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Engineered Naphthalene Diimides as Multimodal G-Quadruplex Interacting Tools.

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In the last 5 years, we engineered three classes of G-quadruplex ligands (naphthalene diimides,[1] polyheteroaryls[2] and anthraquinones[3]), in order to achieve selective covalent modification, visible and NIR (Near InfraRed) fluorescent emission,[4] and singlet oxygen generation.[5] Naphthalene diimides (**NDI**) resulted to be particularly promising as multimodal molecular tools. In fact, the red fluorescent NDI core have been easily conjugated to reactive moieties, by robust and flexible synthetic protocols. Quadruplex *vs* duplex selectivity, efficiency, and G4 base specificity of the target covalent modification have been investigated as a function of the reactive moieties used (quinone methides,[6] oxiranes[7] and phenoxyl radicals[8]). In this seminar, particular emphasis will be placed on our most recent results on a photo-reactive NDI dye targeting the human telomeric sequence Tel22, and several mutated analogues, which has been activated by green light (λ=532 nm). Highly selective covalent modification of G4 *vs* single-stranded and double-stranded DNA was achieved with efficiency up to 64%. Phenoxyl radical was generated and detected by laser flash photolysis, as reactive intermediate targeting loop thymines.[8]

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