

Next-Gen EV Liquid Biopsy: MSP-Enhanced SiMoA Detects HER2 in Metastatic Breast Cancer Plasma

Extracellular vesicles (EVs) represent a promising non-invasive strategy for the continuous monitoring of metastatic breast cancer (mBC) via liquid biopsy. The clinical translation of EV analysis, however, remains challenging due to complex analytical workflows and the low abundance of EVs subpopulations. Here, we introduce a Single Molecule Array (SiMoA) platform enhanced with membrane-sensing peptides (MSPs) as capture agents for the ultrasensitive detection of HER2 on EV membranes (EVs-HER2). The MSP-based SiMoA assay exhibited superior sensitivity and specificity compared with conventional antibody-based methods, enabling detection at lower EV concentrations and discriminating EVs derived from breast cancer patient-derived organoids (BC-PDOs) from those of healthy control-derived organoids (HC-PDOs). Analysis of plasma samples from mBC patients revealed a significant correlation between EVs-HER2 levels and clinical HER2 status assessed by immunohistochemistry, potentially enabling disease-status monitoring from plasma. Our findings indicate that MSP-enhanced SiMoA is an innovative platform for minimally invasive monitoring of rare EV populations within a timeframe compatible with clinical practice.