

# Nanomedicine Holds Promise for New Diagnostics and Therapeutics

Written by Lynne Lederman

When substances are reduced to nanoscale size, they display different properties. Nanoscale phenomena have been recognized for millennia, but the ability to rationally design, build, and manipulate nanoscale objects is fairly recent. Chad A. Mirkin, PhD, Northwestern University, Chicago, Illinois, USA, presented a plenary talk about the promise of nanomedicine, which he described as the convergence of nanoscience and nanotechnology with medicine.

Dr Mirkin predicts that significant advances for nanotechnology in medicine can be expected in the next decade. The creation of tiny structures and the ability to shape them into any desired configuration and adjust their properties will allow the development of high-sensitivity and high-selectivity molecular diagnostics. Nanoscale *in vivo* imaging materials could not only provide better contrast but also have theranostic capabilities; that is, they could combine the ability to diagnose and treat a condition into 1 step. Other applications in nanomedicine could include tools for genetically manipulating cells and making intracellular measurements, as well as novel and better approaches to drug delivery and gene regulation therapy.

Dr Mirkin's laboratory has been working on spherical nucleic acids (SNAs) for > 2 decades. The original SNAs consisted of 40-mer oligonucleotides with chemical groups that react with 13-nm gold nanoparticles so that the oligonucleotides decorate the surface of the gold particle. SNAs can be created that have both multivalency and multifunctionality. They can also be designed with "programmable" properties (eg, cooperative binding or catalysis, depending on the oligonucleotide sequence and structure). Materials other than gold can be used for the core, which will affect the color and electrical properties of the particle, as well as its ability to fluoresce.

SNAs have properties that are distinct from those of linear DNA molecules. SNAs enter cells rapidly and efficiently, whereas linear nucleic acids do not readily enter cells and need to be complexed with polymeric agents for transfection. A drawback of transfection agents is that they are toxic. When SNA labeled with a fluorophore is added to cells, the cells internalize the SNA, and the fluorescent signal is seen within 30 minutes.

One nanostructure-based diagnostic that is currently available is the Verigene System, which has been approved by the US Food and Drug Administration (FDA). This multiplexed nucleic acid diagnostic system detects infections and cardiac-related enzymes. The advantage of nanoparticles for probes is that (1) they can bind targets at low concentrations because of their tight binding constant and sharp melting profiles and (2) they have a very high selectivity in a system that does not use polymerase chain reaction.

SNAs have been multiplexed for detection of nucleic acids specific for viruses, including HIV, Ebola, small pox, and hepatitis B. SNAs are able to simultaneously detect dilute quantities of multiple nucleic acid disease biomarkers with a greater sensitivity than that of linear probes [Stoeva SI et al. *Angew Chem Int Ed Engl.* 2006].

A nanoflare is based on short oligonucleotides with a fluorophore that is quenched when near the gold core. Upon entering a cell and binding the specific target sequence, the fluorophore is released and detectable. Nanoflares have been used to measure mRNA levels in live cells [Prigodich AE et al. *Anal Chem.* 2012]. Nanoflare technology also has the ability to identify a small population of cells based on their properties (eg, a cancer cell from normal cells or stem cells from nonstem cells). Therefore, it could be used for fluorescent-based cell sorting to identify and collect live circulating tumor cells and test therapies by conjugating the fluorophore to a drug candidate to visualize the effect.

Antisense DNA technology has been used in the up- or downregulation of genes. SNAs have the potential to be used as antisense or short interfering RNA-type agents (eg, to downregulate the production of proteins upon which cancer cells depend for growth).

Peer-Reviewed  
Highlights From the

**American Society of  
Nephrology  
Kidney Week**

November 11–16, 2014  
Philadelphia, Pennsylvania

SNAs have been shown to enter most cell lines, primary cells, and organs tested, including neurons; however, mature red blood cells do not take up SNAs, because they are not endocytic. The mechanism appears to be mediated by class A scavenger receptors on cell surfaces that recognize SNAs, facilitating caveolae-mediated endocytosis. Once taken up, SNAs are released into the cytoplasm, suggesting that they can be used therapeutic strategies.

SNAs have been shown to cross the blood-brain barrier (BBB) and penetrate glial cells; they are being studied as a way to improve the prognosis for patients with glioblastoma multiforme (GBM). Bcl2L12 is a therapeutic target in GBM pathogenesis. Bcl2L12 is highly overexpressed in primary GBM tumors relative to normal brain tissues; it inhibits apoptosis by blocking activation of effector caspases 3 and 7; and it blocks p53 transactivational activity. In preclinical models, SNAs designed to knock down Bcl2L12 cross the BBB and blood-tumor barrier, reduce Bcl2L12 expression, and make cells more susceptible to chemotherapy. In mice, after intravenous injection, about 22% of the SNAs cross the BBB, and the majority of that ends up in the tumor. These experiments will be the basis of the first clinical trials of SNAs in GBM. SNAs also show promise for systemically addressing diseases of the brain.

SNAs may also be used to address diseases of the skin because of the high levels of expression of scavenger receptors in keratinocytes. For this application, other SNA cores and structures can be used. Liposomal-based structures are not only possible but desirable, because they would be based on a component that is already FDA approved.

There are many potential medical applications of nanotechnology in diagnostics and therapeutics, and over time, these could become a part of standard practice.

- 37th Annual San Antonio Breast Cancer Symposium**  
December 9–13 • San Antonio, Texas, USA
- 50th American Society of Clinical Oncology 2014 Annual Meeting Science & Society**  
May 30–June 3 • Chicago, Illinois, USA
- Acute Cardiovascular Care 2014\***  
October 18–20 • Geneva, Switzerland
- American Academy of Neurology**  
April 28–May 3 • Philadelphia, Pennsylvania, USA
- American Academy of Ophthalmology 2014**  
May 18–21 • Chicago, Illinois, USA
- American Academy of Orthopaedic Surgeons**  
March 11–15 • New Orleans, Louisiana, USA
- American Academy of Otolaryngology-Head and Neck Surgery Foundation Annual Meeting & OTO EXPO**  
September 21–24 • Orlando, Florida, USA
- American Association for the Study of Liver Disease**  
November 4–7 • Boston, Massachusetts, USA
- American Association of Diabetes Educators**  
August 6–9 • Orlando, Florida, USA
- American College of Cardiology 47th Annual New York Cardiovascular Symposium\***  
December 12–14 • New York, New York, USA
- American College of Cardiology 63rd Annual Scientific Session & Expo\***  
March 29–31 • Washington, DC, USA
- American College of Chest Doctors**  
October 25–30 • Austin, Texas, USA
- American College of Emergency Physicians (ACEP14)**  
October 27–30 • Chicago, Illinois, USA
- American College of Rheumatology 78th Annual Scientific Meeting**  
November 13–18 • Boston, Massachusetts, USA
- American Congress of Obstetricians and Gynecologists 2014 Annual Clinical Meeting**  
April 26–30 • Chicago, Illinois, USA
- American Diabetes Association 74th Scientific Sessions\***  
June 13–17 • San Francisco, California, USA
- American Heart Association Scientific Sessions 2014\***  
November 15–19 • Chicago, Illinois, USA
- American Orthopaedic Society for Sports Medicine\***  
July 10–13 • Seattle, Washington, USA
- American Psychiatric Association 2014 Annual Meeting**  
May 3–7 • New York, New York, USA
- American Psychiatric Nurses Association**  
October 22–25 • Indianapolis, Indiana, USA
- American Society for Microbiology—54th Interscience Conference on Antimicrobial Agents and Chemotherapy**  
September 5–19 • Washington, DC, USA
- American Society for Radiation Oncology**  
September 14–17 • San Francisco, California, USA
- American Society for Surgery of the Hand**  
September 18–20 • Boston, Massachusetts, USA
- American Society of Anesthesiologists Anesthesiology 2014 (ASA)**  
Oct 11–15 • New Orleans, LA, USA
- The American Society of Hematology**  
December 6–9 • San Francisco, California, USA
- American Society of Nutrition Scientific Sessions & Annual Meeting at Experimental Biology 2014**  
April 26–30 • San Diego, California, USA
- American Society of Plastic Surgeons Plastic Surgery The Meeting 2014**  
October 10–14 • Chicago, Illinois, USA
- American Stroke Association 2014 International Stroke Conference\***  
February 11–14 • San Diego, California, USA
- American Thoracic Society 2014 Annual Meeting\***  
May 16–21 • San Diego, California, USA
- American Veterinary Medical Association**  
July 25–29 • Denver, Colorado, USA
- Cardio Alex 2014\***  
June 10–13 • Alexandria, Egypt
- Caribbean Cardiac Society 29th Caribbean Cardiology Conference 2014\***  
July 23–July 26 • Atlantis, Paradise Island, The Bahamas
- Cardiostim EHRA Europeace 2014**  
June 23–26 • Nice, France
- The Endocrine Society—ICE/ENDO 2014\***  
June 21–24 • Chicago, Illinois, USA
- ESMO World Congress on Gastrointestinal Cancer**  
June 25–28 • Barcelona, Spain
- European Association for the Study of Diabetes 49th Annual Meeting**  
September 15–19 • Vienna, Austria
- European Committee for Treatment and Research in Multiple Sclerosis**  
September 10–13 • Boston, Massachusetts, USA
- European League Against Rheumatism 2014 Annual Congress**  
June 11–14 • Paris, France
- European Lung Cancer Conference**  
March 26–29 • Geneva, Switzerland
- European Society of Cardiology ESC Congress 2014\***  
August 30–September 4 • Barcelona, Spain
- European Society of Cardiology EuroEcho 2014\***  
December 3–6 • Vienna, Austria
- European Society of Hypertension 2014 Annual Scientific Meeting**  
June 13–16 • Athens, Greece
- European Society of Medical Oncology**  
September 26–30 • Madrid, Spain
- European Society Traumatology, Knee Surgery, and Arthroscopy**  
May 14–17 • Amsterdam, The Netherlands
- Heart Failure 34th Annual Scientific Sessions**  
May 17–20 • Athens, Greece
- Heart Rhythm Society 34th Annual Scientific Sessions\***  
May 7–10 • San Francisco, CA, USA
- International Federation of Foot and Ankle Surgery/American Orthopaedic Foot & Ankle Society\***  
September 19–23 • Chicago, Illinois, USA
- Kidney Week**  
November 5–10 • Atlanta, Georgia, USA
- Movement Disorder Society**  
June 9–12 Stockholm, Sweden
- North American Spine Society**  
November 12–15 • San Francisco, California, USA
- Obesity Week**  
November 2–7 • Boston, Massachusetts, USA
- Orthopaedic Trauma Association**  
October 15–18 • Tampa, Florida, USA
- Radiological Society of North America**  
November 30–December 5 • Chicago, Illinois, USA
- The Society for Cardiovascular Angiography & Interventions (SCAI)\***  
May 28–31 • Las Vegas, NV, USA
- Transcatheter Cardiovascular Therapeutics 2014 Interventional Conference**  
September 13–17 • Washington, DC, USA

\*Proudly produced in official collaboration with the host society



Click to like us on Facebook  
facebook/mdconferenceexpress