News

Research Highlights

Self-assembled nanostructures mimic biological membranes and show potential for nanomedicine drug delivery

"The novel dendrimersomes are a promising advance in the science of self-assembled nanostructures for both biological and medical applications."

A recent study presents a library of different synthetic biomaterials, created as a result of an international collaboration led by scientists from the University of Pennsylvania (PA, USA). The newly developed synthetic materials are able to mimic biological membranes and as such show promise as safe carriers for targeted delivery.

The study, published in *Science*, describes the preparation, structure, self-assembly and mechanical properties of the biomaterials known as dendrimersomes, which spontaneously form from the exact chemical composition of Janus dendrimers.

The collection of synthetic dendrimersomes are intended to enable targeted delivery of drugs, gene therapies, proteins, imaging and diagnostic agents. However, the precise molecular arrangements needed for these functions have proven difficult to achieve.

The international team has overcome the challenge to create these particular molecular arrangements known as dendrimersomes.

Dendrimersomes are stable bilayer vesicles, which are uniform in size and demonstrate stability in a variety of different media and at a range of temperatures. They have been developed with a range of morphologies, including cubosomes, disks, tubular vesicles and helical ribbons. Researchers confirmed the morphology of the assembled structures using fluorescence microscopy and cryogenic transmission electron microscopy.

Dendrimersomes assemblies offer several advantages when compared with alternative delivery technologies, such as liposomes and polymersomes. Dendrimersomes combine the mechanical strength stability found in polymersomes with the biological activity of phospholipid liposomes. They are also superior in terms of size uniformity, ease of formation monodispersity, tenability and versatility.

"Dendrimersomes marry the stability and mechanical strength obtainable from polymersomes, vesicles made from block copolymers, with the biological function of stabilized phospholipid liposomes," explained Virgil Percec of the University of Pennsylvania.

The new synthetic materials are also tunable by temperature and chemistry. "These materials show special promise because their membranes are the thickness of natural bilayer membranes, but they have superior and tunable materials properties," said Daniel Hammer, also at the University of Pennsylvania. "Because of their membrane thickness, it will be more straightforward to incorporate biological components into the vesicle membranes, such as receptors and channels."

The novel dendrimersomes are a promising advance in the science of self-assembled nanostructures for both biological and medical applications.

Source: Percec V, Wilson DA, Leowanawat P et al.*: Self-assembly of Janus dendrimers into uniform dendrimersomes and other complex architectures.* Science *328(5981), 1009–1014 (2010).*

future medicine part of fsg

Novel liquid formulation developed to deliver nanomedicine treatment for HIV/AIDS

A commercially viable vaccine product to treat HIV/AIDS has been developed by multinational biopharmaceutical company, Genetic Immunity. The company's innovative work to create DermaVir, the first topically administered nanomedicine therapeutic vaccine for HIV/AIDS, has recently been published in the *International Journal of Pharmaceutics*.

The DermaVir vaccine contains a plasmid DNA complexed with a polyethylenimine that is mannobiosylated to enable the nanomedicine to target antigen-presenting cells, so inducing an immune response.

"Biological activity of DermaVir depends upon its nanomedicine formulation that is essential for the potent expression of plasmid-DNA-encoded antigens," commented Julianna Lisziewicz, lead author of the paper and CEO of Genetic Immunity.

"We report here the development of a stable single liquid nanomedicine formulation, a significant milestone in developing DermaVir as a commercially viable global product to treat HIV/AIDS," Lisziewicz explained.

"One challenge in clinical nanomedicine development is to produce a stable formulation with reproducible manufacturing methods," explained Genetic Immunity's Enikö Töke. The result was a new formulation of pDNA surrounded by a chemical polymer, allowing the preservation of both the stability and the activity of DermaVir when kept at 4°C.

Phase II data investigating DermaVir used for initial treatment of HIV-infected individuals has already demonstrated safety and immunogenicity as well as viral load reductions. DermaVir will now enter into Phase II/III human trials as a topically administered nanomedicine therapeutic vaccine.

The work overcame significant hurdles facing the field in order to successfully formulate DermaVir, including systematically investigating the variability of raw materials and their relationship with the product's biological activity.

"It is our belief that DermaVir will become the first nanomedicine vaccine developed to reconstitute HIV-specific immunity with the potential to maintain the health of people living with HIV infection," Lisziewicz concluded.

Source: Tőke ER, Lőrincz O, Somogyi E, Lisziewicz J: Rational development of a stable liquid formulation for nanomedicine products. Int. J. Pharm. *392(1–2), 261–267 (2010).*

Gold nanorods provide effective vehicle for the delivery of immune-boosting antiviral medicines, study suggests

A recent study, carried out by collaborating scientists at the University of Buffalo and the US CDC (NY, USA), has demonstrated a novel nanotechnology approach for the therapy of seasonal and pandemic influenza viruses.

Researchers used gold nanorods to deliver an antiviral treatment to respiratory cells. The antiviral treatment is based on a single-strand RNA molecule able to improve a cell's innate immune response against the influenza virus by boosting production of interferon proteins, which inhibit viral replication.

RNA molecules are generally unstable when delivered into cells. However, the gold nanorods produced at the University of Buffalo enabled the researchers to overcome this problem. By fusing the RNA molecules to the nanorod transporter vehicles researchers were able to effectively deliver the powerful immune-activating medicine.

The study, published in *Proceedings of the National Academy of Sciences,* demonstrated that the GNR-5′PPP-ssRNA nanoplex was an effective antiviral strategy against type A influenza virus. In human respiratory bronchial epithelial cells, the nanoplex was able to activate genes that increased type I IFN and ISGs production and, consequently, this led to a decrease in the replication of H1N1 influenza viruses.

"The gold nanorods protect the RNA from degrading once inside cells, while allowing for more selected targeting of cells," explains Paul Knight III from University of Buffalo School of Medicine and Biomedical Sciences, who worked on the project.

The new nanotechnology approach could be used to target any viruses that are susceptible to the innate immune response triggered by type 1 interferons.

Krishnan V Chakravarthy, an MD/PhD student from the University of Buffalo and the paper's first author, adds: "The novelty of this approach is that most of these kinds of RNA viruses share a common host-response immune pathway; that is what we have targeted with our nanoparticle therapy. By enhancing the host immune response, we avoid the difficulty of ongoing viral resistance generated through mutations."

Further evaluation of biocompatible antiviral nanoplexes for the treatment of seasonal and pandemic influenza viruses is warranted. The University of Buffalo and the US CDC researchers are soon to begin animal studies.

Source: Chakravarthy KV, Bonoiu AC, Davis WG et al.*: Gold nanorod delivery of an ssRNA immune activator inhibits pandemic H1N1 influenza viral replication.* Proc. Natl Acad. Sci. USA *107(22), 10172–10177 (2010).*

Nanoparticle-containing eye drops could simplify eye infection treatment

A new nanoparticle-containing medication could offer an easier course of treatment for patients with the serious eye infection bacterial keratitis.

Bacterial keratitis is a potentially blinding eye infection that affects over 500,000 people worldwide per year. The infection is painful and potentially damaging; it progresses rapidly and causes inflammation of the cornea.

Current treatments are very intensive, requiring patients to use antibiotic eye drops every 5 min at the beginning of treatment and then at 15–30 min intervals for up to 3 days. Patients must also take anti-inflammatory drugs each day. The intensity of treatment regimen means that patients frequently require hospitalization to ensure the method is followed effectively.

The new treatment, reported in the journal *Molecular Pharmaceutics,* combines the antibiotic and anti-inflammatory drug into a single medication. The novel eye drops contain nanoparticles with an average size ranging from 315.2 to 973.65 nm. These nanoparticles are loaded with gatifloxacin (an antibiotic) and prednisolone (an anti-inflammatory) and coated with a bioadhesive polymer substance that allows the eye to retain the medication for longer.

The nanoparticles eye drops showed better bioavailability and sustained action in aqueous humor and corneal tissue when compared with the commercial eye drops. Animal tests revealed that the new drops delivered five-times more medication, which remained in the eye three-times longer than existing medicine.

The new treatment promises to reduce dose frequency and as such is hoped to improve patient compliance with treatment for bacterial keratitis.

Source: Ibrahim HK, El-Leithy I, Makky AA: Mucoadhesive nanoparticles as carrier systems for prolonged ocular delivery of gatifloxacin/prednisolone bitherapy. Mol. Pharmaceutics *7(2), 576–585 (2010).*

New nanoparticle shows promise for prostate cancer detection, study suggests

Researchers have created a targeted gold nanoparticle that has shown potential as an imaging agent for detecting cancer cells.

The team of investigators, led by Raghuraman Kannan and Kattesh Katti (University of Missouri School of Medicine, MO, USA), developed the novel nanoparticles by coating gold nanoparticles with a naturally occurring peptide molecule termed bombesin. *In vivo* bombesin binds to a specific type of receptor, known as a gastrin-releasing peptide receptor, which is abundant on prostate, breast and lung cancer cells.

In the recent study, published in *Proceedings of the National Academy of Sciences*, the new nanoparticles were used to image prostate tumors in prostate tumor-bearing, severe combined immunodeficient mice. The nanoparticles bound to the prostate tumor cells and could then be detected using computed tomography x-ray imaging.

The gold nanoparticle detection method has demonstrated realistic clinical potential in molecular imaging. The particles have a tenfold higher uptake in prostate tumor cells than that of another detection method, currently in clinical trials, which uses bombesin linked directly to a radioactive element termed technetium.

In order to coat the nanoparticles, Kannan and Katti and their team had to develop a new synthetic method for linking the bombesin peptide to the gold nanoparticles.

The researchers also found that injecting the nanoparticles into the peritoneal cavity produced superior results to injecting directly into the bloodstream.

It is thought that the novel nanoparticles may offer a more sensitive and accurate method for detecting early-stage prostate cancer than is currently available. This is particularly important since current methods of prostate cancer screening have little effect on prostate cancer survival.

Source: Chanda N, Kattumuri V, Shukla V et al.*: Bombesin functionalized gold nanoparticles show* in vitro *and* in vivo *cancer receptor specificity.* Proc. Natl Acad. Sci. USA *107(19), 8760–8765 (2010).*

About the News

The News highlights some of the most important events and research in the field of nanomedicine. If you have newsworthy information, please contact: Morag Robertson, Commissioning Editor, *Nanomedicine*; m.robertson@future-medicine.com