So, it really is about people doing spectacular things at a high level. That's the day to day excitement for me.

I see that you can use MeINPs as iron-chelated T1-weighted MRI contrast agents. Would labelling the particle with a radiotracer to enable multimodal PET+MR imaging be a possibility?

[mandragara](#)

In short, yes. Indeed, multimodal imaging has been envisioned and demonstrated in several contexts with this kind of material by several groups now. I'm short on time trying to answer these questions, but I'll dig up a reference for you, and get back to this if I can.

How easy/costly are these nanomaterials to produce right now? Do you think they will be able to be produced in enough quantities to be available/profitable?

Also what differences are there from testing nanomaterials in a lab to testing them in live organisms? Are nanomaterials being tested in humans yet?

[Saltymr](#)

On the first question. The materials are relatively easy to make once you know how to make them form uniform shapes and sizes. This is something that has been worked out by other laboratories, and several postdocs and graduate students in my group have worked hard to hone the process. The materials are also made from simple components, and therefore, can be scaled up fairly easily.

On the second question. I answered this to some extent in an answer above. In short, the differences are vast. Nanomaterials are indeed in human testing. There are many clinical trials, that include combination therapies, and delivery of standard chemotherapeutics.

We share the same last name and I've never, ever had this happen with such an obscure last name. I don't have a question for you unfortunately, but thanks for doing the AMA for people who do.

Keep on making us Gianneschi's look good!

[StrangeBrew710](#)

I've never had that happen either. Keep up the good work mate!

How close are we to being Borg?

[newgraves](#)

Just keep practicing your tennis, and you may have a shot.

Can nano materials be used in conjunction with stem cells to 3d print super organs?

[rvncto](#)

Awesome question. I'd say you have a research project on your hands!

Hey, thanks for doing this AMA. What nanomaterial do you think has incredible untapped potential today?

[WinterCharm](#)

I believe that in terms of nanoscience, nanomaterials and nanotechnology, the biggest impact will be made by the characterization tools. We can make lots and lots of things, but actually fully characterizing them, especially in complex environments following injection, or in solution, is extremely difficult.

My group is working as are many others, on developing techniques for better understanding nanomaterials in solution, as they move around in liquids for example. Over the past 117 years we have seen the tremendous impact of characterization tools on science. From X-ray crystallography and NMR, to biochemical techniques like PCR and ELISA.

The untapped potential today is in the hands of those who will develop the techniques that enable us to peer down, and capture nanoscale processes in action!

Could this be used for diabetics?

[kellaorion](#)

In terms of routine use in chronic disease, nanomaterials present a key challenge. They have the potential to cause an immune response. This fact may limit their use to short term applications. Acute disease, emergency, or otherwise untreatable types of cancer.

As far as traditional methods to administer medicine goes, how does nanomedicine impact the liver and is toxicity/buildup an issue?

[flavianpatrao](#)

Liver toxicity is a frontline concern in the development of any kind of medicine. Nanomedicines have a particular tendency to accumulate in the liver and spleen. In fact, it is very difficult to avoid this fate, as your system is designed to clear the blood of foreign particles and dispose of them.

There are a number of ways people try to design materials to avoid this issue. One obvious one is that you use materials that degrade regardless, and clear, such that they don't "build up". Other techniques include using surface coatings that make them "non-stick" to proteins in the blood that guide the clearance of the particles to the liver.

Regardless, if you are delivering a toxin to cancer tissue, even if it gets to its tumor target, the drug and its byproducts will have to be cleared in some way. Toxicity vs efficacy is always at play.

So you think nanomaterials will one day be able to be applied to parts of the body that wear out overtime due to various factors? Faulty blood valves in the legs would be an example that comes to mind or torn ligaments. Also, I am so excited about your work.

[Flyingwheelbarrow](#)

Yes! This is precisely the kind of thing being investigated.

Would there be any merit to computationally analyzing MeINPs along with organic and biosynthetic molecules to better understand any minute differences between their dynamics?

[NaClBag](#)

Absolutely. The structure of our melanin-like nanoparticles is quite complex. We have a major project in our group dedicated to working out basic structural features of these, and their naturally occurring cousins. Indeed, we work with theoreticians at various levels to grapple with those complexities.

How do you envision your melanosome nanoparticles to be delivered to the skin? Have you started doing in vivo or human skin explant experiments? Have you tried adding PEG to your particles to increase bioavailability and prevent premature clearance?

[Popcornme](#)

We are working on answering these questions and will focus on testing in 3D tissue models.