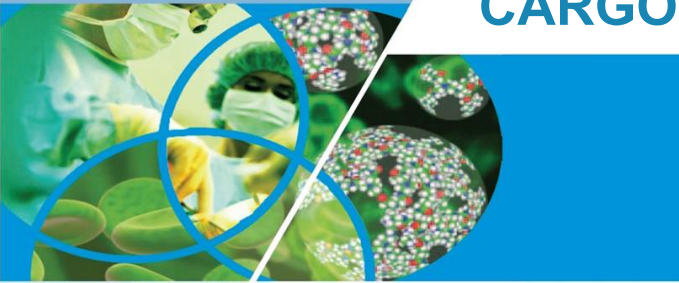
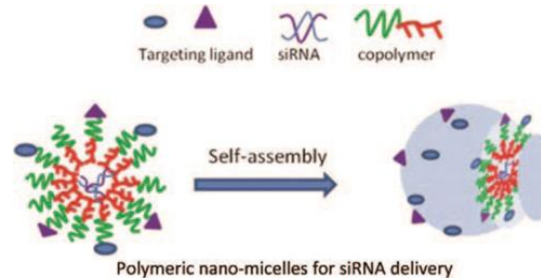


CARGO™ Polymeric Micelle System

Effective *in vivo* Oligonucleotide Delivery



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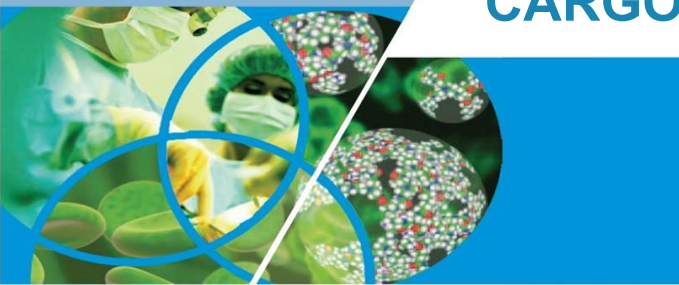
CARGO Advantages

CARGO has been specifically designed for effective delivery *in vivo*. The unique polymeric reagents bind to the nucleic acid and create a stable shell, protecting oligos from degradation, while at the same time providing stealth properties to reduce immune system recognition and elimination. Active targeting is achieved by covalently attaching a ligand to the external surface of the micelle using simple well-established conjugation chemistry. The ligand may be a protein, peptide, carbohydrate or lipopeptide containing functional amine or thiol groups. **CARGO** is extremely flexible, allowing for the attachment of multiple targeting ligands to the surface of the same delivery vehicle. The ligands promote interaction and uptake of the encapsulated siRNA / DNA into the target cells. Once inside, the polymer chemistry provides for intracellular release.

- Self-assembling micelles prevent nucleic acid degradation *in vivo* for prolonged serum stability
- Micelle stealth properties reduce immune system recognition and elimination
- Optimal particle size is proven to reach target tissues
- Multiple active targeting ligands can be attached using simple conjugation chemistry
- Co-delivery of nucleic acids with cellular detection agents and/or small molecules
- Efficient intracellular release of nucleic acids
- Biocompatible and biodegradable components with established history of therapeutic use.

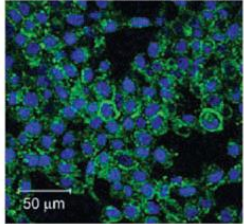
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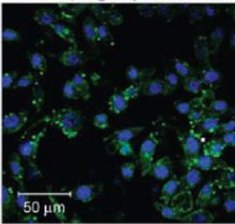


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PEO-b-P(CL-g-SP)/negative siRNA

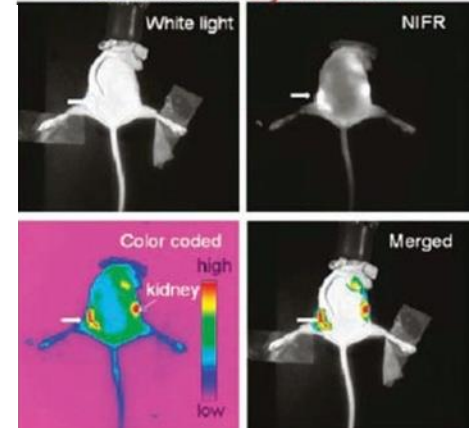


PEO-b-P(CL-g-SP)/MDRI siRNA



Athymic nude mice bearing MDA-MB-435/LCC6 MDRI-resistant tumors injected with RGD-micelles/Dy677-siRNA. MDA-MB-435/LCC6MDR1-resistant cells were transplanted subcutaneously into the right rear flanks of the mice, and tumor was approximately 0.1cm³ 17 days after implant. The mice were imaged at 24 h after injection. The intensity of fluorescence is expressed by different colors, with pink reflecting the lowest intensity (background) and red reflecting the highest intensity. The tumor is indicated by the thick arrow.

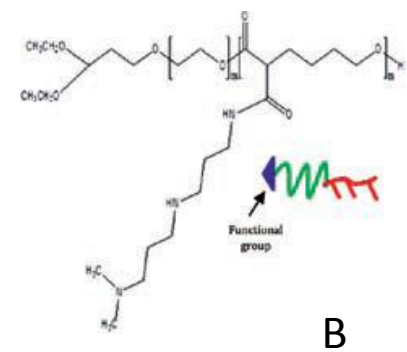
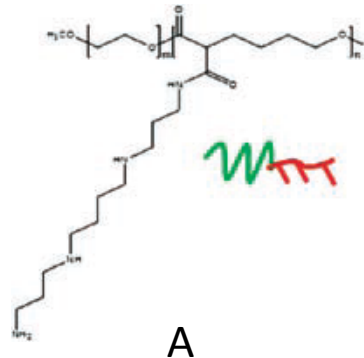
RGD-micelles/Dy677-siRNA



CARGO is comprised of block copolymer poly(ethylene glycol) block-poly(ϵ -caprolactone) (PEG-b-PCL) with pendant spermine (SP) and/or N,N-dimethyl dipropylenetriamine (DP). Diblock copolymers form stable nano-micelles at low concentrations (critical micellar concentrations (CMC) of 3.151J,M).

CARGO Kit Components

- Aqueous buffers
- 0.2 μ sterile filter
- package insert with complete instructions for use
- Kit I (untargeted): MePEG-PCCL-SP polymer
- Kit II (targeted delivery) MePEG-PCCL-SP and Acetal-PEG-PCCL (Structures A and B)



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