

## Studying the Metastatic Potentials of Circulating Tumor Cells and Therapeutic Approaches

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## DESCRIPTION

Circulating Tumor Cells (CTCs) are cancer cells that detach from a primary tumor and enter the bloodstream or lymphatic system. These cells can travel throughout the body and potentially establish secondary tumors at distant sites, a process known as metastasis. The concept of CTCs was first introduced by Dr. Thomas Ashworth in 1869 and since then, they have been recognized as important players in the spread of cancer. These cells can exist as single units or clusters in circulation and their presence is often associated with more aggressive forms of cancer and poorer patient prognosis.

The size of CTCs can vary depending on the type of cancer. For example, CTCs from small-cell cancers, such as small cell lung carcinoma, typically range from 7.2 to 10 microns, while those from solid tumors tend to range from 11.8 to 23.9 microns. CTCs derived from blood cancers generally measure between 8.9 and 15.3 microns. Their ability to move through the bloodstream without losing their metastatic potential is one of the reasons CTCs are of particular interest for cancer diagnosis, prognosis and treatment monitoring.

CTCs can be classified into several types based on their molecular and cellular characteristics, which include.

**Cytokeratin-negative CTCs:** These cells lack cytokeratin and Epithelial Cell Adhesion Molecule (EpCAM), markers typically found on epithelial cells. The absence of these markers can indicate a more undifferentiated or mesenchymal phenotype, a process known as Epithelial-Mesenchymal Transition (EMT). CTCs with these features are often more aggressive and more resistant to treatment. Their ability to evade conventional detection methods makes them challenging to isolate, as they do not express CD45 or cytokeratin markers commonly used for identification.

**Apoptotic CTCs:** These are cells that are undergoing programmed cell death (apoptosis). In patients with metastatic colorectal cancer, apoptotic CTCs are frequently detected in the blood and their presence can be linked to liver metastasis. Researchers have studied the use of apoptotic CTCs as a tool for

monitoring treatment responses. The Epic Sciences method, for example, identifies signs of apoptosis, such as cytoplasmic blebbing or nuclear fragmentation. By measuring the ratio of apoptotic CTCs to normal CTCs before and after treatment, clinicians can gain awareness into the effectiveness of cancer therapies.

**Small CTCs:** These cells are typically CD45-negative and cytokeratin-positive, which makes them resemble white blood cells in size and morphology. However, they harbor cancerspecific biomarkers that classify them as CTCs. Small CTCs are associated with disease progression, particularly in cancers that evolve into small cell carcinomas. These types of CTCs often require distinct therapeutic approaches, as their characteristics differ from those of larger, more traditional tumor cells.

Given that metastasis is responsible for the majority of cancerrelated deaths, CTCs are important in understanding how cancer spreads and how new treatments can be developed to target this process. New therapies aimed at disrupting the behavior of CTCs offer assuring strategies for controlling cancer metastasis. By focusing on CTCs as therapeutic targets, scientists hope to develop treatments that can more effectively prevent the spread of cancer throughout the body.

## CONCLUSION

Despite the potential of targeting Circulating Tumor Cells (CTCs) for preventing metastasis, the technical challenges in effectively eliminating these cells have yet to be fully addressed. To examine this further, a study was conducted where CTCs expressing Green Fluorescent Protein (GFP) were transplanted into mice. Photodynamic Therapy (PDT) was then applied to selectively target and destroy the GFP-expressing CTCs. The results demonstrated that eliminating these CTCs could indeed prevent metastasis and significantly prolong the survival of tumor-bearing mice, highlighting the potential of CTC removal as an effective therapeutic strategy.

The most common and widely used technique for detecting and isolating CTCs involves immune-based methods. This approach relies on the use of antibodies to selectively bind to specific cell

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surface antigens that are unique to tumor cells, enabling their separation from normal blood cells. Since tumor cells express different surface markers compared to circulating blood cells, they can be efficiently isolated from whole blood. One such method uses a rotating disc filter system, which allows for the rapid isolation of CTCs from just 3 mL of blood in under one

minute. After isolation, immunostaining can be performed on the filter to count and identify the CTCs. These techniques provide valuable tools for both research and clinical applications, offering awareness into cancer metastasis and facilitating the development of novel therapies targeting CTCs.