

Role of Immunotherapy in Molecular Pathology

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ABOVE THE STUDY

Immunotherapy has emerged as one of the most transformative advances in modern medicine, reshaping the landscape of disease treatment through its deep integration with molecular pathology. In my opinion, immunotherapy represents a paradigm shift from directly targeting diseased cells to modulating the body's own immune system, guided by molecular insights into disease mechanisms. This convergence of immunology and molecular pathology has enabled more precise, adaptive, and durable therapeutic strategies, particularly in oncology.

At its core, molecular pathology provides the framework for understanding the genetic, epigenetic, and proteomic alterations that define disease states. These molecular signatures are critical for identifying targets that can be recognized by the immune system. Immunotherapy leverages this information to enhance immune recognition and elimination of abnormal cells. For example, tumor cells often express neoantigens derived from genetic mutations, which can be identified through molecular profiling and targeted by immune-based therapies. In my view, this ability to connect molecular alterations with immune targeting is the foundation of precision immunotherapy.

One of the most successful applications of immunotherapy is the use of immune checkpoint inhibitors. Molecules such as PD-1, PD-L1, and CTLA-4 act as regulatory checkpoints that prevent excessive immune activation. However, many tumors exploit these pathways to evade immune surveillance. Checkpoint inhibitors block these inhibitory signals, effectively "releasing the brakes" on the immune system. Molecular pathology plays a crucial role in identifying patients who are most likely to benefit from these therapies, such as those with high PD-L1 expression or increased tumor mutational burden.

Another important advancement is Chimeric Antigen Receptor T-cell (CAR-T) therapy, which involves genetically engineering a patient's T cells to recognize specific tumor antigens. This approach exemplifies the integration of molecular diagnostics with therapeutic design. By identifying tumor-specific antigens through molecular analysis, clinicians can tailor CAR-T cells to

target individual cancers. In my opinion, this personalized approach represents one of the most promising directions in cancer therapy, although challenges such as toxicity and limited applicability to solid tumors remain.

Cancer vaccines and oncolytic viruses further illustrate the role of molecular pathology in immunotherapy. Cancer vaccines aim to stimulate immune responses against tumor-specific antigens, while oncolytic viruses selectively infect and destroy cancer cells while activating immune responses. Both approaches rely heavily on molecular characterization of tumors to identify appropriate targets and optimize therapeutic efficacy.

Beyond oncology, immunotherapy is increasingly being explored in autoimmune diseases, infectious diseases, and chronic inflammatory conditions. Molecular pathology helps identify dysregulated immune pathways and cytokine networks that can be modulated therapeutically. For example, biologic agents targeting specific cytokines such as TNF- α or IL-6 have been highly effective in treating autoimmune disorders. In my view, this highlights the broader applicability of immunotherapy beyond cancer, driven by molecular insights into immune dysregulation.

A key strength of immunotherapy is its potential for long-term efficacy. Unlike conventional therapies that act directly on diseased cells, immunotherapy can generate immunological memory, leading to sustained disease control. However, this benefit is not universal, and response rates vary significantly among patients. Molecular pathology is therefore essential for identifying predictive biomarkers that can guide patient selection and improve outcomes.

Despite its promise, immunotherapy also presents several challenges. One major issue is immune-related adverse events, which can occur when the immune system becomes overactivated and attacks normal tissues. These side effects can affect multiple organ systems and require careful management. In my opinion, understanding the molecular basis of these adverse events is critical for improving the safety profile of immunotherapeutic agents.

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Another challenge is resistance to immunotherapy. Tumors can develop mechanisms to evade immune detection, such as downregulating antigen presentation or altering the tumor microenvironment. Molecular analysis of resistant tumors can reveal these mechanisms and inform the development of combination therapies that overcome resistance.

The tumor microenvironment itself plays a crucial role in determining immunotherapy outcomes. Factors such as hypoxia, metabolic competition, and immune cell infiltration can influence therapeutic response. Molecular pathology provides tools to characterize these complex environments and identify strategies to enhance immune activity within tumors.

Looking forward, the integration of immunotherapy with multi-omics technologies and artificial intelligence is likely to further

refine treatment strategies. Comprehensive molecular profiling can identify novel targets and biomarkers, while computational models can predict patient responses and optimize therapy selection. In my view, this convergence of technologies will drive the next generation of precision immunotherapy.

In conclusion, immunotherapy represents a powerful and evolving approach in molecular pathology, offering new possibilities for treating complex diseases through immune modulation. In my opinion, its success depends on the continued integration of molecular insights with clinical innovation. While challenges such as variability in response, toxicity, and resistance remain, ongoing research is steadily advancing the field toward more effective and personalized therapeutic solutions.