Development of antisense oligonucleotide medicine for the treatment of neuroendocrine cancer

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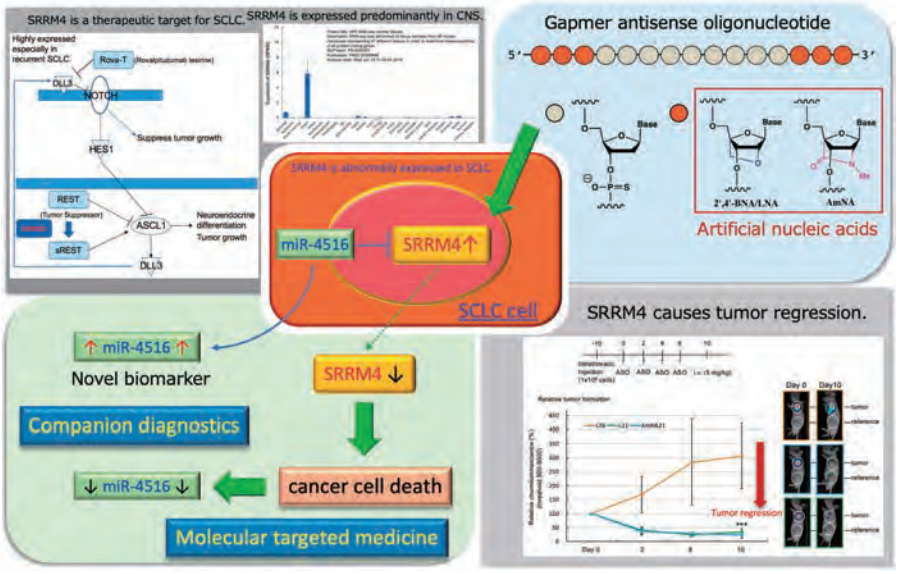
Project Outline

OVERVIEW

Small cell lung cancer (SCLC) is a highly aggressive malignant tumor in lung, which grows rapidly. Although primary chemotherapy is often effective, the 5-year survival rate is extremely poor at less than 10%. Development of effective new therapeutic medicine is thus strongly expected. The research group identified Ser/Arg repetitive matrix protein 4 (SRRM4) is highly expressed in SCLC and induces tumor formation and growth[1]. SRRM4 regulates the alternative splicing of RE1-silencing transcription factor (REST), which suppresses the expression of several neuronal genes. In SCLC, neuroendocrine tumors are formed by high expression of sREST through the alternative splicing of REST produced by SRRM4. We decided to use the gapmer antisense oligonucleotide (ASO) as a therapeutic medicine targeting SRRM4. The ASO contains an amide-bridged artificial nucleic acid (AmNA) developed by Dr. Obika, Osaka Univ. The design used the in silico method established at Osaka Univ and NIBIOHN. SRRM4 ASO showed tumor regression effect in cancer-bearing mice transplanted orthotopically with SCLC-derived cancer cell lines[2]. SRRM4 is also highly expressed in neuroendocrine prostate cancer (NEPC). The clinical trials to make antisense oligonucleotide medicine targeting SRRM4 the world's first antitumor oligonucleotide medicine with excellent efficacy and safety are expected through clinical and non-clinical studies.

[1]Shimojo M. *et al.* Mol Cancer Res. 11:1258 (2013)

[2]Shimojo M. *et al.* Sci Rep. 9:7618 (2019)



Target Disease：neuroendocrine tumour（SCLC、CRPC etc.）

Patent Information：Domestic patent acquired (patent 6467580). PCT/JP2019/030090 pending.

Technical Features：Antisense oligonucleotide

Marketability：New patients worldwide with lung cancer (1.8 million) and with prostate cancer (1.1 million).

Challenges in Development：Non-clinical study

Desired contents of company collaboration：Collaboration and License out