Immunotherapy Research Applications: Circulating Tumor Cell Analysis

By 2040, the International Agency for Research on Cancer estimates that the global cancer burden will grow to more than 27.5 million new cancer cases and 16.3 million cancer deaths.[1] Fortunately, scientific tools for studying, detecting, monitoring, and treating cancer are also on the rise.

Immunotherapy 101

What Are Immunotherapies?

Immunotherapies harness the inherent ability of the human immune system to fight cancer from within. They can use multiple different strategies to help the immune system recognize cancer cells and prime it to launch effective attacks on tumors.

Types of Immunotherapy

Monoclonal Antibodies

Monoclonal antibodies (mAbs) can be designed to bind to specific proteins on cancer cells, labeling them as targets for the immune system's attack cells. Checkpoint inhibitors are a type of immunotherapy that are based on mAbs. Immune checkpoint inhibitors stop the immune system from turning off before cancer is completely eliminated.

Cytokines

Cytokines are naturally occurring proteins that activate the immune system. By artificially introducing higher cytokine levels, scientists can cause a patient's immune cells to attack cancer cells more aggressively.

Vaccines

Vaccines can be used to prime the immune system to attack cancer cells using the same principles used to fight infectious disease. Anti-cancer vaccines can involve introducing cancer cell proteins, genetic sequences, or other components that help immune cells recognize cancer.

CAR T-Cell Therapies

Chimeric antigen receptor (CAR) T cells are human immune cells that have been genetically engineered to express a protein that will bind to cancer cells, attacking them and activating other immune cells to do the same.

What Cancer Types Respond to Immunotherapy?

Immunotherapies have the potential to treat every type of cancer. The FDA has already approved immunotherapies for many major cancer types, including breast, lung, brain, kidney, and colorectal cancer, and many more are in development.

Circulating Tumor Cells

What Are Circulating Tumor Cells (CTCs)?

CTCs are cancer cells that slough off a primary tumor and make their way into the bloodstream and lymphatic systems. Once in circulation, CTCs may seed secondary tumors in other parts of the body. In contrast with a more invasive and localized solid biopsy from a primary tumor, liquid biopsy analysis of CTCs can noninvasively provide representative information about tumor heterogeneity and how cancer is developing.

CTCs are present in most types of cancer that metastasize. However, some cancer types show much higher CTC prevalence in the bloodstream than others (see right graph).

CTC prevalence in the bloodstream also correlates with cancer severity. As a tumor grows or shrinks, the number of CTCs in the bloodstream rises or falls proportionately.[3] As a result, CTCs can provide crucial information about each individual's cancer progression.

Total numbers of CTCs and CTECs identified for various disease types (adapted from Hu, B., et al., Front. Oncol. 02 March 2022, Vol. 12 | https://doi.org/10.3389/fonc.2022.821454) . Center black lines = medians; green, yellow box boundaries = Kruskal- Wallis H-test interquartile range; gray box boundaries = values within 1.5 interquartile ranges of the median

Applications of CTC Analysis in Immunotherapy Development and Cancer Research

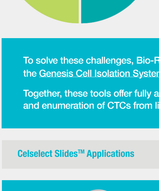
Prognosis

- CTC analysis can provide information that aids researchers in selecting candidates for clinical trials
- CTC enumeration can be used to create disease stratification thresholds
- Downstream genetic analysis of isolated CTCs can enable screening for biomarkers associated with anticipated treatment response

Monitoring

- Since CTC prevalence changes in accordance with tumor size, it can be used to monitor tumor response to treatments
- CTC enumeration in serial liquid biopsy samples can be used to monitor patients for relapse in long-term studies

Analyzing CTCs With Celselect Slides™



Although scientists have been isolating and studying CTCs for decades, legacy technologies present multiple challenges.

To solve these challenges, Bio-Rad scientists developed the Genesis Cell Isolation System with Celselect Slides™.

Together, these tools offer fully automated capture and enumeration of CTCs from liquid biopsy samples.

Celselect Slides™ Applications

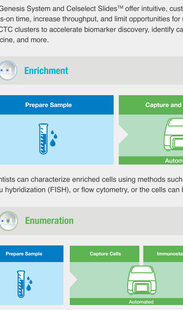
Enrichment

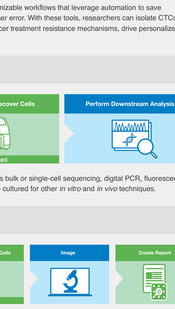
- Capture and retrieval of >80% of CTCs from liquid biopsies
- Removal of >99% of red and white blood cells
- High viability of retrieved cells

Enumeration

- On-slide immunostaining
- Imaging compatibility with automated microscopes
- CTC Analysis Software for result reporting

Because they originate from diverse tissues, different cancer types have different sizes of CTCs relative to healthy blood cells and are generally much larger. Celselect Slides™ are designed with 56,400 microchambers that trap CTCs while red and white blood cells are washed away. As demonstrated in the graph below, Celselect Slides™ pore size is optimized across multiple cancer type CTCs.

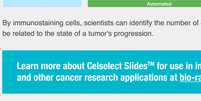




Celselect Slides™ Workflows

The Genesis System and Celselect Slides™ offer intuitive, customizable workflows that leverage automation to save hands-on time, increase throughput, and limit opportunities for user error. With these tools, researchers can isolate CTCs and CTC clusters to accelerate biomarker discovery, identify cancer treatment resistance mechanisms, drive personalized medicine, and more.

Enrichment



Scientists can characterize enriched cells using methods such as bulk or single-cell sequencing, digital PCR, fluorescent in situ hybridization (FISH), or flow cytometry, or the cells can be cultured for other *in vitro* and *in vivo* techniques.

Enumeration

By immunostaining cells, scientists can identify the number of cells with a given expression profile. The number of CTCs can be related to the state of a tumor's progression.

Learn more about Celselect Slides™ for use in immunotherapy development and other cancer research applications at bio-rad.com/celselect.

[1] https://www.cancer.org/research/cancer-facts-statistics/global.html

[2] https://www.clinicaltrials.gov

[3] Alix-Panabières C, Pantel K. Liquid Biopsy: From Discovery to Clinical Application. Cancer Discov. 2021 Apr;11(4):858-873. doi: 10.1158/2159-8290.CD-20-1311. PMID: 33811121.

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