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BOOK REVIEW

THOMAS PROFT (ED.). MICROBIAL TOXINS: CURRENT RESEARCH AND FUTURE TRENDS. UNIVERSITY OF AUCKLAND PUBLISHING, NEW ZEALAND 2009, VIII + 192PP. ISBN: 978-1-904455-44-8.

Toxins are important virulence factors responsible for microbial pathogenicity. Potential applications of toxin research extend beyond simply combating microbial virulence and include the development of novel anti-cancer drugs and other front-line medicines. No less important is the use of toxins as tools in cellular biology and neurobiology. Understanding toxin molecular and cellular biology is critical for the development of new anti-toxin strategies, particularly for those with bioterrorism capability. This well worked book not only provides a general overview of toxins but elucidates in detail recent molecular approaches, achievements and refreshing perspective on the future studies of these molecules. The book is divided into nine chapters and each chapter is written by internationally respected scientists.

Chapter 1. Toxins Carried by Mobile Genetic Elements (José R Penadés and J. Ross Fitzgerald).

Mobile genetic elements (plasmids, bacteriophages, and 'pathogenicity islands') have a profound influence on the emergence of pathogenic clones of these bacteria. The identification of accessory genetic elements has facilitated our efforts to understand the evolution of pathogenic microorganisms. In many cases, toxigenic bacteria including *Staphylococcus aureus, Vibrio cholerae*, or *Escherichia coli* acquired virulence by acquisition of toxin genes carried in mobile genetic elements. Understanding the evolutionary events that lead to the emergence of pathogenic clones may provide new approaches to the control of infectious diseases.

Chapter 2. Botulinum Neurotoxins: Structure and Mechanism of Action (Roshan Kukreja and Bal am Singh).

Botulinum neurotoxins are the most potent natural toxins known to humankind. Botulinum neurotoxins family comprises of seven antigenically distinct serotypes (A to G) that are produced by various toxigenic strains of *Clostridium botulinum*. They act as metalloproteinases that enter peripheral cholinergic nerve terminals and cleave proteins that are key components of the neuroexocytosis apparatus. Botulinum neurotoxins pose a major biological warfare threat due to their extreme toxicity and easy production. Neverheless, they also serve as powerful tools to treat an ever expanding list of medical conditions. A better understanding of the structure-function relationship of clostridial neurotoxins is very important for designing effective specific inhibitors to counter botulism biothreat, and for the development of new therapeutics

Chapter 3. Anthrax Toxin (Francisco J. Maldonado-Arocho, Kathleen M. Averette-Mirrashidi, and Kenneth A. Bradley)

Anthrax toxin is a three-protein exotoxin secreted by virulent strains of the bacterium, *Bacillus anthracis*--the causative agent of anthrax. Anthrax toxin is composed of the cell-binding protein, protective antigen (PA), and two enzyme components, called edema factor (EF), a calcium- and calmodulin-dependent adenylate cyclase and lethal factor (LF), a zinc-dependent metalloproteinase. These three protein components act together to impart their physiological effects. The combination of LF and PA is called lethal toxin (LT), and this toxin inactivates MAPK signal-

ing in the host. Oedema toxin (ET), formed by the combination of EF and PA, produces high cAMP levels in host cells. Both LT and ET are capable of inducing mortality in animal models when injected as purified toxins. This chapter will focus on current trends in LT and ET research aimed at understanding the mechanisms by which they affect the host and alter disease outcome.

Chapter 4. Subtilase Cytotoxin: A New Bacterial AB5 Toxin Family (Adrienne W. Paton and James C. Paton)

Subtilase cytotoxin is the recently-recognised prototype of a new AB5 toxin family. Toxins belonging to the AB5 toxin family are potent virulence factors produced by some bacterial pathogens such as Shiga toxigenic *Escherichia coli and Shigella disenteriae*. These toxins consisiting two protein subunits. Subunit A is a subtilase-like serine protease. Its cytotoxicity for eukaryotic cells is due to a highly specific, single-site cleavage of BiP/GRP78, an essential Hsp70 family chaperone. The B subunit has specificity for glycans terminating in the sialic acid. Subtilase cytotoxin is is lethal for mice and induces pathological features overlapping those seen in the haemolytic uraemic syndrome, a life-threatening complication of Shiga toxigenic E. coli infection.

Chapter 5. Pasteurella multocida Toxin (Joachim H.C. Orth).

Pasteurella multocida toxin (PMT) is the major pathogenic deteriment of *Pasteurella multocida*, Gram-negative, non-motile coccobacillus. It can cause a zoonotic infection in humans, which typically is a result of bites or scratches from domestic pets. The toxin is the causative agent of the economically important atrophic rhinitis in swine. PMT is a 146-kDa mitogenic protein, caused a striking increase in the formation of colonies from single cells in soft agar. Stimulation of several signalling pathways is induced by PMT. In this chapter most recent results on studies of PMT are presented.

Chapter 6. The Multifunctional-Autoprocessing RTX toxins of Vibrios (Karla J. F. Satchell and Brett Geissler).

Multifunctional-Autoprocessing RTX toxins are a unique family of secreted proteins toxins produced by the *Vibrio* sp. This toxin is produced by nearly all clinical and environmental isolates of *V. cholerae*. The toxin is associated with increased epithelial cell damage. Within the eukaryotic cell, this toxin has three distinct biochemical activities: covalent crosslinking of actin, inactivation of Rho-family GTPases, destruction of the actin cytoskeleton. Related toxins produced by *V. vulnificus* and *V. anguillarum* have also been characterized and found to have some similar, but also distinct mechanisms of action. In this chapter, the structure and function of the V. cholerae toxin are discussed in detail. It is shown that the *V. cholerae* toxin is a multifunctional autoprocessing RTX toxin, that represents a larger group of MARTX toxins produced by at least eight gram-negative species.

Chapter 7. Helicobacter pylori VacA Toxin (Timothy L. Cover and John C. Atherton).

Helicobacter pylori, a Gram-negative bacterium that colonizes the human stomach, secretes a toxin known as VacA. Vac A induces the formation of in cultured gastric epithelial cells. VacA also causes several other alterations in gastric epithelial cells and targets multiple types of immune cells. In this chapter, recent progress in understanding three features of VacA: structural properties of VacA, targeting of T lymphocytes by VacA, diversity among VacA proteins expressed by different *H. pylori* strains.

Chapter 8. Staphylococcal Immune Evasion Toxins (Ries J. Langley, Thomas Proft, and John D. Fraser).

Staphylococcus aureus permanently colonizes the moist squamous epithelium of the anterior nares of 20% of the population. Occasionally, the organism can cause superficial skin infections such as abscesses and impetigo, or serious invasive infections such as septic arthritis, osteomyelitis and endocarditis. Novel immune evasion proteins from *S. aureus* were identified. This chapter focuses on some of these proteins and a range of their activities.

Chapter 9. Fungal Ribotoxins: Structure, Function and Evolution Elías Herrero-Galán, Elisa Álvarez-García, Nelson Carreras-Sangrà, Javier Lacadena, Jorge Alegre-Cebollada, Álvaro Martínez del Pozo, Mercedes Oñaderra, and José G. Gavilanes

Ribotoxins are a more widespread group of proteins within the filamentous fungi. There are extracellular ribonucleases which inactivate ribosomes by specifically cleaving a single phosphodiester bond located at the universally conserved sarcin/ricin loop

of the large rRNA. The ribotoxins are specific and potent toxins, of unknown biological function which inhibited protein biosynthesis and cause cell death via apoptosis. Ribotoxins are also able to interact with membranes containing acid phospholipids and altered membrane permeability. The study of structure-function relationships in ribotoxins is of particular interest, since they are postulated as potential therapeutic agents against different human pathologies.

Reviewed book represents rich source of information about microbial toxins and it is possible to recommend it for scientists with an interest in bioterrorism, microbial pathogenesis, and microbial genomics.

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