

Preface

Besides being important pathogens of humans and animals, viruses are obligate intracellular parasites that require host functions to replicate and propagate. This intimate dependence, and the millions of years of co-evolution of viruses and their hosts, are responsible for elaborate attack, defense and counter-attack strategies. The small size of a virus necessitates a small genome. Conservation of sequence space demands a lean (and often mean) viral proteome in which every protein is essential. Some of these proteins often perform more than one function during the viral life cycle, features that make viruses ideal models for more complex living systems (e.g. vertebrates).

Many viruses are associated with one or the other disease. Following an acute infection, the clearance or persistence of viral infection will depend upon how successfully the virus is able to regulate the immune response and cell death (apoptosis) pathway of the host. We now understand that both of these pathways depend critically upon signal transduction. The study of host-virus interactions has yielded rich dividends in terms of basic biological information and intervention strategies. This Special Issue of the *Journal of Biosciences* presents a collection of reviews by prominent workers in this area of research.

The immune response to viral infection consists of innate (nonspecific) and adaptive (specific) defenses. The innate response, which is the first line of immune defense, is composed of natural killer cells, interferons and a complex set of serum proteins termed complement, which when activated destroy virus-infected cells and many virus particles. The first two articles deal with this important pathway. Bernet *et al* review viral mimicry of the complement pathway and discuss strategies used by viruses to neutralize this important innate defense. Jha and Kotwal focus on the vaccinia virus complement control protein and present structure-function data to show how this viral protein can be put to use as an anti-inflammatory drug. Interferons and pro-inflammatory cytokines such as tumour necrosis factor α (TNF α) also regulate the innate response. Zúñiga uses the myxomavirus (a poxvirus) to illustrate how viral immunomodulatory proteins that mimic soluble cytokine receptors control the interferon and TNF α pathways, besides regulating the MHC I and MHC II pathways important in the adaptive immune response.

The adaptive immune response includes antibodies that neutralize extracellular virus particles, cytotoxic T cells that eliminate virus-infected cells, and helper T cells that aid these responses through secretion of appropriate cytokines. Three articles dealing with hepatitis viruses C and B (HCV, HBV) explore viral regulation of the humoral and cellular responses. Pavio and Lai review the role of HCV-encoded proteins in modulating host immunity and the importance of cell signalling in this regulation. The hypervariable region 1 (HVR1) within the envelope glycoprotein 2 of HCV is responsible for immune escape and persistent infection; Mondelli *et al* review new findings to suggest the possibility of inducing a broadly reactive protective immune response to multiple HCV variants. Waris and Siddiqui show how two biologically diverse viruses, HBV and HCV, use common pathways to induce oxidative stress and key transcription factors involved in inflammatory processes.

The human immunodeficiency virus (HIV) is highly adept at evading host immunity and encodes multiple proteins for the purpose. The Nef protein provides an excellent example of one viral protein performing multiple functions. This is the subject of a review by Greenway *et al*. It emphasizes yet again the central role played by signal transduction in host cells and how viruses must interfere with cell signalling to gain an upper hand. Chakrabarti and Krishna carry this theme forward while reviewing molecular interactions of the human papillomavirus E6 and E7 oncoproteins, and show how these can control cell survival, proliferation, differentiation and apoptosis for promoting cellular transformation and tumour formation.

An innate response of the host cell to viral infection is to commit suicide through programmed cell death or apoptosis. This would severely restrict viral infection, and as expected, viruses employ multiple strategies to regulate apoptosis. Hasnain *et al* discuss these strategies and mechanisms in the final article.

It is hoped that this special issue will provide a glimpse into the fascinating world of viruses and their regulatory mechanisms in the quest for survival, replication and propagation.

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