BioPact
bio-pact.com

MGMR, a next-generation carbon nanotube, solves drug development challenges

BioPact's MGMR (Medical Grade Molecular Rebar) offers a safe and scalable nanoparticle platform for controlled and targeted delivery of a wide range of therapeutics.

Carbon nanotubes (CNTs) are created through a complex process in which single carbon atoms are built into a cylinder-like structure consisting of one or many intercalated tubes, each layer just a single molecule thick. This seemingly delicate framework yields surprising qualities not found in other carbon structures: CNTs are stronger yet more flexible than steel, with unique electrical and optical properties. CNTs for medical use hit stumbling blocks early on and, up to now, have failed to deliver commercially. Rising to the challenge, BioPact has developed MGMR, a unique CNT designed specifically for medical use called MGMR, or Medical Grade Molecular Rebar, that addresses past issues with traditional CNTs. With MGMR, BioPact can help pharmaceutical partners breathe new life into clinical programs and products that have hit roadblocks related to systemic toxicity or difficulty reaching the therapeutic target, and possibly help to extend patent life.

Through a proprietary process of mechanical and chemical treatment, BioPact can consistently generate pure MGMR at scale for off-the-shelf use in a wide variety of medical applications. MGMR is a novel vehicle for controlled drug release or targeted delivery of therapeutic small molecules, antibodies, proteins, peptides, or nucleic acids (**Fig. 1**). MGMR formed via the BioPact process is a consistent product composed of individual, dispersed nanotubes, essentially free of residual catalysts and solvents, that can be easily adapted to a variety of needs. In contrast, traditional CNT fabrication yields a tangle of nanotubes and other, less structured matter such as trapped impurities, toxic metals, and nonbiocompatible solvents, which diminish the much publicized theoretical properties of the nanomaterial and reduce batch-to-batch consistency.

Therapeutic loadable structure

The discrete, open-ended nanotubes of MGMR have a high aspect ratio, with a hollow core of ~4–5 nm, an outer diameter of ~12–14 nm, and lengths averaging 900 nm. The interior of MGMR can be readily loaded with a therapeutic payload of choice, and the exterior can be customized to allow for additional functional groups or the attachment of large or small molecules. MGMR's small inner diameter and high surface-to-volume ratio offer advantages for controlled drug delivery: the nanotubes can penetrate cell membranes readily to efficiently transfer a payload to the cytoplasm or nucleus. On the basis of past research with CNTs, MGMR is also expected to cross the blood–brain barrier, which suggests that it could be used to deliver drugs to the central nervous system, as well as other hard-to-target areas.

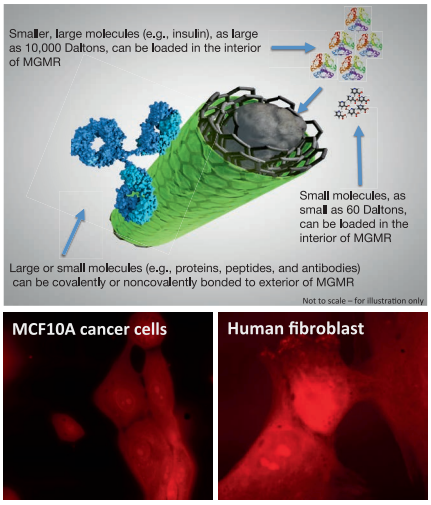

Figure 1: MGMR CNT structure. The diagram illustrates how molecules of various sizes can be loaded into the tube's interior for delivery. Smaller, large molecules on the diagram refer to large molecules that are on the smaller end of the scale, such as insulin and some peptides. The lower two images show MGMR having transported into the cell and localizing to the nucleus.

BioPact has found that MGMR can be loaded with a variety of medically relevant substances with consistency and control. These experiments have included successful attempts to load the interior of the MGMR tube with small molecules or peptides, including chlorambucil, bortezomib, and insulin, and to attach large molecules to the tube's surface. Horseradish peroxidase, for example, has been shown to retain its enzymatic activity when bound to the MGMR surface, whether covalently or noncovalently attached. By adding targeting molecules to the surface or making other modifications, one can tune the location and timing of drug delivery via MGMR. In one experiment, when dextran polymers were added to MGMR loaded with small-molecule dyes, the rate of release was slowed, providing proof of concept for MGMR-based extended-release drug formulations. Targeted drug delivery with MGMR has also been shown using the bisphosphonate alendronate cross-linked with Cy5 dye on the MGMR surface. Both dye and drug were shown to be taken up by bone cells and to retain their functions. Once it has crossed the cell membrane, MGMR preferentially localizes to the nucleus and nucleoli.

Competitive advantages

MGMR offers multiple advantages over other drug delivery systems, particularly liposomes. First, MGMR is simple to manufacture and provides an easy-to-use foundational platform that can be customized for a given therapeutic. In contrast, liposomes require the development of a unique formulation and manufacturing process for each drug. MGMR capacity is high, making large and complex payloads possible, independent of the hydrophobicity of the therapeutic components. The membrane transit time and mechanism also differ from those of other methods, with direct access to the intracellular space provided via endocytosis. And because the nanotube material itself is not biodegradable, it produces no metabolites that might generate unexpected toxicity.

Independent studies commissioned by BioPact and conducted in animals have demonstrated that MGMR is very well tolerated, with a maximum tolerated dose compatible with delivery of a wide range of drugs. In one safety study, mice were injected six times over 18 days with either MGMR or traditional 'medical grade' CNTs from another source. In the MGMR group, no toxicity was observed, although MGMR was detected in the circulation. However, all of the mice exposed to the traditional CNTs died after administration of a single dose. In three transdermal-patch studies, no irritation, contact sensitization, cell lysis, or cytotoxicity was observed in animals whose skin was exposed to MGMR. Finally, a 21-day biodistribution study showed that MGMR delivered as a single intravenous dose reached multiple organs and tissues and was continuously cleared from blood through urine and feces. As in previous studies, no adverse events were observed.

BioPact is seeking partnerships across many therapeutic areas and is currently focusing its internal efforts on applications in oncology, central nervous system, immunology, gene therapy, bone, and metabolism. BioPact works closely with partners to structure feasibility studies on the critical path to developing a licensing agreement tailored to their needs.

contact
Lainie Mulvanny, VP, Business Development
BioPact
Austin, Texas, USA
Tel: +1-800-561-7087
Email: BD@bio-pact.com