Fluorescent nucleobase analogs, a first step towards intrinsically emissive PNAs

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Peptide nucleic acids (PNA) are outstanding chemical biology tools, recognized from decades and deeply applied in basic academic research for targeting nucleic acids substrates.[1,2] PNA, DNA, and RNA easily interact each other thanks to the sharing of the same nucleobase alphabet.[1,2] PNA have been deeply studied in the recent years in antisense and antigene therapies, gene editing but also nucleic acid sensing and imaging.[3,4] In this context, the option to replace natural occurring nucleobases with emissive isomorphic analogs into the PNA sequences represents a unique research field which aims to overcome limitations of the conventional nucleic acid tag with emissive molecules.[5] These intrinsically fluorescent nucleobases have shown extraordinary fluorescence read-outs upon variation of environmental pH and polarity and in the imaging of biological relevant events like duplex formation.[6]

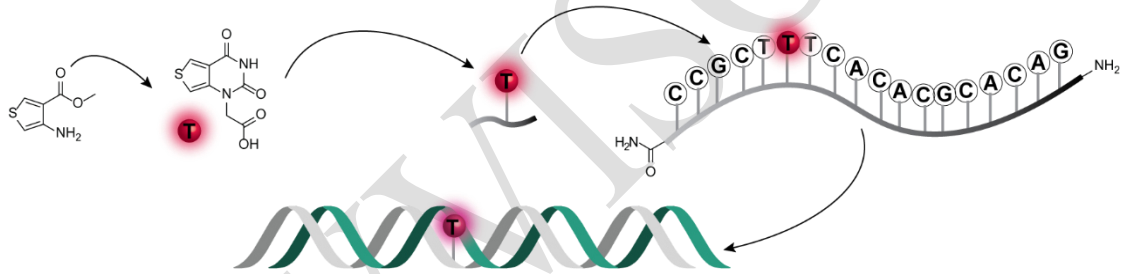

Figure 1. Intrinsically emissive PNA.

Here we present the design, synthesis, characterization and straightforward incorporation into model PNA standard sequences of a thieno[3,4-d]pyrimidine fluorescent analog of thymine to provide intrinsically fluorescent PNAs. The photophysical properties of the emissive PNAs, their ability to form stable heteroduplex with complementary DNAs have been studied by absorption and emission spectroscopies and micro-differential scanning calorimetry. The preliminary results suggest how the replacement of one natural thymine with a fluorescent analog has a minimal impact on the DNA-PNA heteroduplex stability while conferring to PNA remarkable brightness and modular luminescence: excellent properties for future studies in chemical biology assays.

References

[1] P.E. Nielsen, Account of Chemical Research 1999, 32, 624 – 630.
[2] J. Saarbach, P.M. Sabale, N. Winssinger, Current Opinion in Chemical Biology 2019, 52, 112 – 124.
[3] C. Suparpprom, T. Vilaivan, RSC Chemical Biology 2022, 3, 648 – 697.
[4] R. Brazil, ACS Central Science 2023, 9, 3 – 6.
[5] R.W. Sinkeldam, N. Greco, Y. Tor, Chemical Reviews 2010, 110, 2579 – 2619.
[6] A. Rovira, A. Fin, Y. Tor, Chemical Science 2017, 8, 2983 – 2993.