

Preface

The extremely potent substance botulinum neurotoxin (BoNT) has attracted much interest in diverse fields. Originally identified as a cause for the rare but deadly disease botulism, military, and terrorist intended to misuse this sophisticated molecule as biological weapon. This caused its classification as select agent category A by the Centers for Disease Control and Prevention and the listing in the Biological and Toxin Weapons Convention. Later, the civilian use of BoNT as long acting peripheral muscle relaxant has turned this molecule into an indispensable pharmaceutical worldwide with annual revenues >\$1.5 billion. Also, basic scientists value the botulinum neurotoxin as molecular tool for dissecting mechanisms of exocytosis.

This book will cover the most recent molecular details of botulinum neurotoxin, its mechanism of action as well as its detection and application. “[Genetic Diversity Within *Clostridium botulinum* Serotypes, botulinum Neurotoxin Gene Clusters and Toxin Subtypes](#)” explains the genetics of the diverse strains of *Clostridium botulinum* and some other bacteria of the genus *Clostridium* as well as provides an overview of the diverse BoNT family currently including 35 BoNT serotypes and subtypes and their neurotoxin-associated non-toxic proteins (NAPs). “[Assembly and Function of the Botulinum Neurotoxin Progenitor Complex](#)” sheds light on the structural assembly of BoNT with its NAPs yielding stable shield complexes which allow an oral intoxication by an intact passage through the gastrointestinal tract and efficient resorption of BoNT in the gut. “[Uptake of Botulinum Neurotoxin in the Intestine](#)” describes the currently discussed three different routes for resorption of BoNT from the gut. Then the BoNT spreads via the circulation within the body. “[Double Receptor Anchorage of Botulinum Neurotoxins Accounts for their Exquisite Neurospecificity](#)” teaches that BoNT specifically bind to cholinergic motor nerve terminals via a complex dual receptor interaction which is one of the major determinant for their high potency. “[The Elusive Compass of Clostridial Neurotoxins: Deciding When and Where to Go?](#)” illustrates their subsequent endocytotic uptake which decides about the site of action of BoNT and the closely related tetanus neurotoxin. BoNT harness the synaptic vesicle recycling as a Trojan horse and “[Synchronized Chaperone Function of Botulinum Neurotoxin Domains Mediates Light Chain Translocation into Neurons](#)” exhibits the nanomodular machinery which allows

the delivery of the proteolytically active domain (LC, light chain) into the neuronal cytosol. In “[Clostridial Neurotoxin Light Chains: Devices for SNARE Cleavage Mediated Blockade of Neurotransmission](#)”, the extraordinary cleavage specificity of the LC for the members of the SNARE proteins is presented. “[Synaptic Vesicle Proteins: Targets and Routes for Botulinum Neurotoxins](#)” deepens the knowledge about the physiological role of the members of the SNARE proteins susceptible to BoNT hydrolysis. The unusual long persistence of LC activity within the synapses and its molecular basis are elucidated in “[Persistence of Botulinum Neurotoxin Inactivation of Nerve Function](#)”. To counteract intoxications with BoNT, the major efforts of identifying LC inhibiting molecules is explicated in “[Structure-Based Drug Discovery for Botulinum Neurotoxins](#)”. To allow timely and appropriate application of counter measures the most recent advanced techniques for the highly sensitive detection of BoNT are required. These are described in “[Complexity of Botulinum Neurotoxins: Challenges for Detection Technology](#)”. Precise quantitation of potency of BoNT being an active pharmaceutical ingredient using modern cell-based assays is illustrated in “[Progress in Cell Based Assays for Botulinum Neurotoxin Detection](#)”. Exploiting the great body of research data about BoNT to design second generation peripheral muscle relaxants as well as novel targeted secretion inhibitors is highlighted in “[Transforming the Domain Structure of Botulinum Neurotoxins into Novel Therapeutics](#)”. Finally, “[Botulinum Toxin: Application, Safety, and Limitations](#)” deals with the application of BoNT as medicine and describes its extraordinary pharmacological advantages with respect to safety, treatment efficiency, and duration of action.

This book comprehensively covers all major molecular aspects of BoNT and its civilian exploitation written by experts leading in their field. We think it is appropriate for a widespread readership within the BoNT field as well as in related areas of research and medicine. We would like to thank all chapter authors for their high quality contributions and Mrs. Clauss at Springer for the smooth handling of the manuscripts.

Hannover, August 2012

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<http://www.springer.com/978-3-642-33569-3>

Botulinum Neurotoxins

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2013, VIII, 324 p., Hardcover

ISBN: 978-3-642-33569-3