Title (en)

ENHANCED STABILISED PLASMID-LIPID PARTICLE-MEDIATED TRANSFECTION USING ENDOSOMAL MEMBRANE DESTABILISERS

Title (de)

VERBESSERTE VON STABILISIERTEN PLASMID-LIPIDPARTIKELN-MEDIIERTE TRANSFEKTION MIT VERWENDUNG VON DESTABILISATOREN ENDOSOMALER MEMBRANE

Title (fr)

PROCEDES PERMETTANT D'AMELIORER LA TRANSFECTION A MEDIATION SPLP (PARTICULE PLASMIDE-LIPIDE STABILISEE) AU MOYEN DE DESTABILISATEURS DE LA MEMBRANE ENDOSOMALE

Publication

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Application

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Abstract (en)

[origin: WO0180900A2] The present invention provides novel and surprisingly effective methods for delivering nucleic acids to cells. These methods are based upon the discovery that the presence of endosomal membrane destabilizers (e.g., calcium) leads to a dramatic increase in the transfection efficiency of plasmids formulated as SPLP, or "stabilized plasmid-lipid particles."

[origin: WO0180900A2] The present invention provides effective compositions, methods and uses for delivering nucleic acids to cells. The inventive compositions and methods are based upon the surprising discovery that the presence of an endosomal membrane destabiliser in a lipid formulation leads to a dramatic increase in transfection efficiency. The present compositions and methods can be used in vitro or in vivo, and can be used to increase the transfection efficiency of any cell type, including mammalian cells (e.g., humans). In certain embodiments, the conjugated lipid that inhibits aggregation is a "cationic polymer lipid" (CPL). In preferred aspects, the CPL has the formula (I). In formula (I), A is a lipid moiety, W is a hydrophilic polymer, and Y is a polycationic moiety. In certain preferred embodiments, Y is selected from lysine, arginine, asparagine, glutamine, and combinations thereof. In another embodiment, the present invention provides a method for introducing a nucleic acid into a cell, comprising contacting the cell with a nucleic acid-lipid particle composition, wherein the particle comprises a cationic lipid, a conjugated lipid that inhibits aggregation of particles, a nucleic acid; and an endosomal membrane destabilizer. The endosomal membrane destabilizer can be inside the particle, outside the particle, or both inside and outside the particle. In certain embodiments, the endosomal membrane destabilizer contacts the cell before the particle, after the particle, simultaneously or combinations thereof. In still another embodiment, the present invention provides a method for inducing HII phase structure in a lipid bilayer, comprising contacting the lipid bilayer with an endosomal membrane destabilizer, thereby inducing HII phase structure in the lipid bilayer. In certain aspects, the endosomal membrane destabilizer (e.g., Ca<++>ion) acts synergistically or additively with low levels of the cationic lipid to trigger HII phase formation.

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Citation (search report)

See references of WO 0180900A2

Citation (examination)

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