Full spectrum isolation technique-based circulating tumor cells and circulating cancer associated fibroblasts analysis to maximize early cancer diagnosis

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Abstract

Liquid biopsy (LB) is essential in precision medicine, enabling real-time tumor monitoring through repeated sampling. However, its diagnostic sensitivity and accuracy are limited by the low detection rate of circulating tumor cells (CTCs), particularly in early-stage cancers. This limitation arises since existing technologies selectively isolate specific phenotypes of CTCs, failing to capture others, such as mesenchymal CTCs, which are associated with poor prognosis. Mesenchymal CTCs evade detection due to low EpCAM expression and high deformability, while conventional LB methods lack crucial TME insights for effective treatment.

To overcome these limitations, we developed a novel approach that improves LB diagnostic sensitivity and accuracy by (1) creating a technology to isolate all types of CTCs, regardless of marker expression or size, and (2) simultaneously analyzing CTCs and circulating cancer-associated fibroblasts (cCAFs). This dual approach addresses the challenges of low sensitivity and accuracy by enabling the isolation of a broader range of CTCs, including mesenchymal types, and by incorporating cCAF analysis. cCAFs, originating from the TME and circulating in the bloodstream, offer critical tumor microenvironment insights, and their combined analysis with CTCs enhances diagnostic accuracy, particularly in early-stage cancer.

In our study involving 55 breast cancer patients, we demonstrated that while CTCs were undetectable in 42.9% of early-stage patients, cCAFs were detected in all cases and were found to be 10 times more abundant than CTCs. In addition, cCAF subtypes vary with hormonal receptor expression, and their marker analysis allows for 80.9% accurate classification of breast cancer subtypes. We applied this approach to early-stage breast cancer patients, for whom diagnosis through liquid biopsy is particularly difficult, and found that the combined analysis of CTCs and cCAFs achieved a 18% improvement in accuracy compared to CTC analysis alone.

This innovative approach significantly enhances LB by simultaneously isolating all CTC subtypes and incorporating cCAF analysis, thereby offering a more sensitive and accurate diagnostic tool. Beyond improving breast cancer diagnostics, this method has the potential to be applied to other tumor types and could also prove valuable for prognosis prediction and therapeutic response monitoring, ultimately leading to better patient outcomes and more effective cancer treatment strategies.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.