MOF-Derived Fe_3O_4 Nanorods-based Multiplexed Platform for Detecting Ovarian Cancer-Specific Extracellular Vesicles Biomarkers

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Abstract

High-grade serous ovarian cancer (HGSOC) is a highly aggressive malignancy often diagnosed at an advanced stage due to the absence of early symptoms and effective diagnostic tools. Extracellular vesicles (EVs) secreted by tumor cells carry disease-specific biomarkers, offering potential for early detection. However, their low concentration in biological samples poses a challenge for isolation and detection, necessitating a highly sensitive and specific assay for subsequent detection of multiple biomarkers. Herein, we report a metal-organic framework (MOF)-derived porous superparamagnetic Fe_3O_4 nanorods (MOF-IONRs) to construct a rapid and sensitive Surface-Enhanced Raman Scattering (SERS)-based multiplexed assay to detect HGSOC-specific EVs protein biomarkers in clinical samples. The MOF-IONRs facilitate targeted isolation of EVs enriched with key protein biomarkers including Mucin 16, Claudin-3 and Folate receptor α associated with HGSOC progression. Their high porosity and surface area enhance biomarkers capture and enrichment of SERS nanotags for SERS signal amplification. Their superparamagnetic properties enable efficient EVs separation and enrichment, thereby improving assay specificity and sensitivity. Moreover, the use of mesoporous gold nanoparticles (mAuNPs) based SERS nanotags amplify SERS detection signals. The platform achieved a detection limit of 213 EVs/mL with excellent reproducibility (%RSD < 10%, n = 3). Clinical validation successfully distinguished ovarian cancer patients from healthy controls, highlighting its diagnostic accuracy and reliability. This multiplex platform demonstrates potential as a liquid biopsy for early diagnosis of HGSOC by enabling rapid, cost-effective, and highly sensitive analysis of EV-associated biomarkers in complex clinical samples. Its portability and compatibility with point-of-care applications highlight its promise as a transformative tool in ovarian cancer diagnostics, offering new avenues for improved patient outcomes.