

# Preface

The immune responses that can limit or prevent disease induction by viruses are historically divided into innate and adaptive immune responses. Adaptive immunity refers to the selection and rapid expansion of T cell and B cell clones that have rearranged their T cell receptor and antibody genes, respectively, in ways that allow them to effectively recognize and neutralize most viruses or virus-infected cells. In contrast, innate immunity refers to cellular receptors that recognize Pathogen-Associated Molecular Patterns (PAMPs) and then activate signaling pathways leading to the production of interferons. This in turn induces the expression of a large number of Interferon-Stimulated Genes (ISGs), in both the infected cell and adjacent, as yet uninfected cells, many of which are able to alter the cellular environment in ways that inhibit viral replication. Cellular factors involved in PAMP recognition, so-called Pattern Recognition Receptors (PRRs) include the Toll-Like Receptors (TLRs) as well as cytoplasmic PRRs such as the Retinoic acid Inducible Gene-I (RIG-I) protein family, as well as the NOD-like receptors.

In addition to innate and adaptive immune responses, both of which are only activated after pathogen infection, many cells also constitutively express antiviral factors that can act as potent inhibitors of viral replication. These factors are now generally grouped together as mediators of intrinsic antiviral immunity. While several intrinsic immune factors, including APOBEC3G, TRIM5 $\alpha$ , Tetherin, and SAMHD1, were initially discovered by researchers studying the replication of retroviruses, particularly HIV-1, it is now clear that some of these proteins, especially APOBEC3G and Tetherin, are in fact capable of inhibiting a wide range of viral species. In addition, it is becoming increasingly apparent that cells also express intrinsic factors that can limit the replication of other, non-retroviral species, including for example the inhibition of large DNA viruses by DNA damage response proteins. Finally, especially in invertebrate animals and plants, RNA-mediated intrinsic immunity can also play a key role in limiting viral replication and pathogenesis and even in vertebrates, microRNAs can play a major role in either restricting or, in some cases, facilitating viral replication. Because intrinsic immunity is, at least over short time periods, a set of fixed host antiviral mechanisms, it is not surprising that viruses have evolved numerous mechanisms to overcome both protein and RNA-mediated intrinsic immunity in their normal host

species. However, as discussed in the chapter by W. E. Johnson, cellular intrinsic immune factors are also capable of evolution in ways that can circumvent viral countermeasures and this “rapid adversarial co-evolution” is clearly important in defining the host range of viruses.

This volume brings together nine papers reviewing different aspects of antiviral intrinsic immunity from scientists who have made major contributions to this area of research. I believe this field is an important one from several perspectives, including not only the potential design of antiviral drugs but also achieving a better understanding of the coevolution of viral pathogens and their hosts. I hope the reader will find these contributions as interesting as I did.

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