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Editorial: Beyond PD-1: novel checkpoint receptors and ligands as targets for immunotherapy

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Editorial on the Research Topic

Beyond PD-1: novel checkpoint receptors and ligands as targets for immunotherapy

In recent years immunotherapy has become one of the most promising technologies to treat advanced tumors. The idea of modulating the immune system has improved the treatment of cancer patients. While great success has been seen with inhibitors of PD-1, the potential for targeting other cells and ligands in the tumor microenvironment remains vast. This Research Topic emphasizes the potential of targeting both inhibitory and co-stimulatory receptors to reinvigorate anti-tumor immune responses, mainly focusing on receptors other than PD-1.

Some of the most promising research concerns the potential of targeting VISTA, an inhibitory B7 family molecule that can be expressed on tumor cells and myeloid cells in the tumor microenvironment, particularly in immunologically cold tumors. Duan *et al.* explored the role of VISTA in acute myeloid leukemia and multiple myeloma. VISTA co-expresses with other checkpoint receptors (e.g. PD-1, TIM-3) and may influence prognosis, being associated with poor overall survival in pancreatic or prostate cancers, making it a potential target for immunotherapy. *Iadonato et al.* report on the creation of a humanized anti VISTA antibody that was tested in colon cancer and melanoma models, followed by promising toxicology and pharmacokinetics studies in monkeys.

TIM-3 and LAG-3 are inhibitory immune checkpoints implicated in immune modulation that have received growing interest in recent years. In ovarian cancer, TIM-3 affects the immune microenvironment and T-cell function. *Chang et al.* assessed its potential as a therapeutic target, discussing both the regulatory role of TIM-3 and the challenges in developing effective TIM-3-based therapies. *Luo et al.* explored LAG-3 and the promising status of several inhibitors under development, while *Amrane et al.* investigated the potential for HLA-DR, the ligand for LAG-3. While its role in hot tumors may be important, HLA-DR's potential for direct clinical targeting is limited by

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Table of Contents Checkpoint A Novel

1. Understanding the eBook Checkpoint A Novel
 - The Rise of Digital Reading Checkpoint A Novel
 - Advantages of eBooks Over Traditional Books
2. Identifying Checkpoint A Novel
 - 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 Checkpoint A Novel
 - User-Friendly Interface
4. Exploring eBook Recommendations from Checkpoint A Novel
 - Personalized Recommendations
 - Checkpoint A Novel User Reviews and Ratings
 - Checkpoint A Novel and Bestseller Lists
5. Accessing Checkpoint A Novel Free and Paid eBooks
 - Checkpoint A Novel Public Domain eBooks
 - Checkpoint A Novel eBook Subscription Services

- Checkpoint A Novel Budget-Friendly Options
- 6. Navigating Checkpoint A Novel eBook Formats
 - ePub, PDF, MOBI, and More
 - Checkpoint A Novel Compatibility with Devices
 - Checkpoint A Novel Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Checkpoint A Novel
 - Highlighting and Note-Taking Checkpoint A Novel
 - Interactive Elements Checkpoint A Novel
- 8. Staying Engaged with Checkpoint A Novel
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Checkpoint A Novel
- 9. Balancing eBooks and Physical Books Checkpoint A Novel
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Checkpoint A Novel
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Checkpoint A Novel
 - Setting Reading Goals Checkpoint A Novel
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Checkpoint A Novel
 - Fact-Checking eBook Content of Checkpoint A Novel
 - 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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