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B) Molecular Dynamics Simulations of the UACG Tetraloop in the very short Hairpin

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Key words: molecular dynamics simulations, UACG tetraloop

The structure of RNA is as varied as its functions The single-stranded RNA molecule often folds back on itself to form double helical stem capped by a loop of non-Watson-Crick paired or unpaired nucleotides of various sizes, which are thought to provide tertiary recognition sites for both proteins and nucleic acids

The four-base loops cap many double-helical structures in rRNA Although 256 different tetraloop sequences are possible, nearly 70% of all the four-base loops in rRNAs are either UNCG or GNRA (where N is any nucleotide and R is a purine), with extraordinary high melting temperatures in comparison with similar RNA sequences (Woese *et al* 1990)

The goal of our MDS was to make clear remaining questionable structural features of the UACG tetraloop in the very short hairpin (Abdekalfi *et al* 1997), for which an

experimental research produces either inconsistent results (the rA residue conformation), or determination of which is beyond capabilities of contemporary experimental apparatuses (the mode of the hydrogen bond connection in the atypical terminal 1U-rG pair of residues in the tetraloop) Except it, we were interested in the influence of 2'hydroxyls groups on the stabilisation of the hairpin structure due to the creation of hydrogen bonds, either in the mentioned 1U-rG terminal pair of residues or elsewhere, because it seems to be the reason of the substantially higher thermodynamic stability of UNCG tetraloops in comparison with their deoxyoligonucleotide analogues

In our MDS the hairpin structure seemed to be stable in the temperature range up to 285 K with the rA residue in the C3endo/anti conformation In the case of higher temperatures the C3endo/anti conformation of the rA residue changed to the C2endo/syn conformation

One hydrogen bond between RU and 1G bases and the other between the RU 2'hydroxyl group and the rG base stable in both C3endo/anti and C2endo/syn conformations (proposed on the base of NMR results (Allain and Varani 1995) established in the course of our fully solvated MDS This kind of the hydrogen bond connection gives the explanation of higher stability of RNA loops in comparison with the same deoxy- sequences

We found also three other supplementary hydrogen bonds, which formed between 2'hydroxyl and site phosphate groups (in the stem in two cases and once in the loop sequence of the hairpin)

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X-Ray Crystal Structure of GpC phosphonate Analogue: A Promising Unit for the SNAIGE Strategy

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Key words: SNAIGE concept, crystal structure, GpC phosphonate analogue

Several new concepts called, as a whole, the SNAIGE concept (Synthetic Nucleic Acids Interfering with Gene Expression), have been introduced into chemotherapy in recent period of time, such as the idea of "antisense" oligonucleotides

The first X-ray crystal structure of novel-type diribonucleoside monophosphate analogues, the crystal structure of (guanosine-2'-O-phosphonomethyl)-5'-O-cytidine (G-p_cC 2') was determined Structural unit involves two asymmetric molecules of G-p_cC, Mg^{2+} and 13 H_2O, differing in conformation of phosphonate analog of phosphodiester linkage