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## **Food Microbiology and Food Safety Series**

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# Shiga toxins

A Review of Structure, Mechanism,  
and Detection

 Springer

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*This work is dedicated to the memory  
of Dr. William H. "Bill" Vensel.  
He was a remarkable scientist,  
an esteemed colleague, and an inspiration  
who is sorely missed.*

# Foreword

Shiga toxins are a significant cause of human misery throughout the world. In the developing world, they are commonly produced by *Shigella dysenteriae* type 1 and in the developed world they are most frequently encountered when produced by strains of pathogenic *Escherichia coli* that sometimes contaminate food or water. The Shiga toxins produced by these bacteria have similar structures, binding sites on the target cell, and a common mechanism of cell toxicity, but they are produced in very different ways. A single Shiga toxin molecule suffices to kill a target cell, making the bacteria that produce them potent pathogens. There is currently no therapeutic intervention to prevent or ameliorate the effects of Shiga toxins.

Understanding Shiga toxins and their health effects requires a multidisciplinary approach that involves chemistry, proteomics, genomics, virology, microbiology, ecology, and medicine. Many of the examples of outbreaks in this book are drawn from the United States, but examples from Europe and Asia are included, and, together, they reflect the broader worldwide experience. This book also addresses the Shiga toxin-producing *E. coli* (STEC) and their mobile lambdoid phages that present a constantly varying threat, especially via our food supply. In brief, this book describes the properties of Shiga toxins and their threats to human health, and the authors hope that it will be useful to laboratory and clinical scientists from a variety of disciplines.

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# Abbreviations

3D	Three-dimensional
Ab	Antibody
AE	Attaching and effacing
AKI	Acute kidney injury
AMS	Agricultural Marketing Service
Arg	Arginine
Arg-X-X-Arginine	Arginine-amino acid-amino acid-Arginine
Asn	Asparagine
att	Phage attachment site
<i>attB</i>	Site of phage attachment in the bacterial chromosome
attomol	$1 \times 10^{-18}$ mol
CAS	CRISPR-associated genes
CCD	Charge-coupled device
CD <sub>50</sub>	Median cytotoxic dose
CFT	Cell-free translation
CFU	Colony-forming unit
CNS	Central nervous system
CRISPR	Clustered, regularly interspaced, short palindromic repeats
CT-SMAC	MacConkey agar with sorbitol, cefixime, and tellurite
Ctx	Cholera toxin
DAPI	4',6-Diamidino-2-phenylindole dihydrochloride
DNA	Deoxyribonucleic acid
DTT	Dithiothreitol
E	Glutamic acid
eae	Gene that produces intimin
EAEC	Enteraggregative <i>E. coli</i>
EAggEC	Enteraggregative <i>E. coli</i>
EFSA	European Food Safety Authority
EHEC	Enterohemorrhagic <i>E. coli</i>
ELISA	Enzyme-linked immunosorbent assay
EMB	Eosin methylene blue

EPEC	Enteropathogenic <i>E. coli</i>
ER	Endoplasmic reticulum
ERT	Endoplasmic reticulum-routing protein toxins
ESI	Electrospray ionization
FDOSS	Foodborne Disease Outbreak Surveillance System
femtomol	$1 \times 10^{-15}$ mol
FOOD Tool	Foodborne Outbreak Online Database
FSMA	United States Food Safety Modernization Act
fur	Ferric uptake regulator
g	Gram
Gal	Galactose
GAP	Good agricultural practices
Gb3	Globotriaosylceramide
Gb4	Globotetraosylceramide
GFP	Green fluorescent protein
GHP	Good handling practices
Glu	Glutamic acid
GuCl	Guanidinium chloride
HACCP	Hazard analysis and critical control points
HC	Hemorrhagic colitis
HSP-90	Heat shock protein 90
HTH	Helix-turn-helix
HUS	Hemolytic uremic syndrome
HuSAP	Human serum amyloid protein P
IA	Iodoacetamide
IG	Intragastric
IgG	Immunoglobulin G
IgY	Immunoglobulin Y
IMS	Immunomagnetic separation
IP	Intraperitoneal
IS	Insertion sequence
ISt	Internal standard
IV	Intravenous
kDa	Kilodalton
LAMP	Loop-mediated isothermal amplification
LD <sub>50</sub>	Median lethal dose
LEE	Locus of enterocyte effacement
LFA	Lateral flow assay
LFD	Lateral flow device
LOD	Limit of detection
LPS	Lipopolysaccharide
LT	Heat-labile enterotoxin
LT-I	Type I heat-stable enterotoxin
LT-II	Type II heat-stable enterotoxin
mAb	Monoclonal antibody

MAC	MacConkey agar
μL	Microliter
mL	Milliliter
MLD	Minimum lethal dose
MMWR	Morbidity and Mortality Weekly Report
MRM	Multiple reaction monitoring
MS	Mass spectrometry
MS1	First quadrupole of a triple quadrupole mass spectrometer
MS2	Third quadrupole of a triple quadrupole mass spectrometer
ng	Nanogram ( $1 \times 10^{-9}$ g)
NORS	National Outbreak Reporting System
pAb	Polyclonal antibody
PCR	Polymerase chain reaction
PDB	Protein Data Bank
pg	Picogram ( $1 \times 10^{-12}$ g)
Ptx	Pertussis toxin
Q	Glutamine
qPCR	Quantitative PCR
QSR	Quick service restaurant
RCSB	Research Collaboratory for Structural Bioinformatics
RELISA	Receptor/ELISA
RIP	Ribosome-inactivating proteins
RPLA	Reversed passive latex agglutination
rRNA	Ribosomal ribonucleic acid
SLT	Shiga-like toxin
SLT-I	Type I Shiga-like toxin (Stx1)
SLT-II	Type II Shiga-like toxin (Stx2)
SMAC	Sorbitol-MacConkey agar
ST	Heat-stable enterotoxin
STEC	Shiga toxin-producing <i>Escherichia coli</i>
Stx	Shiga toxin
<i>stx</i>	Genes in the Shiga toxin operon
Stx1	Type 1 Shiga toxin
<i>stx1</i>	Genes in the Shiga toxin type 1 operon
Stx2	Type 2 Shiga toxin
<i>stx2</i>	Genes in the Shiga toxin type 2 operon
<i>stxA</i>	Gene encoding the A subunit of Shiga toxin
<i>stxB</i>	Gene encoding the B subunit of Shiga toxin
SubAB	Subtilase cytotoxin
TBX	Tryptone bile X-glucuronide
TPP	Thrombotic-thrombocytopenic purpura
Trp	Tryptophan
Tyr	Tyrosine
USD	United States Dollar (currency)
USDA	United States Department of Agriculture

USDA-FSIS	U. S. Department of Agriculture - Food Safety and Inspection Service
VCT	Verocytotoxin
VT	Verotoxin
VTEC	Verotoxin-producing <i>Escherichia coli</i>
WBDOSS	Waterborne Disease Outbreak Surveillance System
WDOSR	Waterborne Disease & Outbreak Surveillance & Reporting
WGS	Whole genome sequencing
WHO	World Health Organization

## About the Authors

**David L. Brandon** received an A.B. from Harvard College and Ph.D. in biochemistry from Harvard University (Cambridge, MA, USA). He retired in 2016, after 37 years as Research Chemist with the USDA Agricultural Research Service, and has served in leadership and editorial positions in the field of analytical food safety. He is recognized for his research in the areas of toxins and antinutrients in food and feed and immunoanalysis of foodborne contaminants, including bacterial pathogens and drug and pesticide residues. His work has involved significant international collaborations, with applications to food safety, crop improvement, and food defense. Dr. Brandon is author/inventor of over 80 publications and patents, with several technologies licensed to industry.

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