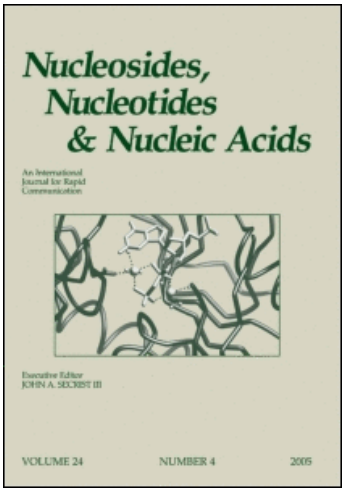

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Inhibition of the Influenza Virus M Protein MRNA Translation in vitro with Complementary Oligonucleotides

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INHIBITION OF THE INFLUENZA VIRUS M PROTEIN mRNA TRANSLATION *in vitro* WITH COMPLEMENTARY OLIGONUCLEOTIDES

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Abstract. Efficient arrest of the influenza virus M protein mRNA translation is achieved with antisense oligodeoxyribonucleotides complementary to the 5'-terminus of the messenger at the initiation codon and the upstream sequences.

Messenger RNAs represent important targets for antisense oligonucleotides. Investigation of the effects of complementary oligonucleotides on translation of different mRNAs is necessary for the elucidation of the general factors which should be taken into account when developing oligonucleotide inhibitors for arbitrary specific mRNAs. We investigated the effect of antisense oligonucleotides on translation of the influenza virus M protein mRNA in a cell-free

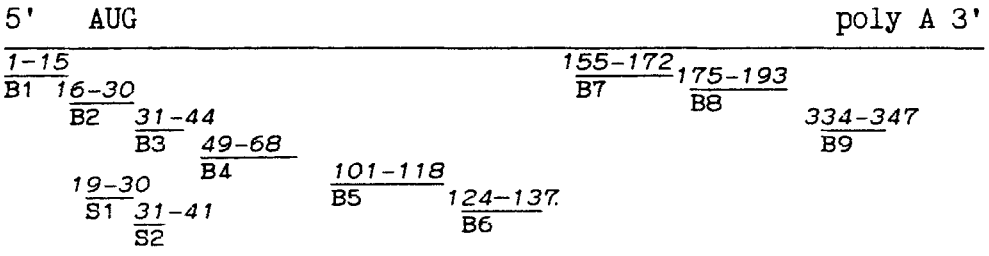

Fig.1.Protein M mRNA and antisense oligonucleotides tested Positions of the nucleotide stretches complementary to the oligonucleotides are shown by figures.

Table 1. Inhibition of the M protein synthesis in the cell free system by oligonucleotides, percents

Oligomer \ Conc.,μM	0	0,6	2	10	25	50	100
B1	0	10	24	30	45	47	
B2	0	5	10	12	16	34	46
B3	0	0	5	12	20	29	55
B1+B2	0	10	10	14	57	61	
B2+B3	0	5	4	50	92	100	
B1+B3	0					57	
B1+B2+B3	0	34	57	96	100		
B4	0						0
B5	0						29
B6	0						41
B7	0					40	41
B8	0						17
B9	0						61
S1+S2	0	0	0	4	46	50	50

system. RNA was isolated from chicken fibroblasts infected with fowl plague virus Weybridge. Oligonucleotides were synthesized by the amidophosphite method and purified by HPLC. Sequences in the mRNA complementary to the oligonucleotides are shown in Fig.1.

The RNA was translated in the presense of [^{35}S]-Met in the reticulocyte cell-free system.The synthesized proteins were resolved by gel electrophoresis and quantitized by densitometry of the autoradiographs of the gels. Results of the experiments shown in Table 1 demonstrate that synthesis of the M protein is suppressed by the oligonucleotides complementary to the 5'-terminus of the messenger at the oligonucleotides concentration of 2-10 μM. Oligonucleotides complementary to the coding region of the mRNA are less efficient in the translation arrest. Powerful inhibition is caused by pairs of oligonucleotides which are complementary to the adjacent sequences of the mRNA and can form contiguous duplex with the target. The identified efficient oligonucleotide ingibitors can be used as basic structures for the design of more efficient derivatized oligonucleotide analogs for arrest of the M protein in infected cells.