Eos Biosciences Inc.

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A smarter way to deliver drugs into cells

Eos Biosciences has developed the Eosome, a versatile drug delivery platform that maximizes efficacy through efficient intracellular delivery of therapeutic payloads. Eosomes can be adapted for many disease indications and for the delivery of a wide variety of drug modalities.

Nanoparticle-based drug delivery systems—assembled using a variety of biological and non-biological molecules as building blocks—have garnered great interest over the past decade as a potential way to increase the efficacy of drug delivery and improve therapeutic indexes. One of the main challenges for current drug delivery systems is the mediation of endosomal escape and reduction of the high rate of lysosomal degradation.

Eos Biosciences Inc., a privately held nanomedicines company, is advancing a unique targeted drug delivery platform, the Eosome, which incorporates a trick borrowed from a virus to effect efficient endosomal escape, resulting in highly improved drug payload delivery. The Eosomes comprise multifunctional recombinant polypeptides specifically engineered to consist of (1) a highly specific cell-targeting peptide that recognizes a cell-surface receptor, (2) a membrane-penetration peptide that causes endosomal lysis and escape, and (3) a therapeutic capturing peptide that can bind a wide range of therapeutic molecules. Because of the modular design of the polypeptides, which allows rapid and efficient substitution of the targeting and therapeutic capture peptides, Eosomes represent a versatile nanoparticle platform that can be adapted for the delivery of a wide variety of therapeutic payloads for multiple disease indications.

"We are harnessing the flexibility of the Eosome platform to develop both a pipeline of in-house therapeutics and a diverse portfolio of high-efficiency drug delivery tools for partnering with other companies interested in improving the efficacy of their drug modalities," said Omar Haffar, founder, president and CEO of Eos.

Eosomes

Eosomes are self-assembling non-liposomal nanoparticles (<50 nm in diameter) initially developed by Lali Medina-Kauwe at Cedars-Sinai Medical Center in Los Angeles and now being advanced by Eos under an exclusive worldwide license[1]. These non-immunogenic nanoparticles are composed of multifunctional recombinant polypeptides designed to incorporate three elements that define their target and payload specificity.

First, a cell-targeting peptide affords the Eosome the capacity to zero in on a particular cell-surface receptor on a diseased or abnormal cell, reducing accumulation of the drug in healthy tissues and improving accumulation at pathological sites. The targeting peptides are typically derived from the natural ligands for cell-surface receptors.

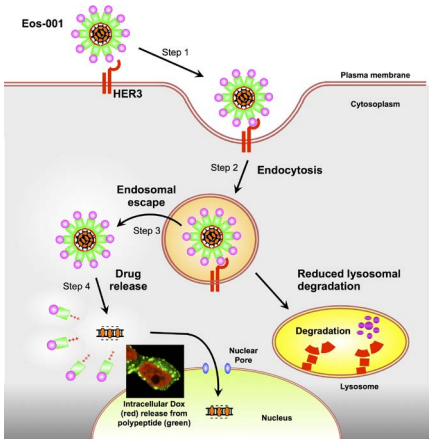

Figure 1: Eos' Eosome platform affords highly efficient drug delivery to specific target cells. Eosomes home to particular receptors overexpressed on diseased or abnormal cells. The adenovirus-derived penton base protein module of the Eosome helps avoid lysosomal degradation of payloads and directs the drugs to the interior compartments of the cell.

The second component is a peptide derived from the adenovirus 5 penton base protein (PB), a capsid protein that triggers rapid release from the endosomes. It is this function of PB that allows Eosomes to efficiently deliver their therapeutic payload to the cytoplasm of cells, evading lysosomal degradation.

The final component is a bridging peptide that is tailored to capture and bind the therapeutic payload non-covalently, thus facilitating its subsequent release once inside the target cell.

Eosomes are stable in circulation and efficiently retain their therapeutic payload, maximizing the dose delivery to the site of disease.

"Their versatility makes Eosomes into a delivery solution for a wide range of therapeutic payloads and indications requiring precise cell-targeting and optimal drug release inside the cells," said Haffar.

Potential payloads tested and validated include small-molecule therapeutics, single- and double-stranded DNA oligonucleotides, siRNA, mRNA and plasmid DNA. Intravenous injection is the current mode of administration, and testing of subcutaneous and intramuscular delivery of Eosomes is planned.

Proof-of-concept Eosomes

Eos has developed a proprietary pipeline of proof-of-concept Eosomes for oncological applications. Eos-001 (**Fig. 1**) and Eos-002, which target HER3-overexpressing cancer cells, are loaded with doxorubicin and a proprietary small molecule, respectively. Two other products, Eos-003 and Eos-004, target c-Met–overexpressing cancer cells, also with doxorubicin and a proprietary small molecule, respectively. Because HER3 and c-Met are overexpressed on a variety of metastatic drug-resistant solid tumors, the Eos product pipeline allows for broad applications for treating cancers that either are underserved or represent an unmet medical need.

In *in vitro* and *in vivo* (animal model) preclinical studies using human $HER2^+$ and $HER3^+$ breast cancer cells, including refractory or drug-resistant lines, Eos-001 has shown greater than tenfold improvement in doxorubicin efficacy compared to free doxorubicin, as well as a substantial reduction in—if not total disappearance of—related cardiac and hepatic toxic side effects. It is anticipated that the therapeutic and safety advantages of Eos-001 may allow for accelerated regulatory approval by the US Food and Drug Administration via a 505(b)(2) regulatory pathway.

In addition to breast cancer, the Eos products have been validated on other human cancer cell lines, including gastric, prostate and glioma. Other potential indications being studied are thyroid, colon, pancreatic, kidney and non–small cell lung cancers.

Next steps

In addition to advancing its proprietary product pipeline, Eos is interested in establishing collaborations to expand the application of the Eosome platform technology to indications other than oncology such as cardiovascular disease, virology, immune disorders, metabolic diseases and genetic disorders. These collaborations could be structured as either licensing agreements or codevelopment partnerships.

To that end, Eos has ongoing projects for testing the delivery of specific RNAi molecules and is in discussion with additional potential collaborators for the delivery of other nucleic acid therapeutics.

According to Haffar, "due to its flexible design, the Eosome platform affords a unique opportunity in the field of nanomedicines to rapidly advance the development of highly effective and safe therapies in a number of therapeutic areas."

1. Agadjanian, H. *et al. Nanomedicine* **7**, 335–352 (2011).

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