

## TRANSPORTER NUCLEIC ACIDS FOR THE INTRACELLULAR DELIVERY OF NUCLEIC ACID AGENTS

### *General*

Apart from the introduction of additional genetic information into the genome of an organism (gene therapy), the development of therapeutic oligonucleotides is in particular being urged forward in human medicine. Particularly if clinical pictures are correlated with incorrectly controlled, greatly increased gene expression or viral gene expression, oligomeric nucleic acid agents can be successfully used as therapeutics. The most promising classes of oligomeric nucleic acid agents include antisense oligonucleotides, double-stranded RNA (siRNA) and ribozymes.

### *Prior art*

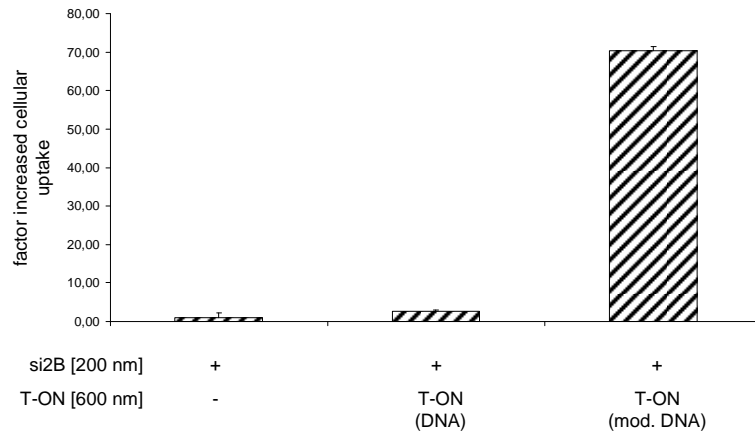
Cellular introduction is one of the largely unsolved, technical requirements for the biological use and therapeutic application of nucleic acid agents. It is e.g. known that antisense oligonucleotides are only slightly or not measurably spontaneously absorbed by target cells. The absorption can in part be improved in that certain carrier substances, frequently peptidic, lipidic or cationic, organic substances are used, which increase the cellular uptake of antisense oligonucleotides and therefore also improve the action of the antisense oligonucleotides applied. In mammals and humans such carrier substances are often toxic and can consequently not be used. Therefore there is a need for suitable methods for the introduction thereof into target cells and target tissue for the clinical application of oligomeric nucleic acid agents.

### *The invention*

The invention relates to a method and a pharmaceutical formation for improving the cellular uptake of nucleic acids, particularly nucleic acid agents.

It is based on the novel finding that nucleic acids modified in a particular way improve the cellular uptake of other nucleic acids, particularly double-stranded RNA (siRNA) and consequently act as transporter nucleic acids.

The cellular uptake of oligonucleotide agents is dependent on the concentration and length of the transporter nucleic acid, but not on its sequence. Fig. 1 illustrates the seventy times increase in the cellular uptake of siRNA through co-incubation with a transporter nucleic acid according to the invention.



**Fig. 1: Improved cellular absorption of siRNA in ECV-304 cells by co-incubation with a transporter nucleic acid. si2B: siRNA, T-ON: transporter oligodeoxyribonucleotide. T-ON (DNA): unmodified transporter oligodeoxyribonucleotide (= neg. control). T-ON (mod. DNA): transporter oligodeoxyribonucleotide modified according to the invention.**

*Advantage/market potential*

Rapidly increasing importance is being attached in science and clinical medicine to the modulation of the gene expression. The effective introduction of nucleic acids is of decisive significance in this connection. Despite a broad spectrum of commercially available transfection reagents there is an increased need for efficient and more particularly toxicologically unobjectionable transfection systems.

*Exploitation concept*

We are seeking the licensing/sale of this invention to an organization which will make the described method marketable and which will take over marketing. If desired, PVA SH GmbH will continue to support the exploitation by arranging contacts with the inventor and the development of a pattern.

*Contact*

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