Multilayered Film for Delivering Proteins and Other Small Molecules into Cells

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a new way of delivering active proteins into cells.

Overview

The ability to deliver proteins into cells has many therapeutic and research applications. However, peptide drugs and therapeutic proteins are notoriously difficult to administer, in part because of the limited permeability and selectivity of the cell membrane.

Polyelectrolyte multilayers (PEMs) have been used to deliver biomolecules into cells. PEMs are essentially thin plastic films with alternating layers of positively and negatively charged polymers. Biomolecules, such as nucleic acids, can be integrated into PEMs, which can be designed to dissolve under physiologically relevant conditions to release the biomolecules into cells.

Previous attempts to use these films to deliver proteins focused mainly on naturally occurring, wild-type proteins. However, this approach is limited because the assembly conditions and film properties are dependent on the charge, isoelectric point and other properties of the proteins and polyelectrolytes used. Many wild-type proteins cannot successfully be integrated into PEMs.

The Invention

UW-Madison researchers have developed a new way of delivering proteins and other small molecules into cells. This approach uses a cationic “anchor” to improve incorporation of proteins into multilayered films.

Before the protein or small molecule is integrated into the film, a cationic protein transduction domain, such as nonaarginine, is attached to it. Appending short, cationic peptides or oligomers to proteins can facilitate their layer-by-layer assembly into PEMs, as well as their uptake by cells.

Then the cationic molecule is incorporated into a polyelectrolyte multilayered film, along with anionic polymers such as sodium polystyrene sulfonate, to result in a multilayered assembly that is preferably about 80 nanometers thick. When this composition is presented to a cell, the film dissolves, delivering the molecule to the cell.

Applications

- Delivering active proteins and other biomolecules, including nucleic acids, drugs, toxins, carbohydrates or metabolites, into cells
- Coating medical devices to provide for the localized release of therapeutics
- Coating disposable research tools, such as pipette tips, tubes and petri dishes

Key Benefits

- Enables the efficient and localized delivery of functional proteins and other biomolecules, including nucleic acids, drugs, toxins, carbohydrates or metabolites, into cells
- Attaching cationic protein transduction domains to proteins provides a straightforward method for conferring cationic charge without compromising protein function, enabling the incorporation of proteins into multilayered films under conditions for which unmodified, wild-type proteins cannot be used.
- Provides a method of controlling the speed at which protein is released
- Promotes the efficient uptake of protein from the surfaces of coated objects, including implanted materials, medical devices and disposable research tools
- Multilayered films are capable of dissolving in physiological media.
- A molecular linker may be attached to the protein transduction domain to attach other molecules for import into cells.

Stage of Development

This film was successfully used to deliver RNase A into cells *in vitro*.

Tech Fields

- Drug Delivery : Other drug delivery technologies
- Medical Devices : Device coatings

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