Enrichment of Epithelial Mesothelioma Cell Clusters for Early Detection and Routine Monitoring of Patients Using Liquid Biopsy

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Objectives:

To validate the potential application of an affordable, non-invasive and early detection of mesothelioma cell clusters by Cluster Isolation Microfluidic Device (CID) enrichment technique.

Background:

Despite new markers to improve mesothelioma diagnosis, about 14-50% of mesothelioma is still misdiagnosed. Above detection device is therefore crucial for early detection of mesothelioma.

Methodology:

Optimization of CID device

1. Detection of mesothelioma cells from spiked-in cells.
2. Detection of mesothelioma cells with clinical patient samples (n=8) and healthy donors. (n=5)

Characterization of detected cells

1. Morphology.
2. Mesothelioma biomarker detection.
3. Recovery, viability and purity of detected cells.

Clinical sample screening

1. Limit of detection (LOD) for specific biomarker.
2. Comparison with current techniques.

Automation of CID system for routine testing

1. Installation of the system in centralized unit.
2. Training of personnel.

Impact:

1. The estimated cost of using the system for routine mesothelioma screening is expected to be 40x less than standard method.
2. The system is in the early phase of clinical testing, further validation and scalability are needed before clinical application.

Result and Conclusion:

1. Cancer cluster was found in blood samples from patients and could be identified by biomarker mesothelin with a reported positive rate up to 100%.
2. Malignant mesothelioma cells were typically large (20-50 μm) with a high nuclear-to-cytoplasmic ratio, nuclear pleomorphism, hyperchromasia, multinucleation, and basophilic cytoplasm, often containing vacuoles. These cells tended to form clusters or papillary structures. In contrast, blood cells were smaller (2-20 μm) and displayed a more uniform morphology, such as erythrocytes (anucleate), neutrophils (segmented nuclei), and lymphocytes (round nuclei).
3. The microfluidic device could increase the concentration of single cells or cluster by 1.8-fold and 2.25-fold respectively.

4. A robust recovery rate of 89% was reported with no significant impact on cell viability. Compared with the commercial CellSearch system with recovery rate of 40% to 80%, the CID device demonstrated a significantly higher recovery rate. Moreover, the label-free detection technology used in the CID system eliminated the reliance on epithelial biomarkers, thereby reducing the false-negative results due to tumor heterogeneity.