The remit of expertise putting nanomaterials to work

Tom Darlington, a Senior Director of Technical Ops and Program Management at nanoComposix developing nanoparticles for drug discovery and therapeutics.

Your PhD is in macromolecular and cellular structure and chemistry. How did you bridge your background into nanomaterial-focused applications?

I started out as an organic chemist with the intention of applying that to biology; thus I moved into a joint programme to work on vaccine development for an oral vaccine. I later went into antibody development in pharma where my role was focused on working with contract manufacturers and on analytics for current good manufacturing practice (cGMP) production. When I came to work with Steve Oldenburg at nanoComposix, we were looking at the toxicity of nanomaterials and developing tox assays. Our work expanded and the team developed the synthesis procedures for what became our catalogue products at nanoComposix. I did not have a formal background in nanomaterials, but I did understand chemistry and was comfortable thinking about macromolecules at the same scale based on my training in structural biology.

You have been at nanoComposix nearly since its inception; how has your role evolved since you first joined?

Early on, we were writing on small business innovation research and using our experience with nanomaterials and backgrounds as research scientists to solve applied research problems. We gained expertise in a variety of materials from silver and iron oxide to polymers and carbon nanotubes. The biggest evolution is that we were a group of 12 or so bench scientists, mostly PhDs, and everyone was hands-on, generating data and working in the lab. We transitioned from research scientists to development scientists, running the technical operations side of the business and building a quality system for cGMP. We had synthesis expertise and knew the unique pitfalls of trying to transfer nanomaterial manufacturing to another group. That set the path to my current role. As we learned, it takes a lot of work to build ISO spaces and a quality system, but we were successful at establishing this infrastructure and cGMP manufacturing has become a core service offering at nanoComposix.

What excites you about nanomaterials and their application to drug delivery and therapeutics?

My core interest is the biomedical applications of particles and getting them into a suitable format to produce for clinical trials and ultimately commercial products. For example, early on we worked with a company called Sienna to produce a novel silver nanoparticle for a topical therapeutic. That product received premarket approval (510k) from the US Food and Drug Administration (FDA) and the science behind it was at the core of our expertise in plasmonic nanoscience with noble metals. More importantly, it was a product that could have a positive impact on people's lives. Personally, the reason I moved into cGMP production of nanomaterials is that you cannot put things into humans without doing so under cGMPs (for very good reasons) and

you cannot use nanoscience to improve people's lives unless you utilise the particles in a drug or medical device.

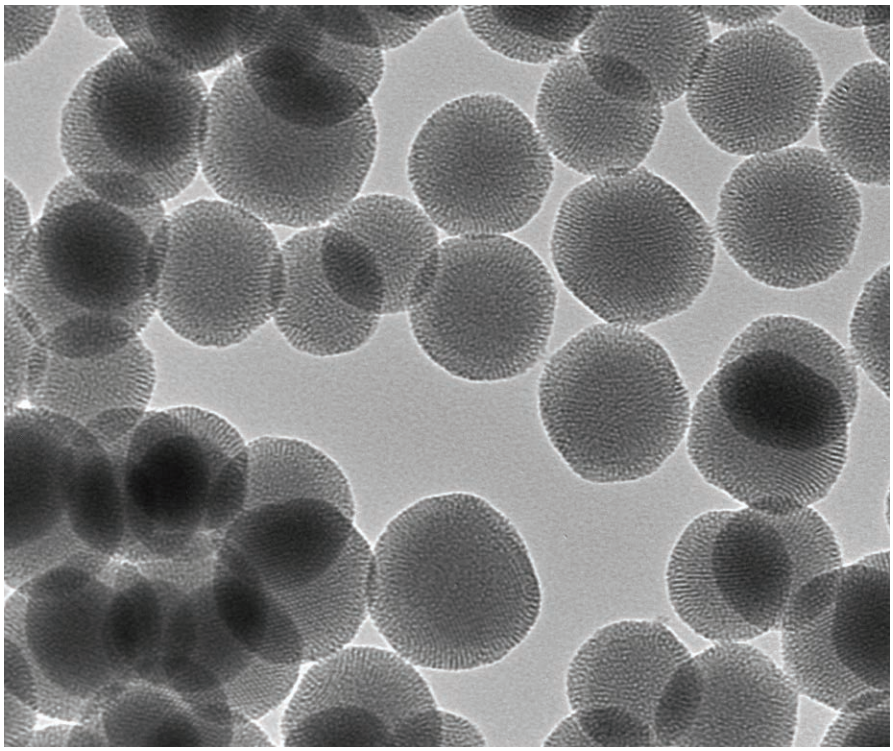
Impacting lives was the reason I went into vaccines during my post-graduate studies. I was making an oral vaccine that was designed to be produced inexpensively and stored without cold chain – the goal being to make it universally available across the globe. In my role at nanoComposix, we take the things that we've worked on for many, many years – silver, gold, iron, silica nanoparticles – and get them into clinic to have an impact on people's lives. To me, that is the most rewarding part of my work. That's why we're building all of these processes and systems. cGMP is entirely about patient safety.

What are some of the key challenges of developing, scaling-up and manufacturing inorganic nanoparticles for regulated applications?

Development is using toolkits from R&D to design a particle with the right properties for the application. For the manufacturing company Sienna, we had invented a new particle and the design input was essentially, "can you make a particle that will absorb laser light and heat for hair removal or acne treatment." We were looking at different sizes and shapes of materials to identify one with the right optical properties.

Developing the right particle might make the process easier but scaling up is a totally different challenge. Some synthesis methods are highly sensitive and work well in an eppi tube, yet are impractical when trying to manufacture even at clinical scale. Mixing and heating are the two big factors that come into play for scale up. For example, if a reaction has fast kinetics, mixing is usually incredibly important – it's often better to have a slightly slower reaction when designing for scale up. Scaling reactions that require heating is especially challenging. If you're heating a small volume and the rate of heating is important, bringing that to a bigger volume is almost exponentially harder as you go up in scale.

When designing for scale up and manufacturing, you begin by carrying out your reaction at small scale in high repetition to understand which factors matter and which do not. Thus, when you scale it up, you know what your critical process parameters are for scaling. When you do enough experiments to develop a deep understanding of your process, you start to understand what ranges you can work within, and in turn, you don't waste time and money controlling parameters that don't matter. You must start with the end in mind; using the types of equipment and reactions as for your final application as early as possible in the process.



What unique capabilities do you and the team at nanoComposix offer, and how do you like to collaborate with clients on challenging manufacturing or development projects?

We are a collaborative group spanning PhD nano chemists, who have spent years in postdocs learning the detailed nuances of various types of nanomaterial chemistry, all the way to individuals who have been in manufacturing and materials for years. We have a team that is up to date on current literature for making the particles and developing new routes, as well as team members who have taken a particle into cGMP production. These groups are always talking to each other and interacting and benefitting from each others' experiences. We take clients through the process from start to finish and hand-off from one team to another based on expertise. We are all available and 'on call' to solve problems. So, when a new therapeutic development project comes in, we get quality involved, or process development, or manufacturing, to understand what will ultimately make the particle manufacturable. We always think with the end in mind. We have both the cGMP production and the R&D groups with deep expertise in nanomaterial synthesis. Both are not usually resident in many organisations and certainly not ones that can do cGMP nanomaterial production. That's the core value that we bring.

Tom Darlington

Tom is a Senior Director of Technical Ops and Program Management at nanoComposix. He is an experienced scientific and operations leader focused on developing and manufacturing nanomaterial-enabled diagnostics and therapeutics. He joined newly-founded nanoComposix in 2005 after manufacturing therapeutic antibodies at Epicyte Pharmaceuticals and developing analytics for biological macromolecules at Chromatin, Inc. Tom has developed technologies in the areas of therapeutic plasmonic particles, targeted nanoparticles for therapies and diagnostics, lateral flow devices, materials science, and analytical instrumentation facilitated by nanomaterials. When nanoComposix and its partners reached the clinical stage of development, Tom led teams to create an ISO 13485:2016-certified QMS and to build a cGMP manufacturing facility for nanomaterial-enabled therapeutics and diagnostics. He obtained his PhD in Macromolecular and Cellular Structure and Chemistry at The Scripps Research Institute.