Dendritic Nanotechnologies, Inc.: The Answer to the Physical Limitations of Nanotechnology

ABSTRACT

Nanotechnology is one of the rare advancements whose impact it is impossible to overestimate. This emerging technology has the potential to change how we work and play, the ways we fight disease, even our life expectancies.

Nanotechnology's move into practical use, however, has been slow because the very nanostructures that hold such promise are neither precise nor physically predictable enough for low-cost mass production. In this article, we will discuss a solution–dendritic polymers, or "dendrimers"–nanostructures with the precision and predictable physical properties necessary for commercialization.

We will also discuss the leading developer and provider of dendrimers, Dendritic Nanotechnologies, Inc. (DNT), which has the intellectual property and strategic relationships to bring nanotechnology to the practical applications sure to change our world.

INTRODUCTION

Imagine a world where nanoscopic probes travel constantly through our bodies, monitoring our health at all times and alerting us at the first sign of danger. Imagine a world where disease is cured safely and painlessly, where invasive surgeries and painful treatments are replaced with nanoparticles sent into our bodies to find diseased cells and destroy them. Of all the areas of our lives in which nanotechnology will soon make an impact, perhaps the most exciting is in the field of medicine–because in this area, nanotechnology will literally be the difference between life and death.

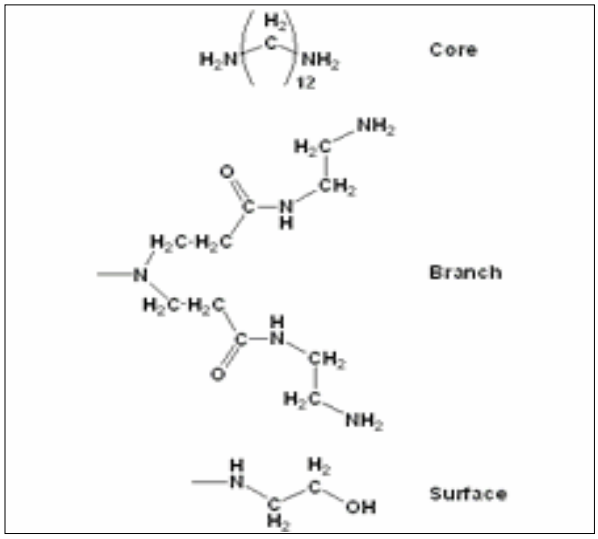
Among nanotechnology's most highly anticipated–and lucrative–applications are disease diagnostics and drug delivery. Engineered nanostructures, however, lack the precision and reproducibility for the vital yet highly delicate art of probing the body to search for disease and unleashing the precise dosage of the required drugs to fight it. The most promising development to overcome this obstacle is a new class of nanostructure called the dendritic polymer, or "dendrimer." With their low-cost, scalable and precision architecture, dendrimers are the ideal agents for targeting disease and delivering the drugs to wipe them out.

I. DENDRIMERS

Dendrimers are nanoparticles that can be precisely designed and manufactured for a wide variety of applications. They are formed by the addition of shells of branched molecules to a central core.

Figure 1: Poly(amidoamine) Dendrimer Structure

Sample dendrimer with a core of 12-diaminododecane, a Poly(amidoamine) or PAMAM branch and an Amidoethanol surface.



Adjusting the chemical properties of their core, shells, and surface layer can tailor dendrimers to fit the needs of specific applications. Because of their precise architecture and construction, dendrimers possess inherently valuable physical, chemical and biological properties, uniquely suited to drug diagnostics and drug delivery. These properties include:

- **Efficient membrane transport**
  Dendrimers have demonstrated rapid transport capabilities across biological membranes.

- **Precise architecture, size and shape control**
  Dendrimers branch out in a highly predictable fashion to form amplified three-dimensional structures with highly ordered architectures.

- **High loading capacity**
  Dendrimer structures can be used to carry and store a wide range of metals, organic or inorganic molecules by encapsulation and absorption.

- **High uniformity and purity**
  The synthetic process used produces dendrimers with uniform sizes, precisely defined surface functionality, and very low impurity levels.

- **Low toxicity**
  Most dendrimer systems display very low cytotoxicity levels.

- **Low immunogenicity**
  Dendrimers commonly manifest a very low or negligible immunogenic response when injected or used topically.

Figure 2: Targeted drug delivery

The high level of control over the dendrimer architecture makes this class of polymers ideal carriers for the active pharmaceutical ingredients in areas such as drug delivery, diagnostic/imaging and gene transfection.

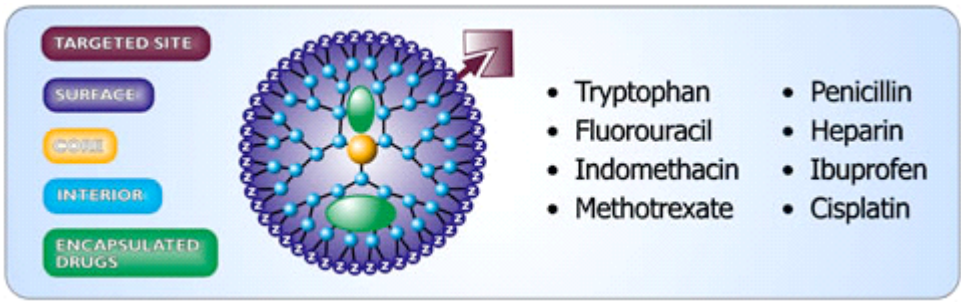


Figure 3: MRI Reagents

Dendrimers have demonstrated excellent potential as metal chelates for MRI. Analysis of dendrimer-chelate structure on retention and distribution has led to the discovery of the unique ability to control pharmacokinetic behavior by tuning dendrimer size and surface functionality.

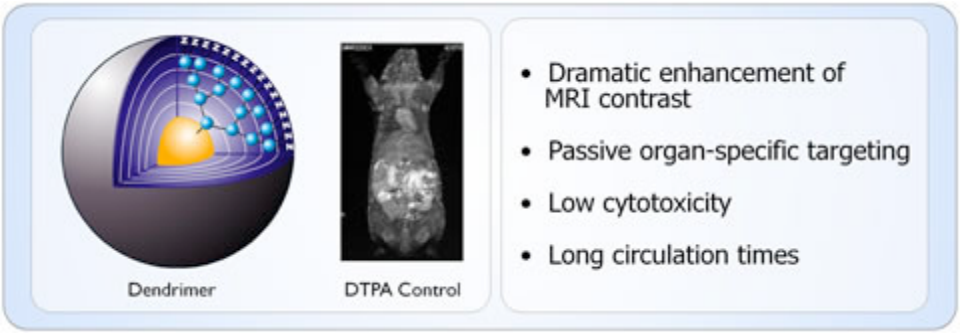
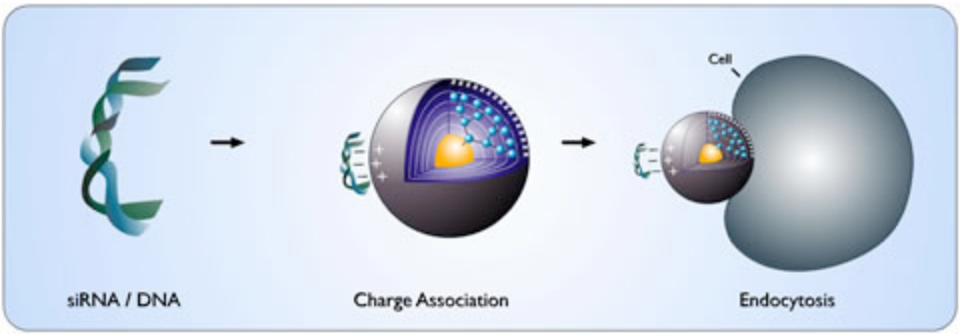


Figure 4: Transfection Agents

Poly(amidoamine) (PAMAM) dendrimers, which have been used to deliver nucleic acids have characteristic novelties associated with a superior, next-generation transfection agent–characteristics such as an amenability to nucleic acid complexation, chemical modification and targeting, transfection enhancing, and/or fluorescent molecule conjugation.



Dendrimers provide the necessary interface between chemistry and biology, possessing the unique traits to act as safe and effective drug-delivery vehicles as well as highly sophisticated diagnostic imaging agents. In the biotechnology and drug fields, these highly adaptable structures have finally taken nanotechnology from the theoretical into the practical. In fact, dendrimers have already been commercialized in products designed for HIV prevention, anthrax detection, cardiac-marker diagnostics and gene transfection.

II. COMPANY BACKGROUND

Dendrimers were actually discovered by Dendritic NanoTechnologies, Inc. (DNT) founder Donald A. Tomalia, Ph.D. In 1979, Dr. Tomalia, then a senior scientist with The Dow Chemical Company, discovered the fourth major class of macromolecular architecture, dendritic polymers. Because of their unique physical properties, these new nanostructures–which Dr. Tomalia would later coin "dendrimers"–heralded great promise for a wide range of real-world applications, most notably in biotechnology and pharmaceuticals. As a result of Dr. Tomalia's work, Dow Chemical was awarded the world's first dendrimer patents.

Two decades later, Dr. Tomalia, serving as co-director of the National Center for Dendrimer-Based Nanotechnology at Central Michigan University, launched DNT in the Applied Research and Technology Center on the CMU campus.

Incorporated in 2003, DNT has quickly established itself as the world's leading developer and provider of dendrimer-based technologies:

- DNT holds the most extensive portfolio of dendrimer-based intellectual property in the world, with over 200 patents in 41 patent families.
- The company has secured more than $9 million in investment capital.
- DNT has established key relationships with Dow Chemical, Australia-based Starpharma Holdings and other firms that provide the company a broad range of licensing opportunities and other revenue sources.
- The company has been awarded over $3.5 million in research contracts from the U.S. Department of Defense, the National Institutes of Health, Pfizer and others.
- DNT is selling and licensing its more than 200 dendrimer products, has several revenue-generating licensing agreements in place, and has achieved positive cash flow.

III. MARKET OPPORTUNITY

Nano-enabled polymeric delivery systems represent the biggest opportunity for nanotechnology companies, according to market-research firm NanoMarkets.[1] The company's recently released report, "Nano Drug Delivery," notes that nanotechnology-enabled drug-delivery systems will generate over $1.7 billion in 2009 and $4.8 billion in 2012. Additionally, NanoMarkets finds imaging agents and nano-enabled cancer drugs will become the most lucrative applications in the nanotechnology field.

[1] "Nano Drug Delivery," market-research report, NanoMarkets, 03/005

IV. BUSINESS STRATEGY

The NanoMarkets recent findings, corroborated by countless other market-research studies of most promising applications for dendrimer-based nanotechnology, speak directly to the value of DNT's uniquely comprehensive portfolio of intellectual property and the soundness of the company's business strategy. DNT's initial market focus is on providing dendrimer technology for imaging diagnostics and drug delivery–likely the two most lucrative opportunities in the field. DNT's two-phase business strategy enables the company to take the lead in delivering these new solutions.

Phase I: Transfection Reagents

DNT's Phase I business objective is to capture early licensing opportunities in (1) imaging contrast agents for new diagnostic solutions for enhancing the findings of MRIs, (2)transfection reagents for RNA-i delivery with improved gene silencing with less toxicity, and (3) encapsulation and release of platinate based anti-cancer drugs to reduce the toxicity and side effects of their use. DNT has existing IP that will be leveraged and licensed in all three areas.

For example, one of the greatest challenges for the use of RNA-i based medicine and conventional therapeutics is finding the appropriate delivery vehicle to transport active pharmaceutical ingredients into the desired area Using the knowledge of genomics and proteomics, researchers are now on the edge of identifying where, when and how diseases are triggered at the molecular level. RNA interference technology offers an extremely efficient tool for identifying and confirming drug targets and for understanding how cells respond when selected genes are shut off. DNT's initial research has indicated that dendritic structures are the ideal delivery vehicle for RNA-i based drug delivery technologies.

As these and other new scientific breakthroughs occur, DNT's dendritic technology will be the key to solving the targeting or delivery components required to bring these technologies to the market.

For an idea of the size of the market opportunity for this initial phase, consider that 40 million MRI imaging procedures were conducted in 2003, with 120 million using contrast agents. Consider also that MRI agents in the U.S. alone generate $365 million in revenue each year.

Phase II: Technology to extend IP and accelerate commercialization

PAMAM and PPI dendrimers, the original gold standards of dendrimer architectures, have been incorporated in thousands of studies by third parties that illustrate the application potential of dendrimers. The cost of synthesizing these precise structures, however, has limited their use in commercial applications.

New technology pioneered by DNT will reduce the cost of synthesis by orders of magnitude and address key limitations of the current PAMAM manufacturing process. DNT has developed a new low cost, scalable class of dendrimer structures and has established an aggressive research agenda that is addressing the synthesis, scalability, and rapid manufacturing of the new dendrimers. The new class of dendrimer structures will set an industry benchmark for precision scalable architecture and will position DNT in the enviable position of controlling a technology that has application in multiple billion dollar markets in multiple industries.

V. CONCLUSION

The medical community is increasingly demanding nanotechnology solutions to improve the detection, treatment and prevention of disease. Dendrimers have emerged as the ideal nanostructures to serve these demands–and are, in fact, expected to become a multibillion-dollar industry in their own right within just the next few years.

At the forefront of this new technology is DNT. The company enjoys an unrivaled intellectual-property portfolio, a strong customer base, a broad range of key partnerships and positive cash-flow. The discoverer of dendrimers himself serves as the company's president and chief technology officer. With a significant competitive advantage as the world's leading developer and provider of dendritic polymers, DNT is poised to continue to drive this industry-changing technology.