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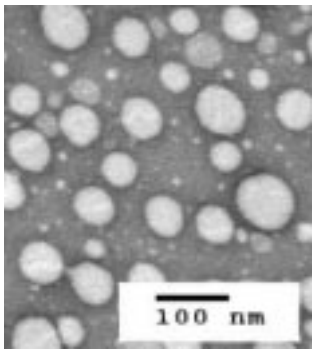
SPOTLIGHT:
NanoMed Pharmaceuticals

By Stephen Benoit

With the rush to add "nano" as a prefix to company names and technology descriptions, and venture capitalists and private equity investors using their Blackberries® to check email at "Investing in Nano" conferences from New York City to San Diego, one cannot be faulted for suggesting that the current hype surrounding nanotechnology is reminiscent of a time not so long ago when "dot com" was every company's corporate suffix. To be sure, much of the nano-hype is just that; hype. However, the application of nanotechnology in drug delivery is also very real and this reality is taking shape today.



Nanoparticles containing gadolinium that are <100 nm, stable in blood, and are comprised of as high as 50% pure gadolinium.

In this issue, we spotlight NanoMed Pharmaceuticals; an early-stage start-up company, developing novel nanoparticle-based advanced drug delivery systems.

Size matters, in drug delivery. Smaller is better, in targeting biotech therapeutics to specific cells and tissues. Size matters. Smaller is better. This was the thinking of NanoMed's scientific co-founders, Russell J. Mumper, Ph.D., and Michael Jay, Ph.D., faculty members at the University of Kentucky, College of Pharmacy, and the Assistant Director and Director, respectively, of the University's Center for Pharmaceutical Science and Technology. In 1999, Drs. Mumper and Jay set out to develop a novel nanoparticle manufacturing technology that would avoid the problems associated with polymeric nanoparticles and liposomes, and instead, combine the unique advantages of these systems with the advantages of microemulsions to engineer nanoparticles that could be targeted to specific tissues and cells. The overriding development criteria were that any new manufacturing technology had to be inexpensive, reproducible, and scalable.


Scientific Founders of NanoMed Pharmaceuticals, Inc. Dr. Russell Mumper (left) and Dr. Michael Jay (right) are currently faculty members in the College of Pharmacy at the University of Kentucky in Lexington, Kentucky. Dr. Mumper and Dr. Jay are inventors of Nanotemplate Engineering.

Dr. Mumper's and Dr. Jay's work resulted in the development of *Nanotemplate Engineering*, a platform manufacturing technology which enables the production – in minutes – of well-defined, uniform, solid nanoparticles less than 100 nanometers in diameter. These nanoparticles are made using all pharmaceutically-acceptable excipients and can be engineered to contain or carry small molecules, peptides, proteins, plasmid DNA, diagnostic agents, and radio- and bio-sensors.

The ability to rapidly and consistently produce sub-100 nanometer particles is a significant process development milestone since below 100 nanometers, materials exhibit different, more desirable physical, chemically, and biological properties. These enhanced properties are important, if not essential, when trying to create so-called next generation vaccines that stimulate both humoral and cellular immune responses, or formulating drugs that can be delivered systemically and subsequently targeted to the brain.

In 2000, NanoMed Pharmaceuticals, Inc., was formed. In 2001, the Company obtained from the University of Kentucky Research Foundation the exclusive, worldwide rights to the *Nanotemplate Engineering* technology invented by Drs. Mumper and Jay. Today, NanoMed is using this novel platform technology to develop nanoparticle-based drug delivery solutions for pharmaceutical and biotechnology partners to deliver drugs to the brain, and create the next generation of vaccines. NanoMed's development programs focus on therapeutics that will stop the progressively debilitating effects and ultimate outcome of neurodegenerative conditions like Alzheimer's and Parkinson's disease, stroke, and brain tumors; and prophylactic vaccines that will provide immunity against infectious diseases like HIV and hepatitis C.

More than 50 million people worldwide are infected with HIV and hepatitis. More than 10 million people worldwide are suffering from the progressively debilitating effects of Alzheimer's and Parkinson's disease, stroke, and brain cancer (collectively, neurodegenerative diseases). Unfortunately, the prognosis for these individuals is poor.

To delay the progression or stop the ultimate outcome of Alzheimer's, Parkinson's, stroke or brain cancer, a drug needs to be able to cross the blood-brain barrier (BBB) and get to the right part of the brain or brain tumor. 95% of today's therapeutics

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cannot cross the BBB and must be delivered via direct injection into the brain or cerebrospinal fluid, or utilize approaches that involve temporarily 'opening' the BBB, or be released from a device that has been implanted into the brain.

To provide immunity to HIV, a therapeutic (protein antigen) needs to get into the immune cells that stimulate – both – the production of protective antibodies and so-called killer T cells that seek out and destroy the virus. Today, no such vaccine exists.

NanoMed's founders are committed to improving the outlook for people with Alzheimer's disease or HIV by solving the needs of pharmaceutical and biotechnology companies seeking to deliver drugs to the brain or create the next generation of vaccines. In working with such companies, NanoMed has learned that alternative nanoparticle carriers do not appear to be able to be routinely or easily manufactured in a size range that is well-suited for cell- and tissue-specific targeting. Moreover, these alternative systems appear to employ processes that are intrinsically more complex, slower, less flexible, and potentially damaging to the therapeutics they intend to deliver.

In contrast, *Nanotemplate Engineering* has been shown to consistently produce nanoparticles that can: be coated with plasmid DNA or protein antigens; entrap plasmid DNA or model proteins; contain up to 33%-80% w/w low Mw drug with entrapment efficiencies of 80% to 100%; increase drug solubility up to 10,000-fold; are stable in biological fluids at 37°C; can be sterile-filtered and lyophilized; and can be formulated with various types of adjuvants, endosomolytic agents, and ligands (which are critical for cell- and tissue-specific targeting).

More significantly, NanoMed has generated extensive peer-reviewed data demonstrating: *in-vitro* receptor-mediated tumor cell uptake of folate-targeted gadolinium-entrapped nanoparticles in human KB cells (nasopharyngeal epidermal carcinoma); *in-vitro* receptor-mediated cell uptake and transfection of human dendritic cells with plasmid DNA nanoparticles; *in-vivo* (genetic) vaccine studies in mice showing significant enhancements of humoral, Th1-type, and proliferative immune responses with dendritic cell-targeted nanoparticles; and *in-situ* BBB transport of nanoparticles and absence of nanoparticle toxicity at BBB with uptake comparable to existing CNS therapeutics.

NanoMed's founders' labs are located at the University of Kentucky's Center for Pharmaceutical Science & Technology ("CPST") and Advanced Science & Technology Commercialization Center ("ASTeCC"). The CPST is a fully integrated analytical and formulation development and FDA-registered pharmaceutical clinical manufacturing facility utilizing current Good Manufacturing Practices (cGMP). The facility employs 24 trained professionals and occupies approximately 3,700 square feet. ASTeCC is the University of Kentucky's incubator for multidisciplinary collaborations and start-up ventures. This $17 million, 80,000-square-foot facility is located in the heart of the University of Kentucky campus.

Collectively, NanoMed's management team represents a unique balance of commercial and academic experience; large and small company experience; start-up and operating general management experience; and broad expertise in developing advanced drug delivery systems. Most importantly, each member of the team has a strong background in product development.

In addition to a strong management nucleus, NanoMed has attracted a group of scientific advisors that augments the Company's strengths in developing advanced drug delivery systems with expertise in the physiology and function of the blood-brain barrier with primary focus on drug delivery to the central nervous system, polymers for supplementing or stimulating the immune system, cell interactions with polymers, and global experience in all phases of clinical development, including supervision of more than three hundred clinical trials across numerous therapeutic areas and drug classes.

Dr. Michael Jay (left) and Dr. Russell Mumper (right) are testing the viscosity of a nanotemplate suspension used to engineer nanoparticles that are being developed by NanoMed as a potential new vaccine for AIDS.

NanoMed is following a growth strategy proven successful by today's leaders in the drug delivery industry. The Company will enter into strategic alliances with pharmaceutical and biotechnology company partners and is now performing seven feasibility studies involving nanoparticle-based drug delivery solutions that capitalize on NanoMed's competitive strengths in brain delivery and vaccine development. As NanoMed grows, it will seek opportunities to use its proprietary drug delivery systems to develop and independently market its own drugs. Consistent with this longer-term phase of its growth strategy, NanoMed has initiated the development of proprietary products for neurodegenerative diseases and a next generation HIV-1 vaccine.

Size matters. Smaller is better. The application of nanotechnology in drug delivery is happening today, and is manifested in NanoMed Pharmaceuticals nanoparticle-based advanced drug delivery system. The successful utilization of this system by NanoMed and its pharmaceutical and biotechnology partners will mean a brighter outlook for persons suffering from many neurodegenerative and infectious diseases. •