

Oligonucleotide agents for therapy of tumour diseases

General information

Despite significant advances in the understanding of carcinogenesis, effective treatment of cancer remains one of the most urgent problems of contemporary medicine. E.g., with a 5-year survival rate of 0.4%, prognosis for pancreatic carcinomas is extremely bad. Therefore, development of effective anti-tumour substances is still of utmost importance.

State of the art

Oligodeoxyribonucleotides (ODN) have recently proved to be a group of promising substances. High expectations were raised by the so-called antisense-oligodeoxyribonucleotides (ASODN), which are meant to suppress the expression of a specific protein, e.g. an oncogene. In spite of these expectations so far only one ASODN has been approved as a medical drug. Starting from the original idea of a steric blockade of the relevant process of ribosomal translation, a much more sophisticated picture of possible modes of action of ASODN has developed. Meanwhile, unspecific biological properties have also been reported for ODN that do not exhibit a target-specific sequence of an ASODN.

The invention

The present invention relates to certain non-sequence-specific oligonucleotides, pharmaceuticals containing these oligonucleotides, and their therapeutical use. The oligonucleotides according to the invention e.g. are able to inhibit the proliferation of pancreatic tumour cells *in vitro* in cell cultures by up to 96% (fig. 1) and *in vivo* in an orthotopic xenotransplant model by up to 50% (fig. 2).

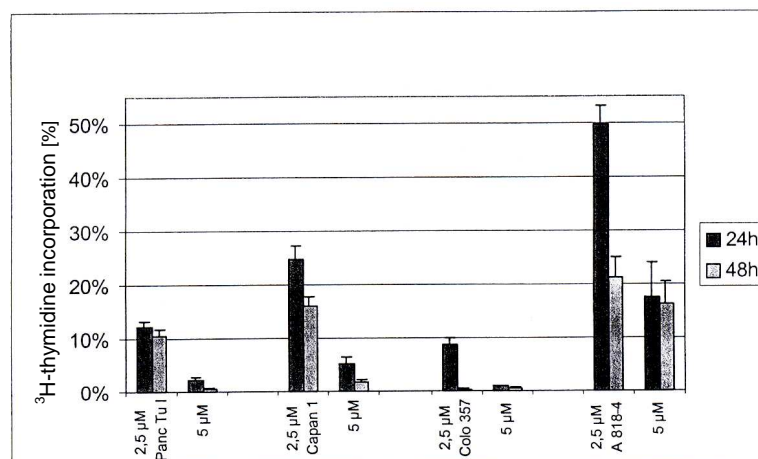


Fig. 1: Tumour cell proliferation (measured by ³H-thymidin-incorporation) as a function of the dosage of the inventive oligonucleotide agent MON1 in relation to the relevant untreated control(=100%): PancTu1, Capan1, Colo357, A818A: tumour cell lines



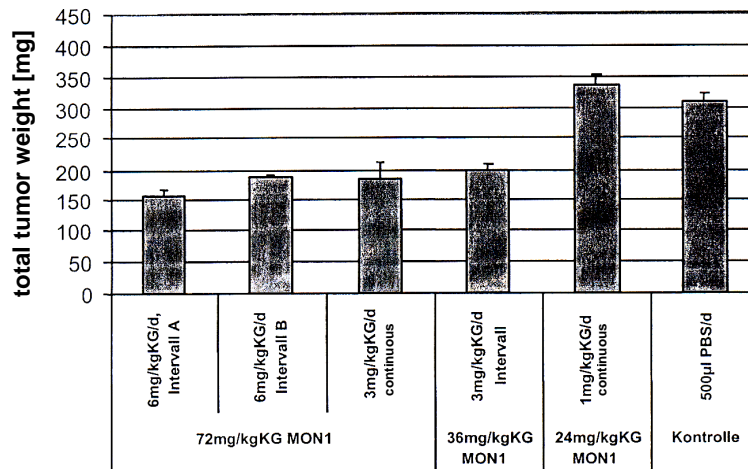


Fig. 2: Overall tumour weight in xenotransplanted SCID-mice as a function of the application rhythm and the dosage of the inventive oligonucleotide agent MON1: interval A: 3 day therapy + 3 day break; interval B: 6 day therapy + 12 day break

The oligonucleotides that have proved to be especially effective are those that show a covalent bond in the terminal 3'- and/or 5'-positions, lipophilic molecular entities, and a modified backbone. The oligonucleotides according to the invention are comparatively short and can thus be produced inexpensively through well-established methods of synthesis.

Utilisation concept

Licensing of this invention is sought to a company that will bring to market and distribute the oligonucleotide agents described and the pharmaceutical preparations containing them. If desired PVA SH GmbH will further assist utilisation through arranging contact with the inventor and financing development of a sample.

Contact

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