Small Molecules for Targeting and Imaging Nucleic Acid Structures.

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For many years our research efforts have been focused on the design of structure and fluorescent probes for nucleic acids. Our targets are more specifically alternative secondary structures such as G-quadruplexes that can be found in G-rich regions and local pairing defects such as base mismatches that result from base misincorporation or damages. These structures are involved in various genomic dysfunctions and may ultimately cause genetic instability related to cancer development. Our aim is to provide chemical biology tools for better understanding the roles of these structures and their processing by proteins. In parallel the new compounds may be considered as prototypes for anticancer drug development.

Along these lines, we have developed a number of new heterocyclic scaffolds that have been engineered to display on the one hand selective recognition of the target DNA structure and on the other hand a switchable fluorescence emission acting as reporter. Selected examples illustrating our main achievements in the field will be described:

1) Design of bisquinolinium scaffolds acting as G-quadruplex DNA probes [1,3]
2) Design of Cyclobismacrocycles binding to homopyrimidine mismatches [4,6]
3) Design of Vinyl-Triphenylamine dyes shaped for two-photon absorption and AT-rich regiospecificity.[7,9]

In each case, we will give a short overview of the synthetic approaches, the structure of the interaction with DNA identified by NMR or modelling and the practical applications for in vitro analysis and in-cell probing.

References:

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[9] B.Dumat et al. DNA switches on the two-photon efficiency of an ultrabright triphenylamine dye with exquisite AT regiospecificity. *Submitted*.