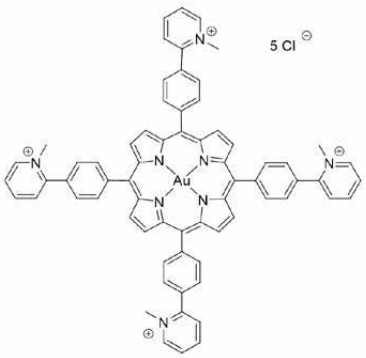
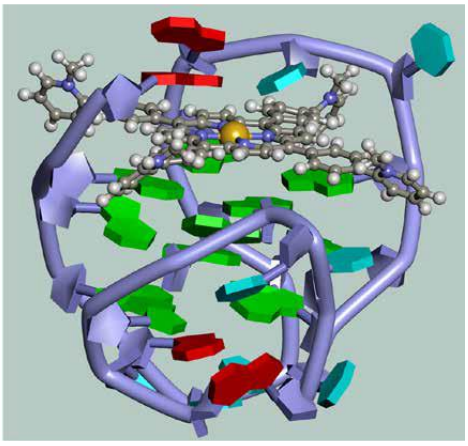
OUR RESULTS FOR THE YEAR 2022

The role played by RNA G-quadruplex in HIV-1 infection





G-quadruplex nucleic acids are secondary structures of RNA or DNA with four strands found in guanine-rich sequences. They are formed by pairing of guanines by trays of four guanines. These structures are involved in the regulation of many biological processes but their role in viruses is less known. The genome of the HIV-1 virus contains 10 sequences that can form a G-quadruplex. It should be noted that these sequences are highly conserved in the HIV-1 virus, which suggests a vital role for the virus.

We have prepared metal complexes based on gold(III) porphyrins to target G-quadruplexes specifically. These complexes inhibit viral proliferation at concentrations of the same order of magnitude than AZT (zidovudine), a standard antiviral drug for the treatment of HIV-1 virus. However, their pharmacological target is different as demonstrated in the study. Indeed, we were able to show that the target of porphyrins was G-quadruplex RNAs which are formed in the very first steps of the viral cycle, during the initiation of the reverse transcription of the viral RNA in the infected cell. This work has thus allowed to demonstrate on the one hand, the importance / existence of G-quadruplex structures on the RNA of the virus during its infection and on the other hand, the possibility of targeting these elements with small molecules opening the way to potential drugs with an original mechanism of action compared to what currently exists in antiviral therapy.

Deciphering RNA G-quadruplex function during the early steps of HIV-1 infection.

S. Amrane, C. Jaubert, A. Bedrat, T. Rundstadler, P. Recordon-Pinson, C. Aknin, A. Guédin, A. De Rache, L. Bartolucci, I. Diene, F. Lemoine, O. Gascuel, G. Pratviel, J.-L. Mergny, M.-L. Andreola, *Nucleic Acids Res.* **2022**, 50(21), 12328-12343
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