

**ANTI-TUMOR IMMUNITY AND ONCOMARKERS:
A COMPREHENSIVE OVERVIEW**

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Annotation. *Cancer remains one of the leading causes of morbidity and mortality worldwide. Recent advances in immunology have led to a deeper understanding of the body's immune response to tumors, giving rise to the field of tumor immunology. Anti-tumor immunity refers to the immune system's ability to recognize and eliminate cancer cells. This article explores the mechanisms of anti-tumor immunity, the role of oncomarkers in cancer diagnosis and prognosis, and the potential for harnessing these responses in therapeutic strategies.*

Key words: *tumor immunology, the immune system, Innate Immunity, adaptive immunity, oncomarkers, diagnosis.*

Introduction. The immune system is a complex network of cells and molecules that work together to defend against pathogens, including viruses, bacteria, and malignant cells. This comprehensive overview highlights the intricate relationship between anti-tumor immunity and oncomarkers, drawing attention to the significance of continuing research and interdisciplinary collaboration to advance cancer therapies and improve patient outcomes.

It comprises two main branches:

- **Innate Immunity:** This is the body's first line of defense, providing immediate but non-specific responses to infections and abnormalities. Key components include natural killer (NK) cells, macrophages, and dendritic cells.
- **Adaptive Immunity:** This system provides a specific response to pathogens and involves two major types of lymphocytes: T cells and B cells. Adaptive immunity is characterized by memory, allowing for a stronger response upon re-exposure to the same antigen.

The Role of Immune Cells in Anti-Tumor Immunity

Several immune cells play vital roles in anti-tumor immunity:

- **Dendritic Cells (DCs):** Act as professional antigen-presenting cells, capturing, processing, and presenting tumor antigens to T cells, initiating an adaptive immune response.
- **T Cells:** Both CD4+ (helper T cells) and CD8+ (cytotoxic T cells) are crucial. CD8+ T cells can directly kill tumor cells, whereas CD4+ T cells provide help to other immune cells.

- **NK Cells:** These are part of the innate immune response and can recognize and destroy tumoral cells, especially those that have downregulated major histocompatibility complex (MHC) class I molecules.
- **Macrophages:** Tumor-associated macrophages (TAMs) can exhibit pro-tumor (M2) or anti-tumor (M1) polarization, influencing the tumor microenvironment.

Mechanisms of Anti-Tumor Immunity

The mechanisms of anti-tumor immunity include:

- **Recognition of Tumor Antigens:** Tumor cells often express unique proteins (tumor-specific antigens) and altered forms of normal proteins (tumor-associated antigens) that can be recognized by the immune system.
- **T Cell Activation and Proliferation:** Upon encountering tumor antigens presented by dendritic cells, T cells become activated, expand in number, and gain effector functions to kill tumor cells.
- **Cytokine Production:** Activated immune cells produce cytokines, which modulate the immune response and enhance the anti-tumor activity.
- **Immune Memory:** After the initial immune response, memory T cells can persist, providing a rapid response upon re-exposure to the same tumor antigens [1].

Immune Evasion by Tumors

Despite the body's anti-tumor immunity, cancer cells can develop mechanisms to evade immune detection and destruction:

- **Antigen Loss or Modification:** Tumors may lose expression of major antigens, making them less recognizable to the immune system.
- **Immunosuppressive Microenvironment:** Tumors can create microenvironments rich in immunosuppressive factors (e.g., transforming growth factor-beta [TGF- β], interleukin-10 [IL-10]) that inhibit immune responses.
- **Regulatory T Cells (Tregs):** These cells can inhibit the function of effector T cells, contributing to immune tolerance toward tumors.
- **Checkpoint Molecules:** Tumors may express or induce ligands that activate immune checkpoint pathways (e.g., PD-1/PD-L1, CTLA-4), which dampen T cell activity.

What are Oncomarkers?

Oncomarkers, or tumor markers, are substances that can be detected in blood, urine, or tissues and are associated with the presence of cancer. They are often proteins, but can also be nucleic acids or other molecules. Oncomarkers can originate from the tumor itself or be produced by the body in response to cancer.

Types of Oncomarkers

- **Tumor-Specific Antigens (TSAs):** Unique to cancer cells, these antigens arise from mutated proteins. An example is the mutant p53 antigen.

- **Tumor-Associated Antigens (TAAs):** These are normal proteins that are expressed at higher levels in cancer cells. For example, carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) are considered TAAs.
- **Circulating Tumor DNA (ctDNA):** Fragments of DNA shed from tumor cells into the bloodstream can be used for non-invasive cancer detection.

Clinical Applications of Oncomarkers

- **Diagnosis:** Elevated levels of certain oncomarkers in blood can indicate the presence of cancer. For instance, elevated prostate-specific antigen (PSA) levels can indicate prostate cancer.
- **Prognosis:** The presence and levels of oncomarkers can provide information about the aggressiveness of cancer and its likely course. For instance, high levels of HER2/neu are associated with poorer outcomes in breast cancer.
- **Monitoring Treatment Response:** Changes in oncomarker levels can indicate how well a cancer treatment is working. A decrease in tumor markers may suggest a positive response to therapy, whereas stable or rising levels may indicate treatment failure.
- **Recurrence Monitoring:** Regular measurement of oncomarkers can help detect cancer recurrence early, allowing for timely intervention.

Immuno-Oncology: Harnessing the Immune System

Immuno-oncology is an emerging field that focuses on manipulating the immune system to fight cancer. Understanding anti-tumor immunity and utilizing oncomarkers play critical roles in developing immunotherapies [2].

Immune Checkpoint Inhibitors

Immune checkpoint inhibitors (ICIs) are a class of drugs that block inhibitory pathways in T cells, enhancing anti-tumor immunity. Commonly used ICIs include:

- **Anti-PD-1/PD-L1 Therapies:** Pembrolizumab and nivolumab block PD-1, while atezolizumab and durvalumab block PD-L1, allowing T cells to recognize and attack tumor cells.
- **Anti-CTLA-4 Therapies:** Ipilimumab blocks CTLA-4, enhancing T cell activation and proliferation.

Personalized Cancer Vaccines

Cancer vaccines aim to stimulate an immune response against specific tumor antigens. The use of defined oncomarkers allows for personalized vaccine development, tailoring therapies to individual patients based on their tumor profile [3].

Adoptive Cell Therapy

Adoptive cell therapy involves the infusion of T cells that have been engineered to recognize tumor antigens. This approach can leverage oncomarkers to select the most effective T cells for infusion.

Combination Therapies

Combining different therapeutic approaches, such as ICIs with oncovaccines or chemotherapy, may provide synergistic effects in enhancing anti-tumor immunity and improving patient outcomes.

Advances in Biomarker Discovery

The exploration of novel oncomarkers is crucial for the development of precision medicine in oncology. Advanced technologies such as next-generation sequencing and proteomics are paving the way for identifying new tumor-related antigens and biomarkers [4].

Challenges in the Clinical Implementation of Oncomarkers

Despite their potential, several challenges hinder the widespread use of oncomarkers in clinical practice:

- **Standardization of Tests:** The lack of standardized methods for measuring oncomarkers can lead to variability in test results.
- **Sensitivity and Specificity:** Many oncomarkers lack sufficient sensitivity or specificity for reliable diagnosis, leading to false positives or negatives.
- **Integration into Clinical Practice:** Incorporating oncomarker testing into routine clinical practice requires interdisciplinary collaboration among oncologists, pathologists, and laboratory specialists.

The Role of Artificial Intelligence and Machine Learning

Artificial intelligence (AI) and machine learning technologies offer great potential in oncology for improving diagnostic accuracy, predicting treatment responses, and identifying novel biomarkers from large datasets. These technologies can significantly enhance how clinicians interpret oncomarker data in the context of broader patient profiles [6].

Ethical Considerations. The use of oncomarkers and immunotherapies raises ethical questions concerning data privacy, informed consent, and the equitable access of cancer treatments. Balancing innovation with ethical considerations is essential for the responsible advancement of cancer therapies [7,8].

Conclusion. Anti-tumor immunity represents a crucial aspect of cancer biology, with the potential for significant implications in therapeutic strategies. Oncomarkers provide valuable insights into cancer diagnosis, prognosis, and response to treatment. The combination of enhancing anti-tumor immunity through immunotherapies and utilizing oncomarkers for personalized cancer treatment forms the cornerstone of modern oncology. Continuous research and collaboration across disciplines are vital to overcome the challenges faced in the successful integration of these approaches into clinical practice, ultimately improving patient outcomes in the battle against cancer.

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