Novel CPP-compatible phosphate oligonucleotides

Value proposition and Field of application

A key issue within antisense oligonucleotide (ASO) therapeutics is that cell-penetrating peptides (CPPs) cannot be used for delivery into cells of phosphate-based ASOs. Our technology makes CPP-compatible phosphate-based ASOs possible and opens CPP delivery to the broader ASO field.

Technological description

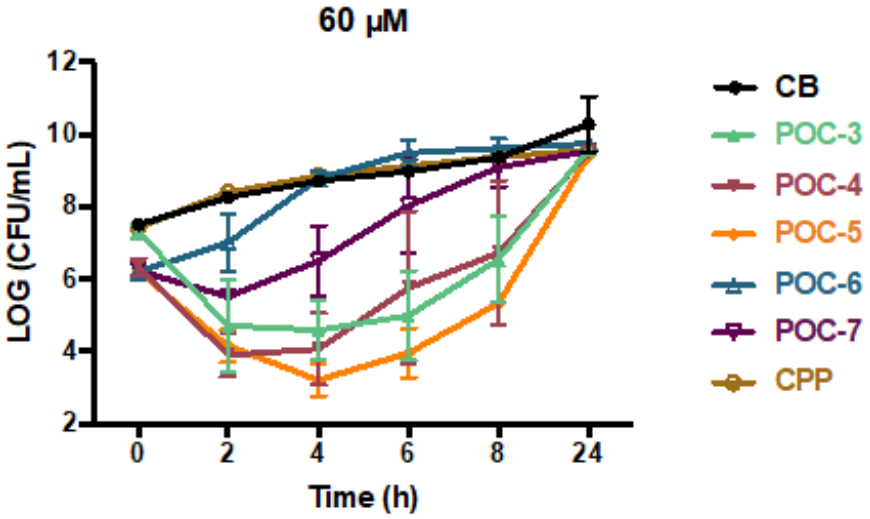
Cell-penetrating peptides (CPP) are promising vectors for the delivery of antisense oligonucleotides (ASOs) into animal and bacterial cells.
CPPs are typically positively charged amphipathic peptides that easily penetrate biological membranes in a receptor-independent way. Due to the positive charge of CPPs, chemical conjugation and purification with negatively charged ASOs (phosphate-based ASOs composed of monomers like DNA, 2'-O-(2-Methoxyethyl)-RNA (MOE-RNA), 2'-O-Me-RNA and Locked Nucleic Acid (LNA) has proved to be challenging.
The key challenge for such for gene silencing in bacterial, animal or human cells is that interaction between the typically negatively charged ASO and the typically positively charged CPP. This results in lack of efficient gene silencing due to aggregation and low solubility.

So, CPPs have been almost exclusively used with ASOs composed of the neutrally charged monomers peptide nucleic acid (PNA) or phosphoramidate morpholino oligomer (PMO).
Unfortunately, PNAs and PMOs cannot be combined with eg. DNA, RNA, LNA or MOE monomers in mixmer ASOs. So, there's a great need for a solution that provides a greater range of possibilities in ASO design and makes conjugation of phosphate-based ASOs with CPPs possible.

Our technology is a solution to this key challenge: It enables conjugation of CPPs with phosphate-based ASOs composed of monomers like DNA, MOEs, 2'-O-Me-RNA and LNA.
We have demonstrated efficient silencing in bacteria and in mammalian cells.

Current state of development

We have evidence of efficient gene silencing by peptide-oligonucleotide conjugates in cell cultures of *E. coli* and human cancer cells.



Team

The inventor team includes Professor Jesper Thagaard Wengel (University of Southern Denmark), who has also invented LNA and Assistant Professor Nuno Filipe Azevedo (University of Porto) who has extensive experience working with bacterial cell cultures.

Intellectual property rights

International application no. PCT/DK2022/050248 was filed on 25 November 2022. University of Southern Denmark is searching for external partners on behalf of the IP owners (University of Porto and University of Southern Denmark).

Business opportunity and Call to action

We are looking for one or more partner(s) or licensee(s) to further establish the usefulness of the invention and eventually market it.

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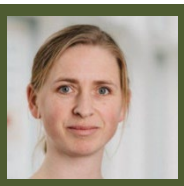

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