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Special Issue: Molecular Mechanisms of Immunity

Editorial

Moving Pieces in Molecular Immunology

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During the publication of this issue, we have witnessed the full-blown effects of the global severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) 2020 pandemic. Such an event presses us to quickly and robustly attempt to find scientific connections and mechanistic insights that can lead to us to better grasp the human host's immune response to this virus, how to fight disease and defeat this pathogen, and to define the best avenues for designing efficient vaccines against it. At the same time, scientific research in other areas of molecular immunology are thriving and, in turn, can offer us a respite from the current turmoil of virology overload.

Seminal discoveries in molecular immunology have been achieved in recent years; by drawing inspiration from the 2019 Federation of American Societies for Experimental Biology (FASEB) summer research conference, we present a themed special issue on 'Molecular Mechanisms of Immunity'. The reviews and opinions in it provide pointed examples of the state of current research in different subfields: evolution, epigenetics, gene expression and signaling, lymphocyte differentiation and function, as well as disease. Describing novel findings and molecular details, this timely issue gathers discussions that unveil key research avenues. We have aimed to highlight new technologies and hypotheses in the field and have explored experimental approaches geared towards gaining genomic, mechanistic, and therapeutic insights to improve our understanding of the immune response during homeostasis and disease.

We begin our special issue with a TrendsTalk interview; in it, six experts in molecular immunology – also members of our advisory board – provide us with a fresh and exciting overview of salient questions in their subfields.

Two spotlight articles showcase exciting new research: Kris Hogquist and Maude Ashby comment on the importance of transcription factor Eomes in CD8⁺ memory phenotype T cell precursors during murine thymic development and antitumor immunity. Peggy Goodell and colleagues examine new data on chronic inflammation and the competitive clonal dominance of myelodysplastic syndrome hematopoietic stem progenitor cells, which contribute to malignancy progression stemming from changes in the NF- κ B/TLR-TRAF6/A20 pathway.

Pierre Pontarotti, Jim Kaufman, and coworkers present a compelling opinion piece on the hypothetical evolutionary origins of vertebrate adaptive immunity and its derivation from innate immunity, focusing on the emergence of the recombination-activation gene (RAG) system, and the rise of MHC polymorphisms.

From another angle, Kate Jeffrey and Isabella Fraschilla examine the function of a certain class of chromatin 'readers'; based on the role of various Speckled Protein (SP) family members in human immunological diseases, the authors provide an informative review of these factors along with future SP targeting approaches that may be relevant to treating certain pathologies and/or immunodeficiencies due to dysfunctional SP proteins. The authors also suggest that these proteins can act as key regulators of gene silencing, helping to establish immune cell identity and function.

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Intrinsic to our knowledge of B cell biology and humoral immunity is an interrogation of diverse transcriptional changes accompanying B cell differentiation. In a review article, Silvia Bolland and colleagues lead us down the path of B cell development, specifically focusing on the transitional and mature stages of this process. In their overview, they highlight previously unrecognized pathways of cell fate decisions as well as new advances in the field.

Continuing with our understanding of humoral immunity, an essential component to the generation of antibody diversity is the enzymatic action of activation-induced cytidine deaminase (AID), which leads to affinity maturation, somatic hypermutation, and class switch recombination. To commemorate the twentieth anniversary since the discovery of AID, Alberto Martin, Javier Di Noia, and coworkers review the most up-to-date information regarding AID biochemistry and function, highlighting the nuances of mutagenesis during DNA repair as well as how chromatin landscapes modulate AID-mediated genomic targeting.

A key component of adaptive immunity is the cooperation between B and T cells to control the quantity and quality of antibodies during an immune response. In a review bearing a related theme, Roger Sciammas, Sarah Cook, and coauthors tease out the transcriptional processes that govern B and helper CD4⁺ T cell fates, narrowing on the description of a conserved, synchronous, and perhaps ancient IRF4 transcription factor-dependent gene regulatory network. This network depends on transcription factor graded expression and antigen receptor signaling strength, ultimately coordinating cell fate dynamics and leading to an optimal antibody response.

A prevalent conceptual theme in this issue is that of B lymphocyte differentiation and function. Thus, the issue ends with a review article that revises the paradigm of B cell development at the pre-B cell checkpoint, updating the model to include the coordinated action of not two, but three receptors (IL-7R, pre-BCR, and CXCR4) that properly incite B cell progenitors to respond to cell-intrinsic and -extrinsic cues, progressing through the pre-BCR checkpoint towards their development in the murine bone marrow.

Our special issue has assembled some of today's trends and offers updated information on emerging technologies, approaches, and paradigms to inform on different facets of immunity at a mechanistic level. We have also left you with provocative ideas to ponder. Due to space limitations, other key topics and subfields of molecular immunology were not discussed but are by no means less important. We are excited to highlight many outstanding questions that have emerged from previous laid-out queries, and we acknowledge the present and future strong research efforts from our scientific community. We hope you enjoy and feel refreshed by the many moving pieces of molecular immunity in this special issue. Many thanks to all readers for their interest and support, and to all authors, reviewers, and advisory board members for their continued contribution and insight. Please send me your comments at immunology@cell.com or @TrendsImmuno. In the meantime, keep on reading and stay safe!