

Title: Nucleic Acid-Linked Immune-Sandwich Assay (NULISA): A Double-Capture Mechanism Achieving Attomolar Sensitivity for Liquid Biopsy Applications

Abstract:

The development of highly sensitive and accurate diagnostic platforms is crucial for early disease detection and monitoring. We introduce the Nucleic Acid-Linked Immune-Sandwich Assay (NULISA), a novel technique that combines the simplicity of ELISA with superior sensitivity and specificity, outperforming existing methods such as Proximity Ligation Assay (PLA), Proximity Extension Assay (PEA), Single Molecule Array (SiMoA), and Single Molecule Counting (SMC).

NULISA employs a double-capture mechanism using antibody-oligonucleotide conjugates, which bind to two distinct epitopes of a target biomarker. This interaction generates a specific coding bridge that ensures accuracy and minimizes false positives. Sequential washing steps effectively reduce background noise, achieving attomolar sensitivity and enhancing signal purity to over 90%. This method has been validated for protein-level biomarker detection and shows promise for application to exosomes biomarkers, enabling non-invasive liquid biopsies.

We aim to establish NULISA as a transformative tool for detecting low-abundance biomarkers with unmatched precision. Its capability to detect cancer stem cell biomarkers at both protein and exosomes levels will be evaluated, offering potential for disease diagnosis earlier than current protein synthesis-based methods. This work represents a significant step forward in precision diagnostics, with implications for cancer research and beyond.