

## **Unraveling metastatic mechanisms: from circulating tumor cell detection to molecular insights**

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### **Abstract**

Recent studies on metastasis and circulating tumor cells (CTCs) have provided new insights into understanding cancer progression and dissemination, along with potential strategies for inhibition. Specifically, in-depth studies on the interactions between the tumor microenvironment and the pre-metastatic niche are enhancing our understanding of metastatic processes. Furthermore, the development of high-resolution imaging technologies and next-generation sequencing (NGS) has significantly improved the detection and analysis of trace amounts of CTCs in the bloodstream.

However, most detection methods rely solely on markers, making it challenging to analyze extremely small quantities of CTCs. In particular, NGS-based analyses, such as 10x Genomics Chromium, have faced significant difficulties in detecting trace amounts of CTCs. Nevertheless, our research team collected and analyzed samples from multiple metastatic cancer patients, successfully detecting CTC clusters using 10x Genomics' Chromium. These clusters exhibit characteristics where some epithelial cell markers are expressed, and a majority of the cells are annotated as epithelial cells using correlation-based cell type annotation tools. When we compared these CTCs with primary and metastatic tumors, we confirmed the expression of previously reported AST markers such as IKZF1 and IRF8. Additionally, we identified genes and pathways that exhibit differential expression depending on the tumor detection site, allowing us to explore their association with metastasis.

By understanding the molecular characteristics and heterogeneity of CTCs, we aim to elucidate metastatic mechanisms and develop personalized therapeutic strategies based on these findings.

### **Do you have any conflicts of interest?**

No, I do not have a conflict of interest.