Charge-Dynamic Polymers for Delivering Anionic Compounds, Such as DNA, into Cells

View U.S. Patent No. 7,883,720 in PDF format.

WARF: P03393US

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing cationic polymers that undergo dynamic changes in charge states (from cationic to less cationic) to trigger the "unpackaging" of anionic molecules like DNA from condensed interpolyelectrolyte complexes.

Overview

The safe and efficient delivery of DNA into cells is essential for the clinical success of gene therapy. Synthetic polymers are considered long-term alternatives to virus-based gene delivery agents because they exhibit low immunogenicities and can be easily modified. Of particular interest are cationic polymers. These molecules spontaneously self-assemble with anionic DNA to form condensed interpolyelectrolyte complexes (IPECs) that cells can efficiently internalize. However, once inside the cell, conventional cationic polymers cannot dissociate readily or promote the release of bound DNA.

The Invention

UW-Madison researchers have developed polymers that allow temporal control over the dissociation of DNA from polymer/DNA interpolyelectrolyte complexes. The cationic polymers undergo dynamic changes in charge states (from cationic to less cationic) to trigger the "unpackaging" of anionic molecules from IPECs. The polymers possess cationic charge densities that result from the number, type, and position of functional groups attached to the backbone; specifically, cationic charge densities decrease when one or more of the functional groups is removed.

In one embodiment, side chain esters are introduced to linear poly(ethylene imine) (PEI) via conjugate addition chemistry. The PEI is then complexed with an anionic molecule such as DNA. When the pendant ester groups are hydrolyzed, the cationic charge density of the polymer is reduced, promoting the dissociation of the polymer/DNA complex and efficient release of DNA.

Applications

- Can potentially deliver polynucleotides, proteins, small molecules, antigens or drugs to a patient
- Provides controlled, sustained release of an encapsulated agent
- Allows the initial formation of polymer/DNA complexes and later facilitates the efficient and timely unpackaging of DNA in the intracellular environment

Key Benefits

- Would allow more complete utilization of existing technologies that address other barriers to gene delivery
- Can be designed so the charge shift of the polymer occurs on a desired time scale
- Cell/tissue delivery can be *in vivo* or *in vitro*

Additional Information

Related Intellectual Property

- View Continuation Patent in PDF format.
- View Divisional Patent in PDF format.

Publications

- Saurer E.M., Flessner R.M., Sullivan S.P., Prausnitz M.R. and Lynn D.M. 2010. Layer-by-Layer Assembly of DNA- and Protein-Containing Films on Microneedles for Drug Delivery to the Skin. Biomacromolecules 11, 3136–3143.

Tech Fields

- Drug Delivery : Other drug delivery technologies

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854