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Commentary

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OncoProfiler - A Multi-Cancer Early Detection (MCED) Assay

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Abstract

Laser fabricated SERS nanosensors, OncoProfiler, demonstrated detection sensitivity that sufficient to sense trace amount of tumor-associated content from unprocessed plasma or buffy coat. OncoProfiler enabled the discovery of new biomarkers for cancer detection, which are undetectable with conventional bioassay-based methods. A single test with OncoProfiler could sense multiple biomarkers, which provides high diagnostic accuracy as well as a holistic representation of the spatial and temporal heterogeneity of a tumor. Due to high sensitivity, OncoProfiler has the potential to lead to a non-invasive blood based Multi-Cancer Early Detection (MCED) assay meant for cancer screening and therapeutic monitoring.

Keywords: *Diagnostic Technics and Procedures; Blood; Cancer Early Diagnosis; Raman Scattering*

Introduction

Early cancer detection has been a persistent issue in cancer research for decades. Although liquid biopsy has the potential to solve this ever-persistent issue, conventional liquid biopsy approaches such as DNA microarray, next-gen sequencing, and reverse transcriptase PCR cannot always be reliable due to the low sensitivity, specificity, and extensive sample treatment, usually leading to high false-positives-rate [1], thus skepticism regarding the clinical utility of this technology [2]. In addition, the clinical application of liquid biopsy is hindered by biological barriers such as the lack of cancer-specific biomarkers for asymptomatic cancers, significantly lower biomarkers in circulation at early stages of cancer [3], the short half-life of these biomarkers (up to 3 hours) [4], and the high similarity between healthy and cancer-derived circulating biomaterials [5].

Nanomaterials can aid in developing rapid, cost-effective, and simple substitutes for conventional liquid biopsy approaches since they do not require modification of the analyte using enzymes or multiple amplification steps. Surface-enhanced Raman scattering technology (SERS) has been investigated intensively since it offers essential signal enhancement with high sensitivity, rapid and multiplexing capability, and the ability to provide real-time molecular information without labels [6,7].

Discussion

One of the vital components of SERS is the sensor that amplifies Raman scattering so that ultrahigh sensitivity can be achieved. It is extremely difficult to design and fabricate SERS sensors to function in the biological environment. Most of the SERS-based biosensors made of either noble metal or semiconductors. The former lacks of reasonable reliability and repeatability and the latter provides weak signal [8-11]. It is in this context that we designed a new type of non-metallic SERS nanosensor, OncoProfiler [12-14], using ultrafast laser synthesis. The nanosensor demonstrated limit of detection down to femtomolar concentration with various tumor-associated markers, such as cancer cellular DNA and proteins [8,15]. The chemical stability of the nanosensor and high repeatability [10,16-18] of test make it a clinically applicable tool to diagnosis cancer using patient blood as a primary model.

Figure 1 illustrate the workflow of OncoProfiler. In contrast to existing bioassays, OncoProfiler does not require pre-processing patient blood other than standard blood fractionation. Moreover, comprehensive information of the tumor, including tissue of origin, metastatic states, and prognosis, could be obtained from a single test. Test results could be available within hours of blood

withdrawal from patients. Importantly, OncoProfiler is a single piece of equipment, thus, does not require centralized facilities. Taken together, we believe OncoProfile is well suited for low-cost rapid diagnosis of cancer.

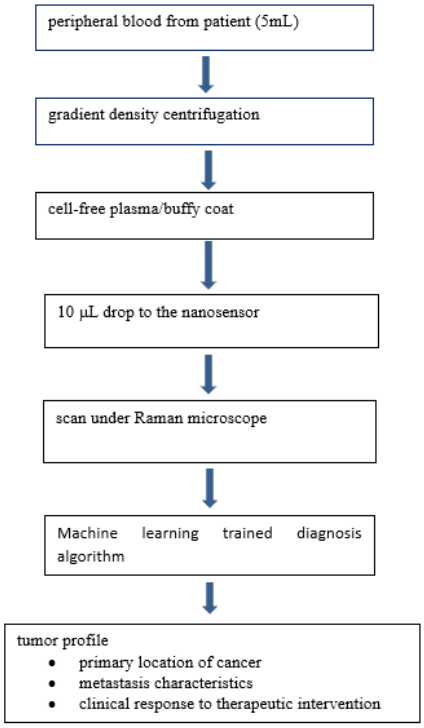

Figure 1: Workflow of OncoProfiler in a clinical setting.

The ultra-sensitivity of Onco Profiler enabled us to discover four tumor associated biomarkers that were hard-to-detect with any other methods, such as, global DNA methylation, extracellular vesicles and components of immune cells [12-14,17,19-20]. The pilot validation of OncoProfiler was tested with a small set (22-75) of patient blood samples for 5 different cancer types with diverse tissues of origin. The sensivity and specificity is given in (Table 1). The reported results are based on a single tumor-associated biomarker. If multiple biomarkers are used simultaneously, we can expect a holistic representation of the spatial and temporal heterogeneity of a tumor [16-18] as well as high diagnostic accuracy.

Table 1: Detecting the presence of cancer from blood samples collected from patient with confirmed diagnosis(stage II-IV cancers); blood sample from healthy adult was used as control.

Type of cancer	Specificity	Sensitivity	Tumor-associated biomarkers	Reference
Breast Cancer	92%	86%	ct DNA, NK cell profiling	[13,17]
Lung Cancer	96%	83%	ctDNA, Exosome profiling, NK cell profiling	[13,17,19]
Colorectal Cancer	92%	75%	ctDNA, Exosome Profiling, NK cell profiling	[13,17,19]
Glioblastoma	100%	93.3%	T cell profiling, Immune exosome profiling	[12,14,20]
Low Grade Glioma (Astrocytoma and Oligodendroglioma)	92.15%	98%	Immune exosome profiling	[14]

Minimally invasive cancer diagnostic methods hold great potential for early cancer diagnosis. However, identifying a set of cancer-specific biomarkers with sufficient specificity and sensitivity for early diagnosis of asymptomatic cancers is highly challenging. Although novel biomarkers, such as CSCs, increase the specificity required for early diagnosis, the percentage of biomarkers in a tumor is usually less than 0.1% of the total tumor cells. Hence, only a trace number of tumor-associated biomarkers will be in circulation. The conventional diagnostic methods cannot detect the trace amount of tumor content in circulation since it is beyond their analytical sensitivity. Therefore,

existing technologies show only a 10-35% sensitivity to detect Stage I breast cancer [21]. OncoProfiler successfully detected the presence of various types of cancer, including hard to detect types, with reasonable sensitivity and specificity from untreated patient blood. It may address the technical challenge of detecting a trace number of tumor-associated biomarkers at the early stage of tumor growth.

Conclusion

OncoProfiler is fabricated using an ultrafast laser-assisted manufacturing technique, which provides the ease of scalability for large-scale mass production. In the future, with the essential preclinical validation studies, the OncoProfiler has the potential to lead to a non-invasive blood test meant for early detection of asymptomatic cancers in a high-risk population and potentially reduce the cost associated with cancer management in the healthcare system.

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