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Predicting breast cancer recurrence risk through spatial-minimal residual disease (sMRD)

Stanford researchers have developed tissue-based profiling by deep sequencing for detection of Minimal Residual Disease (MRD) by tracking patient-specific tumor mutations in post-chemotherapy tissue samples, enabling a highly sensitive, molecular-level assessment of residual cancer.

Breast cancer is the second most common cancer in the U.S, with over 260,000 cases diagnosed annually. Despite advancements in treatment, more than 40,000 Americans still die each year due to metastatic breast cancer. Neoadjuvant chemotherapy (NAC) is essential for shrinking tumors before surgery in locally advanced cases, yet current methods to detect residual disease post-NAC lack sensitivity. Pathological assessments and circulating tumor DNA (ctDNA) tests often miss microscopic traces, leading to undetected residual disease and undertreatment of patients. A more accurate detection method is urgently needed to guide patient selection for adjuvant treatments, inform targeted therapies, and reduce recurrence risks.

To address this need, Stanford researchers have developed tissue-based deep sequencing for Minimal Residual Disease (MRD) detection, which offers a highly sensitive approach to identify residual cancer cells in tumor tissue after NAC. Unlike traditional pathology, which relies on visual examination, spatial-MRD (sMRD) uses ultra-deep sequencing to detect molecular traces of cancer across different regions of the tumor tissue, even when no residual cells are detectable under the microscope. In pilot studies, s-MRD demonstrated superior accuracy and sensitivity compared to traditional pathology, detecting molecular residual disease in resection tissues where pathology was negative but the cancer later recurred. With its potential to outperform existing methods, s-MRD represents a promising

advancement for improving breast cancer outcomes and making it a valuable tool for global oncology care.

Stage of Development: Pre-clinical

Applications

- Cancer diagnostics
- Prognostic tool for personalized treatment
- Companion diagnostic in drug trials

Advantages

- High sensitivity detection of minimal residual disease at a molecular level
- Personalized profiling of residual cancer
- Alternative to manual pathology, especially beneficial in resource-limited settings
- Adaptable to multiple cancer types beyond breast cancer

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