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Triplex-Peptide Nucleic Acid (PNA) biological systems investigated through advanced computational methods

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Peptide Nucleic Acids (PNAs), introduced by Nielsen et al. in 1991, are synthetic DNA/RNA analogues and represent a promising tool for gene modulation in anticancer treatment[1]. In the PNA structure, repetitive N-2-aminoethyl-glycine units replace the traditional sugar-phosphate DNA backbone, and the polyamide chain is connected to nucleobase covalently via carboxymethyl spacer. Thanks to their uncharged peptidyl backbone and resistance towards chemical and enzymatic degradation, PNAs can form hybrid complexes with complementary DNA or RNA strands [2-3]. In this view, advanced computational methods based on both conventional and accelerated Molecular Dynamics (cMD and aMD, respectively) simulations were helpful to accurately elucidate the atomistic structural organisation of two differently protonated PNAs structures wrapped into triplex DNA/PNA. In particular, aMD allowed us to improve the conformational space sampling by reducing energy barriers separating different states of a system, thus observing atomistic details about the conformational changes of the two triplex systems. In fact, although the mechanistic aspects for the formation of PNA-DNA triplexes are known, detailed structural information on the PNA-DNA heterotriplexes are still missing. Our findings are in agreement with experimental data and lay the foundation for a further development of novel PNAs in anticancer therapy.

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