Isomorphic Fluorescent Nucleosides

Yitzhak Tor, University of California, San Diego

The photophysics of RNA and DNA is unique among biomolecules that possess aromatic building blocks. Unlike proteins, which contain intrinsically fluorescent amino acids, the canonical nucleosides, and hence nucleotides and oligonucleotides, are practically non-emissive. We develop emissive nucleoside surrogates that facilitate the monitoring of nucleoside-, nucleotide- and nucleic acid-based transformations at a "nucleobase-resolution" in real time (Figure). The lecture will articulate the fundamental challenges and will present the design, synthesis and photophysical features of emissive nucleosides as well as selected examples for their utilization in fluorescence-based biophysical and discovery assays.



Figure. Fluorescent nucleoside analogs (R=D-ribose, 2'-deoxy-D-ribose)

Selected References

Fluorescent Analogs of Biomolecular Building Blocks: Design, Properties and Applications Sinkeldam, Greco and Tor, Chem. Rev. **2010**, 110, 2579

Emissive RNA Alphabet Shin, Sinkeldam and Tor, J. Am. Chem. Soc. **2011**, 133, 14912

Enzymatic Interconversion of Isomorphic Fluorescent Nucleosides: Adenosine Deaminase Transforms an Adenosine Analogue into an Inosine Analogue Sinkeldam, McCoy, Shin and Tor, Angew. Chem. Int. Ed. **2013**, 52, 14026

Chemical mutagenesis of an emissive RNA alphabet Rovira, Fin and Tor, J. Am. Chem. Soc. **2015**, 137, 14602

Emissive synthetic cofactors: An isomorphic, isofunctional and responsive NAD⁺ analogue Rovira, Fin and Tor, J. Am. Chem. Soc. **2017**, 139, 15556–15559

Polymerase-mediated site-specific incorporation of a synthetic fluorescent isomorphic G surrogate into RNA

Li, Fin, McCoy and Tor, Angew. Chem. Int. Ed. 2017, 56, 1303

Inherently Emissive Puromycin Analogues for Live Cell Labelling Hadidi et al., Angew. Chem. Int. Ed. **2023**, 62, e202216784

Isomorphic Fluorescent Nucleosides Tor, Acc. Chem. Res. **2024**, 57, 1325