PREFACE

Baculoviruses are perhaps unique among viruses in the breadth of their biotechnological applications. These insect-specific viruses are used not only for insect pest management purposes but also as laboratory research tools for production of recombinant proteins and for protein display and as potential vectors for human gene therapy. Although the biotechnological use of insect viruses has historically been dominated by the baculoviruses, the development of technologies from other insect virus families, such as the *Polydnaviridae* and *Tetraviridae*, is gaining momentum. In addition to highlighting recent advances, this volume provides a comprehensive review of the biotechnological applications of these and other insect viruses.

Although there is some overlap, the chapters in this volume are divided into the following sections: (1) Insect Viruses as Laboratory Research Tools, (2) Applications to Human and Animal Health, and (3) Insect Pest Management. While chapters on stably transformed insect cell lines (Douris *et al.*, pp. 113–156) and mammalian glycosylation in insect cells (Harrison and Jarvis, pp. 159–191) describe "spin-off" technologies from baculovirus research, all other chapters deal with application of the insect virus itself or virus-derived genes for technological purposes.

Given that baculoviruses comprise the most widely used of the insect viruses within the biotechnological arena, it is appropriate that this volume begins with a personal chronicle of the milestones leading to the use of baculoviruses for recombinant protein expression and as genetically optimized insecticides (Max D. Summers, pp. 3–73). This chronicle was written by Max Summers, a leader in the development and implementation of the baculovirus expression vector system (BEVS), and provides some historical background for many of the subsequent chapters. Angelika Fath-Goodin *et al.* describe a cutting-edge technology for enhancement of the BEVS by using a polydnavirus gene that prolongs the longevity of baculovirus-infected cells (Fath-Goodin *et al.*, pp. 75–90), and Anna Mäkelä and Christian Oker-Blom provide an overview of baculovirus display technologies for display of proteins either on the budded virus or on the surface of baculovirus-infected cells (Mäkelä and Oker-Blom, pp. 91–112). Applications of these display techniques range from production of monoclonal antibodies, to study of protein–protein interactions, and targeting of gene therapy vectors to specific cell types. Vassilis Douris *et al.* describe the use of stably transformed cell lines for recombinant protein production and for high-throughput screening for drug and insecticide discovery, including a detailed description of expression cassettes available for specific applications that employ various baculovirus-derived promoter and enhancer elements (Douris *et al.*, pp. 113–156).

The differences between mammalian and insect glycosylation compromise the biomedical value of glycoproteins produced by using the BEVS. In their chapter, Robert Harrison and Donald Jarvis (pp. 159–191) describe insect glycosylation pathways and efforts to engineer both baculovirus vectors and insect cell lines to remedy the problem of inappropriate glycosylation of mammalian proteins. Monique van Oers (pp. 193–253) describes different approaches and tailoring of the BEVS for production of vaccines against viral and parasitic disease. Descriptions of the first vaccine for animal use produced in insect cells, and the development of tests that distinguish between immunized and infected individuals, highlight the potential for application of the BEVS toward development of effective vaccines.

The broad range of mammalian cells that are permissive to baculovirus transduction provides the foundation for research described in chapters by Condreay *et al.* (pp. 255–286) and Andy Hu (pp. 287–320). Pat Condreay *et al.* (pp. 255–286) address the use of baculoviruses for automated screening of chemical libraries in mammalian cell-based assays. This chapter describes the use of the BacMam system both for basic research and therapeutic intervention with a focus on nuclear receptors, transporters, G-protein–coupled receptors, ion channels, and viral targets. Andy Hu (pp. 287–320) provides an overview of the use of baculoviruses as potential vectors for both *in vitro* and *in vivo* gene therapy including the benefits and limitations of this system. Baculovirus gene therapy vectors have potential for use in hybrid vectors for stable integration of expression cassettes into the host genome and for delivery of dsRNA for RNA interference-based gene silencing.

In the final section, which deals with biotechnological application of insect viruses for the management of insect pests, Bora Inceoglu *et al.* (pp. 323–360) provide a historical overview of the development of recombinant baculovirus insecticides and an assessment of the prospects for their use. Genetically enhanced baculovirus insecticides are now competitive with pyrethroid insecticides under field conditions, and, as public acceptance of genetically modified organisms increases, could be adopted as an integral part of modern pest management programs. In their chapter, John Carlson *et al.* (pp. 361–392) describe the potential use of densoviruses as transducing vectors to directly combat mosquito-borne disease agents and also highlight the potential use of densoviruses for management of mosquitoes. With the emergence of mosquito-borne diseases, such as that caused by *West Nile virus* and dengue hemorrhagic fever, management of both the disease agent and the insect vectors are increasingly important goals.

In the final three chapters, Gill, *et al.* (pp. 393–426), Liu *et al.* (pp. 427–457), and Gordon and Waterhouse (pp. 459–502) address transgenic plant-mediated delivery of insect virus-derived genes and insect viruses themselves for pest management purposes. Torrence Gill *et al.* describe the intricate biology of the parasitoid wasp–polydnavirus–host insect interactions, and the potential use of both polydnavirus and wasp genes that disrupt the physiology of the host insect, for pest control purposes. Of particular note is the use of the Cys-motif genes derived from the *Campoletis sonorensis* ichnovirus and wasp teratocytes as transgenes for plant protection against lepidopteran pests. Sijun Liu *et al.* (pp. 427–457) describe the potential for use of other virus-derived genes for production of insect-resistant transgenic plants, particularly virus genes that have evolved to counter the physiological defenses of the host insect. These authors also describe the use of plant lectins for appropriate delivery of toxins that act within the insect hemocoel, from a transgenic plant. This delivery system allows for exploitation of intrahemocoelic toxins that have effectively been screened for efficacy during the optimization of recombinant baculovirus insecticides (described in chapter by Bora Inceoglu *et al.*, pp. 323–360). In the final chapter, Karl Gordon and Peter Waterhouse (pp. 459–502) describe the potential for use of the relatively little studied, small RNA viruses of insects for pest management. In addition to their classical use as insecticidal agents, the authors describe efforts to develop transgenic plants that express the *Helicoverpa armigera* stunt virus and the resulting encounters with the RNA-based antiviral immune response of plants. However, the virus-like particles of small RNA viruses assembled in plants have potential for delivery of dsRNAs for silencing of genes in target insect pests. This novel biotechnological application of small RNA viruses that does not require plant expression of a viable virus is likely to stimulate a good deal of interest for plant protection purposes.

The assembly of the 13 chapters within this volume highlights the remarkable versatility of insect viruses for a diverse range of applications. Not covered in this volume are a number of other important insect virus-derived tools, which include (1) the baculovirus gene *P35*, an inhibitor of apoptosis identified by Lois Miller and colleagues that is the most broadly acting caspase inhibitor protein known (Clem, 2001; Clem *et al.*, 1991), and (2) the transposon *piggyBac*, which was isolated from a baculovirus and which, among other applications, has been widely adopted for production of transgenic insects (Handler, 2002). Aside from the myriad applications of baculoviruses and baculovirus-derived genes, the internal ribosome entry site (IRES) sequences of the *Dicistroviridae* have been extensively studied both for their novelty (Jan, 2005) and for construction of dicistronic expression vectors (Royall *et al.*, 2004).

This volume on the biotechnological applications of insect viruses was inspired in part by a Virus Division symposium on "Insect Expression Systems, Gene Therapy, and Vaccine Development" held at the annual meeting of the Society for Invertebrate Pathology in Alaska, Anchorage in 2005. I would like to thank the participants of that symposium, in addition to all other authors who have contributed to this volume. With the exponential increase in insect genomic efforts, growth in the study of insect virus–host interactions, and discovery of new insect viruses, the continued development of biotechnological products from these viruses is assured.

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