

## The Molecular Basis for Immunology Meets the Electronic Basis for Scientific Discovery

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### Editorial

As an immunology instructor, I and my colleagues that teach our undergraduate immunology course recommend and often use Janeway's Immunology as a guide and reference textbook for the class. We refer to it as the "encyclopedia of immunology", and it certainly is the most comprehensive and widely used textbook in undergraduate immunology courses nationwide. It provides a great overview of the human immune system, and is a great reference tool for a basic understanding of human immunology on a whole organismal and system level. It even offers some pretty comprehensive details on cellular immunity. However, for more detailed, integrated information on cellular and molecular immunology, I prefer Abbas, Lichtman and Pober's Cellular and Molecular Immunology. It focuses primarily on the cellular, and especially the molecular, mechanisms of immunity. I use this textbook, in conjunction with primary literature, to teach graduate level immunology courses. Both Janeway's Immunology and Abbas et al., Cellular and Molecular Immunology are excellent resources, but have distinct focus areas. I draw the same analogy between the Journal of Immunology and this new Omics journal, Journal of Molecular Immunology. JMI is the mothership for research immunologists. It is arguably the most impactful journal in the field of Immunology. It publishes reports on every aspect of Immunology, from basic research into immune response to pathogens, to comparative evolutionary immunology, to yes cellular and molecular mechanisms of immunity. The Journal of Molecular Immunology focuses on molecules of the immune system, and their function, importance and interplay among other immune molecules. JMI will most certainly have a deeper, more comprehensive focus on molecular mechanisms underpinning the host immune response to pathogens than JI. I envision JMI to be the preeminent journal for publishing impactful research into the molecules of the immune system and their interplay with each other, as well as other molecules of various other organ systems, including the gastrointestinal, reproductive, endocrine and nervous systems, to name a few. JMI will rapidly expand into the molecular immunology field by disseminating reports using the open access model, the data-sharing concept revolutionizing scientific communication worldwide. Immunology sits at the crossroads of several important molecular biological processes, including signal transduction, transcription, translation, genome editing, protein modification and cell activation. The early innate immune response relies heavily on defensins, complement, toll and rig-I-like receptors (TLRs and RLRs) and cytokines. These molecules represent the oldest elements of the human immune system. Many of them link innate and adaptive immune responses. TLR ligands can act as potent second signals for T cell-independent B cell activation. Complement receptors CD21/35 lower the B cell activation threshold 10,000-fold. Complement activation also produces anaphylotoxins C3a, C4a and C5a that can stimulate mast cells and, like chemokines, set up

biomolecular gradients to promote inflammation. Adaptive immune responses rely on MHC-TCR, and CD28-CD80 interactions for optimal T cell activation. B cells receive activation signals via MHC-TCR and CD40-CD40 ligand interactions with T helper cells. B cells expand rapidly into effector and memory cells as a result of these molecular cues, and undergo profound changes in their genetic loci encoding immunoglobulins. A diversity of cytokines help activate, control or suppress both innate and adaptive immune responses. These and other immune responses characterize the immune system as one of the most intricate, dynamic and important organ systems in animals. Understanding these immune responses means understanding the molecular bases for them. Application of the latest cutting-edge technologies accelerates discovery and understanding of the complexities of the underlying molecular mechanisms of immune responses. New disciplines like transcriptomics, proteomics, glycomics, lipidomics and metabolomics complement genomics (the omics granddaddy!) to drive this accelerated discovery. Even genomics research continues to accelerate with the advent of lightning-fast next-generation sequencing, incredibly sensitive deep sequencing and high-throughput digital droplet PCR. These powerful tools enhance classic vaccine development and drug discovery by propelling immunology into new frontiers of research and therapeutics. Researchers use these new omics strategies to obtain vast amounts of data that will reveal new developmental, metabolic and signaling pathways as potential therapeutic targets. Combinatorial medicinal chemistry and detailed pharmacological studies accelerate new drug discovery and testing. Induced pluripotent stem cells (IPSCs) promise to revolutionize experimental model construction and offer host-specific designer therapies for everything from autoimmunity and immunodeficiency to infectious disease and cancer. Generating antigen-specific dendritic and T cells from a patient's own IPSCs requires detailed and precise understanding of the molecular mechanisms that drive pluripotency and differentiation. These immune cells can then be engineered to express the appropriate molecular profile to effectively stimulate both cellular and humoral immune responses via antigen presentation and processing and T helper cell activation. T regulatory (Treg) cells can be engineered to resolve these immune responses, as well as inappropriate ones that cause autoimmune, allergic or other hypersensitivity reactions. But accomplishing this requires discovering and manipulating the molecules responsible for Treg development, or the regulatory cytokines like IL-10 and TGF- $\beta$  that they express. These examples of generating host-specific immunotherapies using IPSCs reinforce the importance of molecular immunology in this process. Understanding the extremely complicated mammalian immune system can be a daunting, sometimes overwhelming task. Taking a big picture view helps to give perspective and allows observation and identification of key components and general themes: Defensins, Complement, TLRs and RLRs in the innate immune system; and MHC, antibody, TCR and accessory signaling molecules in the

adaptive immune system; and a network of cytokines orchestrating the entire process from activation to resolution. But to truly understand the complex interplay of all of these different aspects of immune responses, one must dig deep to the fundamental molecular bases of these responses. JMI facilitates this understanding by focusing

specifically on the molecular basis of immunology and using the Open Access model to expedite dissemination and discussion of important new discoveries in molecular immunology. We look forward to the journey.