AMANY as a conjugated flexible intercalator to improve the hybridization efficiency of therapeutic triplex forming oligonucleotides

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Technological field
Biotechnology – health, medico-technical

Business opportunity
- Licensing
- Investment
- Partnership

The technology
With the decoding of the human genome and with an increased knowledge of the genes functions the necessity for sequence specific recognition and targeting of double stranded DNA for diagnostic applications and therapeutics are of high interest.
The anti-gene strategy involves a triplex forming oligonucleotide (TFO) which is able to target the genome via the major groove of the duplex forming a triple helical structure (triplex). The TFO consists of either pyrimidine or purine bases.
Bulge insertions of flexible intercalators into the DNA triplex structure are found to give a dramatic contribution to the triplex stability. On the other hand insertions of conjugated intercalators are found to diminish quadruplex structures and in this way breaking down the self association of G-rich oligonucleotides under physiologically potassium ion conditions.

In the present invention AMANY has been synthesized as a flexible intercalator in a cheap, short and efficient synthetic route.

Compared to previous examples, AMANY has a completely new design in the structural feature. Thermal melting studies showed that the AMANY intercalator has extraordinary high thermal stability of Hoogsteen-type triplexes and duplexes with a high discrimination of Hoogsteen mismatch.

Current state of the technology
The chemical synthesis has been accomplished and the AMANY amidite needed for the oligo synthesis is ready for custom synthesis in 100 gram scale or more.

Applications
- Antigene therapy of untreatable diseases like pancreas cancer
- Agents capable of directing mutagenesis
- Purification of DNA plasmids (double-stranded DNA)
- Non-denaturating Fluorescence In Situ Hybridization (FISH) gene repair

Intellectual property right
IPRs are owned by the University of Southern Denmark. A US provisional application has been filed, 2008.

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The group of Erik Bjerregaard Pedersen currently consists of one Post doc, one Ph.D student, one Master student, one laboratory technician and one academic secretary. The research in the group concentrates on synthesis of modified nucleic acids for use in antigen therapy, for example triplex-forming oligonucleotides and intercalator-based transcription inhibitors. Furthermore, the group is devoted to synthesis of non-nucleoside reverse transcriptase inhibitors, nucleoside monomers and prodrugs directed at identification of new anti-HIV and anti-AIDS agents.

Publications relevant to the invention:
Flexible intercalators which were published in *Nucl. Acids Res.* **2008**, *38*, 3496-3507 and *J. Am. Chem. Soc*. **2005**, *127*, 14849-14858

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