

Loligomers: Targeted Intracellular Drug Delivery Vehicles

Overview of Technology:

The effective routing of therapeutic agents through cell membranes and into distinct cell compartments remains a constant challenge for the pharmaceutical and biotechnology industry. Loligomers are multi-tasking, peptide-based shuttles able to penetrate cells and self-localize into distinct cellular compartments. These molecules are branched peptides that can be rapidly assembled by solid phase methods. Loligomers offer the opportunity of enhancing cellular signaling, cellular routing or recognition events through avidity mechanisms as a result of presenting one or more distinct peptide signals on each of its arms.

Confocal microscopy, EM and flow cytometry, has confirmed that peptide signals introduced on the arms of such peptides can guide the import and localization of such constructs into cells. Loligomers can act as carriers of cytotoxic groups, peptides or macromolecules. Their uptake of large molecular entities such as plasmids was demonstrated using vectors harboring reporter genes suggesting that such constructs can act as non-viral transfection agents. They have also been shown to enhance the potency of a photodynamic cytotoxic agents. Use of alternative signals may allow targeting of endoplasmic reticulum, cytosol or other vesicular compartments.

Related Publications:

Sheldon, K., Liu, D., Ferguson, J., and Gariépy, J. (1995) Loligomers: Design of de novo peptide-based intracellular vehicles. *Proc. Natl. Acad. Sci. (USA)* 92, 2056-2060.

Singh, D., Kiarash, R., Kawamura, K., LaCasse, E.C. and Gariépy, J. (1998). Penetration and Intracellular routing of nucleus-directed peptide-based shuttles (loligomers) in eukaryotic cells. *Biochemistry* 37, 5798-5809.

Singh, D., Bisland, S., and Gariépy, J. (1999) Peptide-based intracellular shuttle able to facilitate gene transfer in mammalian cells. *Bioconjugate Chem.* 10, 745-754.

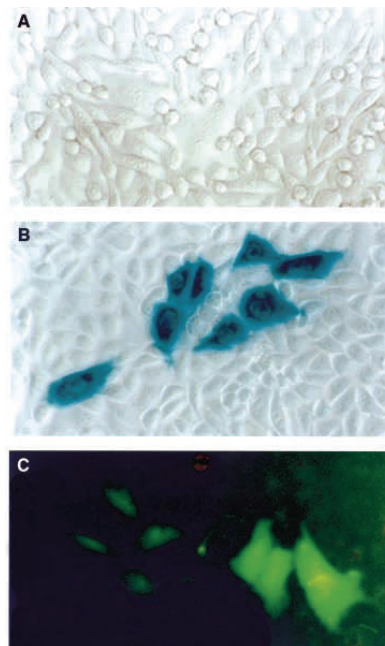
Bisland, S.K., Singh, D. and Gariépy, J. (1999) Potentiation of chlorin e6 photodynamic activity in vitro with peptide-based intracellular vehicles. *Bioconjugate Chem.* 10, 982-992.

Patents:

US5,674,977 and CA2,191,862 - Patents Granted

Inventor:

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Expression of β -galactosidase and GFP in CHO cells. (A) CHO cells transfected with the naked plasmid pCMV β -gal showing no indigo staining of cells. (B) Indigo-colored cells are observed in this preparation of CHO cells transfected with loligomer 4-pCMV β -gal plasmid. (C) Fluorescent green cells were visualized in a field of CHO cells transfected with loligomer 4-pGFP plasmid.
From *Bioconjugate Chem.* 1999, 10, 745-754

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