



Editorial

# Advances, Limitations and Future Challenges in the Management of Immunotherapy for Hematological Diseases and Solid Tumors

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Our immune system is able to attack cancer cells by recognizing cellular mistakes and destroying them. To date, we still do not have sufficient knowledge on how well the immune system can fight degenerate cells that are developing. The idea of utilizing the patients' own immune system to fight tumors has led to the remarkable progress in the field of cancer therapy in the last decade [1]. However, errors during the cell division process and multiple genetic mutations promoting oncogeneses allow the damaged cells to escape the immune system, which usually patrols and eliminates such cellular mistakes before they become uncontrollable. This Special Issue reviews diverse immunotherapeutic strategies, approved treatments and possible methods to predict therapeutic response. The experts in the field do not only summarize the recent breakthroughs and successful evidence in many types of cancers, but also the failures and the unexpected limitations in clinical practice. The contents should help us better understand the mechanisms of different immunotherapies and intend to discuss the challenges and opportunities in improving current strategies.

Capietto and colleagues have focused on the mutated peptide ("neoantigens") induced by oncogenic events and presented on the histocompatibility complex (MHC) molecules to evoke potent anti-tumor immune responses [2]. The tumor-specific neoantigens can be generated from different sources: single-nucleotide variations or small insertions/deletion, gene fusions, alternative splicing variants and post-translational modifications. Since such cancer-specific neoantigens are known to induce potent immune response, numerous efforts to modulate the neoantigen expression, and different approaches to enhance the anti-tumor-specific T cell response are made [3,4]. Capietto and colleagues describe in their review the recent updates on the identification of neoantigens and prediction methods for therapeutic responses, as well as studies showing promising results for the DNA/RNA aberrations as novel sources of neoantigens [2]. One of the mentioned challenges was, for example, the identification and modulation of neoantigens arisen from non-coding DNA regions, e.g., long and short non-coding RNA transcripts (lncRNA) or pseudogenes. lncRNA influence the processes of regulation of transcription, splicing and translation, and pseudogenes can regain the lost protein-coding function in tumor cells. Moreover, the T-cell response varies with the type of neoantigens or targeting approaches, and may not be sufficient enough to fight the tumor cells effectively. The improvement of antigen quality and overcoming some manufacturing challenges requires more studies in this field.

From a therapeutic perspective, certain dysregulated kinase signaling cascades found in tumors, which could mediate different immune responses by targeting, are discussed by Kim and colleagues [5]. Among others, the Rho-kinase (ROCK) pathway is known to promote tumor cell progression, migration, metastasis, and extracellular matrix remodeling. ROCK is a serine/threonine kinase [6] and has two isoforms, ROCK1 and ROCK2, which are differentially expressed in specific tissues [7]. In tumors, an increasingly stronger expression of Rho-K with tumor progression has been observed [5]. There are already two



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## **Table of Contents Advances Computerinfo Sci 98**

1. Understanding the eBook Advances Computerinfo Sci 98
  - The Rise of Digital Reading Advances Computerinfo Sci 98
  - Advantages of eBooks Over Traditional Books
2. Identifying Advances Computerinfo Sci 98
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Advances Computerinfo Sci 98
  - User-Friendly Interface
4. Exploring eBook Recommendations from Advances Computerinfo Sci 98
  - Personalized Recommendations
  - Advances Computerinfo Sci 98 User Reviews and Ratings
  - Advances Computerinfo Sci 98 and Bestseller Lists
5. Accessing Advances Computerinfo Sci 98 Free and Paid eBooks
  - Advances Computerinfo Sci 98 Public Domain eBooks
  - Advances Computerinfo Sci 98 eBook Subscription Services
  - Advances Computerinfo Sci 98 Budget-Friendly Options
6. Navigating Advances Computerinfo Sci 98 eBook Formats

- ePub, PDF, MOBI, and More
  - Advances Computerinfo Sci 98 Compatibility with Devices
  - Advances Computerinfo Sci 98 Enhanced eBook Features
7. Enhancing Your Reading Experience
    - Adjustable Fonts and Text Sizes of Advances Computerinfo Sci 98
    - Highlighting and Note-Taking Advances Computerinfo Sci 98
    - Interactive Elements Advances Computerinfo Sci 98
  8. Staying Engaged with Advances Computerinfo Sci 98
    - Joining Online Reading Communities
    - Participating in Virtual Book Clubs
    - Following Authors and Publishers Advances Computerinfo Sci 98
  9. Balancing eBooks and Physical Books Advances Computerinfo Sci 98
    - Benefits of a Digital Library
    - Creating a Diverse Reading Collection Advances Computerinfo Sci 98
  10. Overcoming Reading Challenges
    - Dealing with Digital Eye Strain
    - Minimizing Distractions
    - Managing Screen Time
  11. Cultivating a Reading Routine Advances Computerinfo Sci 98
    - Setting Reading Goals Advances Computerinfo Sci 98
    - Carving Out Dedicated Reading Time
  12. Sourcing Reliable Information of Advances Computerinfo Sci 98
    - Fact-Checking eBook Content of Advances Computerinfo Sci 98
    - Distinguishing Credible Sources
  13. Promoting Lifelong Learning
    - Utilizing eBooks for Skill Development
    - Exploring Educational eBooks
  14. Embracing eBook Trends
    - Integration of Multimedia Elements
    - Interactive and Gamified eBooks

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