

Novel approach to PK bioanalysis of oligonucleotide therapeutics using Nucleic Acid Nanorobotics (NANs).

Maria Oranges

Nanovery Ltd, United Kingdom

Background: Oligonucleotide therapeutics represent a groundbreaking approach to treat a wide range of diseases. This class of therapeutic molecules introduces a unique and complex scientific challenge in the field of pharmacokinetic (PK) bioanalysis due to the incorporation of chemical modifications, ligand conjugates, and need for direct quantification in various biological matrices.

Method: Nucleic acid nanorobotics (NANs), driven by dynamic DNA nanotechnology, quantify oligonucleotide therapeutics via an enzyme-free, isothermal and user-friendly approach. NANs eliminate cumbersome pre-analytical steps such as RNA extraction, magnetic bead isolation and capture probe processes by directly quantifying oligonucleotide therapeutics in a wide range of samples including, serum, plasma and various tissue homogenates.

Results: This study demonstrates the performance detecting antisense oligonucleotides (ASOs) comprised of various chemical modifications and patterns including 2'-O-Methoxyethyl (2'MOE), 2'-O-Methyl (2'OMe), 2'-Fluoro (2'-F), Phosphorothioate (PS), Locked Nucleic Acids (LNA), and Peptide Nucleic Acids (PNA). Moreover, NANs are not only used for ASOs quantification, they can also detect double stranded nucleic acids, specifically small-interfering RNA (siRNA), aptamers and sgRNA.

Conclusion: Taken together, this research shows the potential of NANs to support oligonucleotide therapeutic PK bioanalysis and beyond to other emerging nucleic acid therapies.