

Tuesday, May 20 at 10:00 am (BBS Amphitheatre)

Structuration and Functionalisation of oligonucleotides for biomimetic applications

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To modulate the biological or biotechnical properties of oligonucleotides (ON), the group has focused on the introduction of modifications at the under-exploited 5'-position of nucleosides. First, the 5'-carbon was connected in a stereo-controlled manner to the phosphate moiety of the nucleotide chain. The resulting conformationally constrained nucleotides bear a 1,3,2,-dioxaphosphorinane ring within the sugar-phosphate backbone, locking the conformation of torsional angles either into canonical or non-canonical values, leading to the enhanced stabilization of the targeted DNA secondary structures.¹ Meanwhile, the synthetic development of 5'-C-propargyl nucleotides led, after SPS, to convertible ON (CvON). Their post synthetic conjugation by CuAAC reaction gave access to functionalized oligonucleotides (FuON) modified to

expand their catalytic repertoire towards biomimetic reactions. In the challenging field of protease-like DNA catalysts, those nucleic mimics were designed to ultimately be able to perform the hydrolysis of the amide bond. Inspired by the serine proteases relying on a catalytic triad of three cooperative amino acids, serine, histidine and aspartate, the azide molecules bearing the corresponding side chain-like residues (carboxylate, imidazole and aspartate), alongside a synthetic organocatalyst presenting the three required groups, were conjugated onto CvON.² Then, by taking advantage of the controlled folding of DNA, the resulting FuON were assembled into different secondary structures with the goal of reproducing the active site of the serine proteases. The results and perspectives of this approach will be then presented.

[1] C. Chardet, C. Payrastra, B. Gerland, J.-M. Escudier, Convertible and Constrained Nucleotides: The 2'-Deoxyribose 5'-C-Functionalization Approach, a French Touch, *Molecules* 2021, 26.

[2] a) C. Addamiano, B. Gerland, C. Payrastra, J. M. Escudier, DNA Three Way Junction Core Decorated with Amino Acids-Like Residues-Synthesis and Characterization, *Molecules* 2016, 21. ; b) C. Chardet, S. Serres, C. Payrastra, J.-M. Escudier, B. Gerland, Functionalized oligonucleotides, synthetic catalysts as enzyme mimics, *Comptes Rendus. Chimie* 2024, 26, 1-13.

Host: Valérie Desvergnès, ARNA laboratory