nature immunology

Looking forward

***Nature Immunology* turns 10 years old in July. What new immunologic insights will the next decade bring?**

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In this 10th anniversary issue, we commemorate the launch of *Nature Immunology* in 2000. This new journal represented a commitment by Nature Publishing Group to provide the immunology community with a journal dedicated to publishing the best immunology research. Ten years later, the aim remains the same: to publish fundamental new insights in all areas of immunology that lead the field significantly forward.

How protective immune responses are elicited and how pathologic processes arise because of tolerance breakdown remain core questions in immunology. Answers to these questions will aid in understanding allergies and autoimmunity, inherited defects and environmental triggers that lead to immunodeficiency or cancer. *Nature Immunology* remains interested in studies that examine these basic concepts. Cellular communication has a key role in orchestrating immune responses. Understanding how communication occurs between innate or parenchymal cells and adaptive immune cells in nonlymphoid tissues and between antigen-presenting cells and lymphocytes to prime antigen-specific responses and engender immunological memory or tolerance is of prime importance. Addressing such questions requires identification of the cell types involved and their location and lineage development, as well as knowledge of the receptors, ligands and signaling pathways that convey information from one cell to another.

Looking back, we see that tremendous strides have been made in the past decade. It will come as no surprise that among the top-cited papers published in *Nature Immunology* are those that describe the activation and signaling pathways of Toll-like receptors, the identification of the factors necessary for regulatory T cell generation and function, and the great diversity of helper T cell subsets associated with distinct effector function. More recently, the identification of sensors that detect intracellular pathogens or damage to promote inflammatory responses have sparked interest. Pathogenesis studies have mirrored this trend by identifying the triggers or evasion strategies used by microbes to subvert host immunity. Similarly, the discovery of microRNAs and their role in the post-transcriptional regulation of gene expression has opened new avenues of exploration of their role in regulating immune cell function. Our journal has also placed an emphasis on publishing robust human immunology papers.

Like other scientific disciplines, immunology has emerged from an age of identifying and characterizing individual molecules and cell types to one of understanding the roles of each under contextual situations and the regulatory networks that govern interactions of immune cells. *Nature Immunology* emphasizes the need to demonstrate physiological relevance. Advances in the use of multicolor flow cytometry and the generation of highly specific fluorescent molecular probes have allowed the prospective isolation and analysis of primary cells. Advances in vector-mediated delivery of target genes or short hairpin RNAs to interfere with gene expression have made it feasible, in many cases, to undertake rigorous studies of primary human cells. In animal models, advances in imaging technologies, such as intravital microscopy, have paved the way to allow real-time visualization of immune-cell interactions in living tissues. Advances in automated DNA-sequencing capacities now allow genome-wide analysis of chromatin modifications and transcription factor binding by 'ChIP-Seq' approaches. Thus, tools are now in place and continue to be developed that will allow the investigation and manipulation of real immune cells with far greater resolution than was possible even a decade ago.

To help celebrate this 10th anniversary issue, we asked several prominent scientists to imagine what the next decade of immunology research might bring. Medzhitov discusses innate immune–recognition pathways. He predicts that as with pathogenic species, the recognition of commensal microorganisms is probably an active process that triggers immunological tolerance rather than immunity. Finlay and colleagues discuss the mucosa as an integrated organ system that is immunologically unique because of its function as a physical barrier. Because many pathogens enter their hosts at mucosal sites, there is great interest in how to elicit protective mucosal antigen-specific immunity. Both Medzhitov and Finlay emphasize that much remains to be learned about the complexity of symbiotic microbial communities and how their interactions with the host organism shape immune responsiveness.

Such a systems approach to immunology is also emphasized by Krummel, as autoimmunity or tolerance does not arise from cells acting alone. Instead, immune responses form through the integration of multiple simultaneous and often transient inputs from a suite of participants, including the tissues themselves. As discussed by Krummel, visualization of immune cells in their environment is needed to explore how specific immune responses occur in real time. Tracey analyzes the largely unexplored interactions between cells of the immune and neural systems. These interactions represent a more ancient form of chemical communication that contributes to the regulation of innate immune responses and inflammation. He suggests by studying neural reactions during immune responses, it may be possible one day to therapeutically modulate immunity by targeting neural cells.

Finally, Tarakhovsky focuses on how cells epigenetically 'remember things past'. Epigenetic chromatin modification regulates the specification of cellular identity and function. He argues that intracellular pathogens can target the 'readers' of epigenetic information to subvert immune responses.

This collection represents but the tip of the iceberg and is not meant to delimit the interests of *Nature Immunology*, as many other exciting areas remain to be explored. Our motto remains "Immunology. All of it." We are pleased that the immunology community has embraced *Nature Immunology* and made it a success. We hope you share our enthusiasm and will continue to support the journal during the next 10 years and beyond.