Studies review relationship between immune system and cancer

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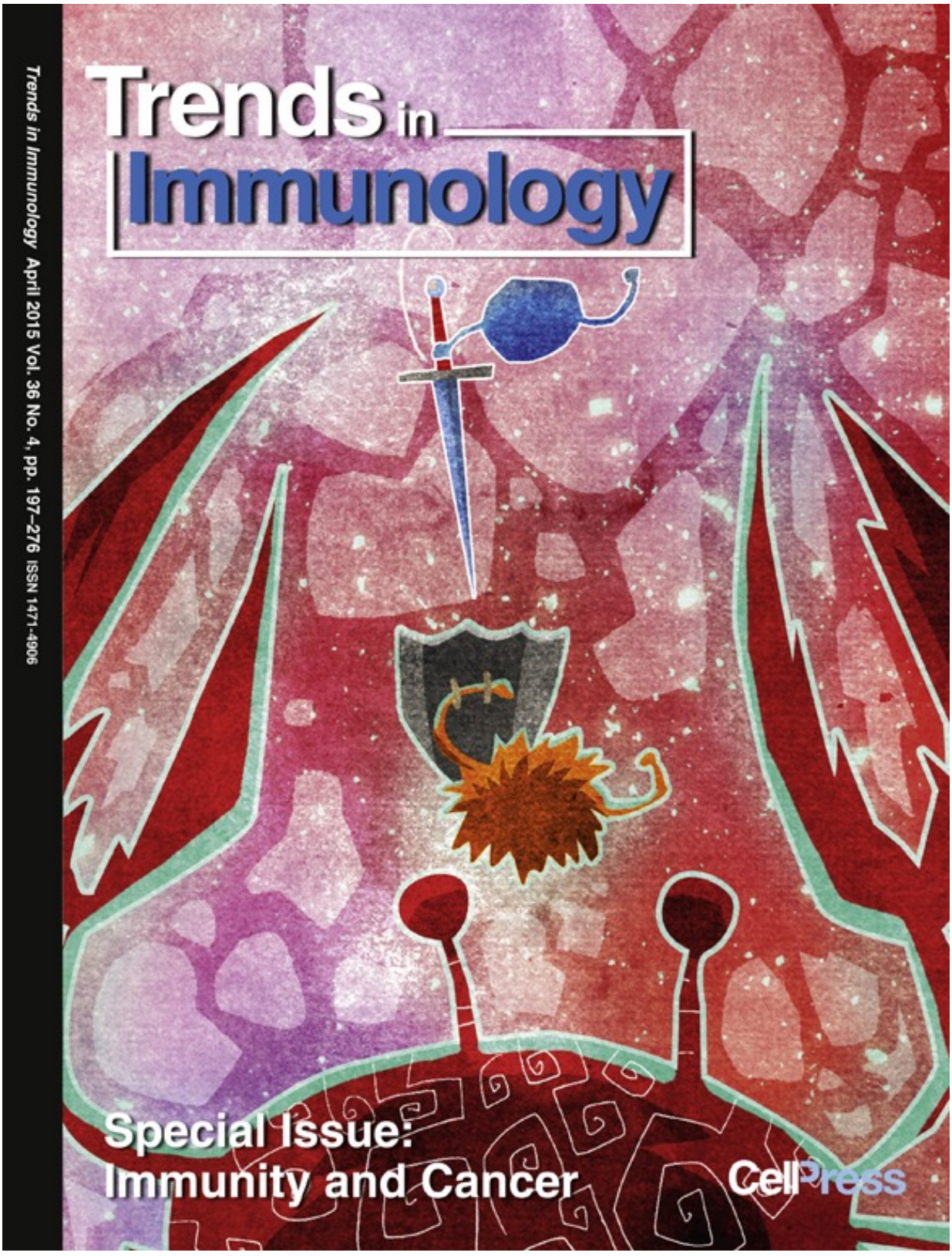
Trends in Immunology
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Cover for *Trends in Immunology*'s joint special issue on immunity and cancer with *Cancer Cell*. Credit: *Trends in Immunology* 2015

The last ten years have seen a renewed interest in how cancer evades the immune system and how white blood cells can be used therapeutically to help patients, even with late-stage diagnoses. In an April 13 joint special issue on cancer, immunity, and immunotherapy, *Cancer Cell* and *Trends in Immunology* explore the history of this work and review how immunology and cancer research currently intersect. Articles explore drugs that eliminate cancer's hold on the immune system, as well as the ways the immune response is affected by anti-cancer therapies and vice versa.

"In these coordinated special issues, we explore the complex relationship between the immune system and cancer and the potential of harnessing anti-tumor immunity for the treatment of disease," write *Trends in Immunology* Editor Fabiola Rivas and *Cancer Cell* Editor Li-Kuo Su. "We approach these topics from different perspectives and expertise, but with the joint aim of providing a meeting ground for discussion and exchange between the cancer biology and immunology communities."

A History of Immunotherapy

"Research, not specifically designed to bring relief or cure to any particular disease, can, when creatively exploited, lead to spectacular results in the management of cancer," write Jacques Miller and Michel Sadelain in a comprehensive review of the work that led to immunotherapy—a treatment strategy that primes a patient's immune system to kill tumors. The authors trace the incremental discoveries, such as a 1963 study that found that mice with their thymus surgically removed were more susceptible to cancer, the cancer vaccine efforts of

the 1990s, and eventually the immunotherapy drugs that earned "breakthrough" status in the 2010s.

"While some key molecular pathways and cellular interactions have been decoded, much more is yet to be discovered," conclude Miller, of Australia's Walter and Eliza Hall Institute of Medical Research, and Sadelain, of New York's Memorial Sloan Kettering Cancer Center. "In the meantime, immunology has spawned immunotherapy, which is about to claim a seat in the therapeutic pantheon of oncology, next to surgery, radiation therapy, and chemotherapy."

Cancer Cell, Miller, J., and Sadelain, M.: "The Journey from Discoveries in Fundamental Immunology to Cancer Immunotherapy" http://dx.doi.org/10.1016/j.ccell.2015.03.007

How Immunotherapy Drugs Work

Cancer drugs that target the unique mutations that cause a normal skin cell to start dividing uncontrollable have found success in the clinic, but only a limited range of patients qualify for any given treatment. Immunotherapy drugs, which target cells in the immune system—essentially by shutting down the signals that tell a white blood cell that a tumor is friendly—can be a "common denominator," holding promise for the treatment of many different cancers. In a review of recent studies of these drugs, Suzanne Topalian, Director of the Melanoma Program at Johns Hopkins University School of Medicine's Sidney Kimmel Comprehensive Cancer Center, and colleagues discuss the similarities and differences between immunotherapy drugs and what treatments are on the horizon.

"The successful application of the immune checkpoint blockers anti-CTLA-4 in melanoma and anti-PD-1/PD-L1 in multiple cancer types has established immunotherapy as a viable treatment option for patients with

advanced cancers and has opened the doors to developing a new generation of immune modulators that may be most effective when employed in treatment combinations," the authors write. "Armed with a new understanding and unprecedented opportunities, the field of immunotherapy is now standing on the threshold of great advances in the war against cancer."

Cancer Cell, Topalian et al.: "Immune Checkpoint Blockade: A Common Denominator Approach to Cancer Therapy"
http://dx.doi.org/10.1016/j.ccell.2015.03.001

How Anti-cancer Therapies Affect the Immune System

The idea for chemotherapy can be traced back to the trenches of World War I, when it was noticed that soldiers exposed to mustard gas experienced a severe loss of bone marrow and white blood cells. The observation led to experiments in mice using mustard gas to slow the growth of lymphatic cancer. Eventually, the procedure was tested in humans, and the use of agents to therapeutic stop cancer cell division took off.

Today, it is clear that anti-cancer therapies and patient immune systems are able to influence each other. White blood cell count can even be used to predict how well someone will respond to a particular cancer treatment. But according to a review by Karin de Visser and Seth Brandon Coffelt of The Netherlands Cancer Institute, there is still a lot more to know about how this relationship is affected by treatment timing and resistance, as well as the role that metastasis plays.

"It is difficult to deduce one over-arching conclusion from these studies, because of the overwhelming complexity and the diversity of immune

cell responses to specific anti-cancer therapies," de Visser and Coffelt write. "What we can say for sure is that the involvement of immune cells is largely dictated by tumor type, mutational signature, tumor model and tumor location, and generalizing immune cell response to a particular anticancer therapy across multiple tumor types or locations should be avoided."

Trends in Immunology, de Visser, K., and Coffelt, S.: "Immune-mediated mechanisms influencing the efficacy of anticancer therapies" http://dx.doi.org/10.1016/j.it.2015.02.006

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