



# Type Vi Secretion

**Brian Thomas Ho**



## Type VI Secretion

**Structure and Diversity of the Type VI Secretion System** Romain Kooger,2019

**Dissecting the Puncturing Device of the Type VI Secretion System** Francesca Romana Cianfanelli,2016

*Protein Secretion in Bacteria* Maria Sandkvist, Eric Cascales, Peter J. Christie, 2020-07-02 Protein transport into and across membranes is a fundamental process in bacteria that touches upon and unites many areas of microbiology including bacterial cell physiology adhesion and motility nutrient scavenging intrabacterial signaling and social behavior toxin deployment interbacterial antagonism and collaboration host invasion and disruption and immune evasion A broad repertoire of mechanisms and macromolecular machines are required to deliver protein substrates across bacterial cell membranes for intended effects Some machines are common to most if not all bacteria whereas others are specific to Gram negative or Gram positive species or species with unique cell envelope properties such as members of Actinobacteria and Spirochetes *Protein Secretion in Bacteria* authored and edited by an international team of experts draws together the many distinct functions and mechanisms involved in protein translocation in one concise tome This comprehensive book presents updated information on all aspects of bacterial protein secretion encompassing Individual secretory systems Sec Tat and T1SS through the newly discovered T9SS Mechanisms structures and functions of bacterial secretion systems Lipoprotein sorting pathways outer membrane vesicles and the sortase system Structures and roles of surface organelles including flagella pili and curli Emerging technologies and translational implications *Protein Secretion in Bacteria* serves as both an introductory guide for students and postdocs and a ready reference for seasoned researchers whose work touches on protein export and secretion This volume synthesizes the diversity of mechanisms of bacterial secretion across the microbial world into a digestible resource to stimulate new research inspire continued identification and characterization of novel systems and bring about new ways to manipulate these systems for biotechnological preventative and therapeutic applications

**Type VI Secretion System Effectors** Thi Thu Hang Le, 2017 Here we analyzed the Enteric aggregative *Escherichia coli* Sci 1 T6SS toxin effectors We identified Tle1 a toxin effector encoded by this cluster and show that Tle1 possesses phospholipase A1 and A2 activities required for the inter bacterial competition Self protection of the attacker cell is secured by an outer membrane lipoprotein Tli1 which binds Tle1 in a 1:1 stoichiometric ratio with nanomolar affinity and inhibits its phospholipase activity The protein 435 from the pathogen AIEC LF82 has been predicted to be a phospholipase of the Tle3 effector family with PLA1 activity from a T6SS1 gene cluster Its toxicity can be neutralized by the cognate immunity protein 434 that is a putative Tli3 by forming Tle3/Tli3 protein complex The two separated proteins and their complex were then called Tle3AIEC/Tli3AIEC and Tle3AIEC/Tli3AIEC complex proteins respectively In order to further investigate the related mechanism of Tle3AIEC and Tli3AIEC we performed expression purification characterization crystallization of the two proteins and preliminary X ray crystallographic studies of the Tle3AIEC/Tli3AIEC complex in order to understand how Tle3AIEC protein recognizes and binds to its cognate Tli3AIEC effector and inhibits its activity X ray diffraction data were collected from selenomethionine derivatized Tle3AIEC/SeMet/Tli3AIEC crystals to a resolution of 3.8 Å

Characterization of the Antibacterial Activity of the Type VI Secretion System Brian Thomas Ho,2014 This pathway also induced T6SS counterattacks in response to mating pair formation associated with type IV secretion system T4SS mediated DNA conjugation as well as treatment with membrane disrupting natural product polymyxin B suggesting that the signal needed to induce T6SS activity was mechanical perturbation of the P aeruginosa cell membrane Interestingly these T4SS induced counterattacks were able to confer resistance to the acquisition of horizontally transferred foreign DNA by selectively killing conjugative donor cells As such the T6SS of P aeruginosa may represent a type of general bacterial innate immune system capable of responding to a wide range of exogenous threats

**Mechanisms of Delivery and Mode of Action of Type VI Secretion System Effectors** Peter David Ringel,2018

**Structural Studies on the Type VI Secretion System and Human CLN3p** Dennis Quentin,2018\*

*Bacterial Effectors as Drivers of Human Disease: Models, Methods, Mechanisms* Teresa Thurston,Jaclyn Suzanne Pearson,Gunnar Neels Schroeder,2021-09-13

**Posttranslational Regulation and Effector Specificity of the Type VI Secretion System** Julie Michelle Silverman,2013 Bacteria mediate interactions with their surroundings by exporting a variety of proteins into the extracellular environment Gram negative bacteria have evolved at least six dedicated secretory pathways to accomplish this task each exporting a discrete set of proteins through complex and genetically divergent systems One such system is the type VI secretion system T6SS which is a contact dependent protein export pathway that delivers toxic effectors into target bacterial and eukaryotic cells The export of effectors is controlled by sophisticated regulatory networks that can be triggered by specific environmental cues The characterization of these regulatory pathways has yielded new insight into the physiologically relevant conditions in which these systems are active In this thesis work the Hcp secretion island I HSI I encoded T6SS H1 T6SS of the opportunistic pathogen Pseudomonas aeruginosa was used as a model system to investigate the factors that govern T6S activity Specifically this work describes two distinct posttranslational regulatory pathways mediated by H1 T6SS associated proteins that coordinate T6S apparatus assembly and effector export One of these regulatory pathways the threonine phosphorylation pathway TPP is stimulated when P aeruginosa is subjected to surface associated growth conditions In contrast the second pathway which is mediated by a negative regulator TagF does not respond to surface or planktonic growth conditions and instead is likely stimulated by an unknown cue As productive H1 T6S dependent toxin delivery requires close cell contact the presence of these regulatory pathways may provide a means to efficiently initiate H1 T6S activity under appropriate environmental conditions Another important aspect of the T6SS and secretion systems in general is the mechanisms used to specifically select substrates for export This thesis work has uncovered a mechanism for substrate recognition by the T6SS I found that specific interactions between T6S effectors and a secreted T6S component Hcp haemolysin co regulated protein are essential for effector export Thus Hcp plays a central role in T6S substrate discrimination Together these findings have advanced our understanding of the T6SS and have shed light on the diverse mechanisms by which proteins can be exported by bacteria

*Structure and Function of Type VI Secretion System Dependent Amidase Effector/immunity Proteins from Pathogenic Bacteria* Juliane Benz,2014

*Exploring the Effector Loading Mechanisms of a Type Vi Secretion System in Agrobacterium Tumefaciens* □□□,2018

**Type VI Secretion System Dependent Interactions and Diversity in Vibrio Fischeri** Peyton Moore,2022 Many animals rely on symbioses with microorganisms for normal development and health Symbiont populations usually consist of multiple species and or strains that exhibit diverse traits and these characteristics impact their fitness for establishing and maintaining symbiosis These traits include mechanisms that promote interactions between cells specifically competitive interactions to obtain space and resources within habitats in the host A gap in knowledge currently exists regarding how diversity in these traits impacts formation of symbiont populations To address this knowledge gap this study characterizes a natural isolate of Vibrio fischeri which is a bacterial symbiont that forms a multi strain symbiosis with the Hawaiian bobtail squid Euprymna scolopes This characterization contributes to our understanding of strain diversity within a system Specifically we investigate the diversity of a molecular mechanism that promotes interference competition among V fischeri in the host called the type VI secretion system T6SS which is a contact dependent nanomachine that delivers toxic effectors into neighboring cells T6SS positive T6SS cells prevent self intoxication by co expressing immunity proteins that neutralize the toxins How non isogenic T6SS strains interact with each other remains poorly understood which prevents the ability to predict which strains can coexist within the same habitats This study showcases diversity among T6SS effectors to highlight factors that potentially influence population organization We showcase that strains can readily utilize adopted toxins and foreign toxins from competitor cells can cause inhibition of kin cells despite harboring immunity proteins Taken together these findings support a model in which T6SS strains inhibit each other using diverse effectors which provides insight into how different T6SS strains can occupy the same habitat

**Protein-protein Interactions in the Bacterial Type VI Secretion System** Asma Ahmad,2014

**The Comprehensive Sourcebook of Bacterial Protein Toxins** Joseph E. Alouf,Daniel Ladant,Michel R. Popoff,2005-12-20 This book describes the major achievements and discoveries relevant to bacterial protein toxins since the turn of the new century illustrated by the discovery of more than fifty novel toxins many of them identified through genome screening The establishment of the three dimensional crystal structure of more than 20 toxins during the same period offers deeper knowledge of structure activity relationships and provides a framework to understand how toxins recognize receptors penetrate membranes and interact with and modify intracellular substrates Edited by two of the most highly regarded experts in the field from the Institut Pasteur France 14 brand new chapters dedicated to coverage of historical and general aspects of toxinology Includes the major toxins of both basic and clinical interest are described in depth Details applied aspects of toxins such as therapy vaccinology and toolkits in cell biology Evolutionary and functional aspects of bacterial toxins evaluated and summarized Toxin applications in cell biology presented Therapy cancer therapy dystonias discussed Vaccines native and genetically engineered vaccines featured Toxins discussed as biological weapons comprising chapters on anthrax diphtheria ricin etc

**Biogenesis and Membrane Anchoring of the Type VI Secretion Contractile Tail** Abdelrahim Zoued,2015 Among the broad weaponry of bacteria the recently identified type VI secretion system T6SS emerges as one of the key player in bacterial competition T6SS is a versatile machinery that targets both eukaryotic and prokaryotic cells This molecular weapon assembles two evolutionarily different sub assemblies One complex anchors the machinery to the cell envelope while the second acts as a molecular crossbow The mechanism of action of the T6SS is similar to other known contractile machineries such as bacteriophages the contraction of a sheath propels an arrow constituted of a tail tube capped by a cell puncturing device directly into the prey cell to deliver effector toxins My Ph D project was to provide mechanistic details on the structure and biogenesis of the two T6SS sub complexes and to understand how they are connected using entero aggregative Escherichia coli as model bacterium I have demonstrated that the membrane complex is assembled first and starts with the positioning of the outer membrane TssJ lipoprotein and proceeds inward from the outer to the inner membrane through the sequential recruitment of the TssM and TssL subunits After assembly the membrane complex recruits an assembly platform called the baseplate We identified and characterized the components of this baseplate which serves as assembly platform for the tail We further demonstrated that the functional and physical interaction between the T6SS membrane complex and the baseplate is mediated by multiple contacts Finally we identified and deciphered the role of TssA a protein that coordinates the polymerizations of the tail tube and sheath

**Dynamics of the Type VI Secretion System in Pseudomonas Aeruginosa** Martina Liuzzo,2018

*Characterisation of Putative Type VI Secretion System Effector Proteins from Burkholderia Cenocepacia* ,2014

*Antibacterial Effectors of the Type VI Secretion System* Alistair Brian Russell, 2014 With the advent of high throughput culture independent sequencing it has become increasingly apparent that bacteria often live in complex communities both in the environment and in association with the human body Moreover in polymicrobial settings there is often fierce competition for both space and resources the results of which can have drastic effects on community composition The evolutionary pressure exerted by competition is reflected by the significant portion of the coding capacity of many bacterial genomes dedicated to the production and regulation of antagonistic pathways One such pathway the type VI secretion system T6SS has emerged as a mechanism mediating the delivery of potent antibacterial effectors between contacting Gram negative bacteria granting the attacking organism a fitness benefit over sensitive neighbors Initial studies of interbacterial T6S provided evidence that this system plays an important role in antagonism however its mechanism of action on recipient cells remained elusive This thesis describes the first biochemical characterization of antibacterial T6SS effector proteins finding that they compromise basal features of bacterial physiology such as cell envelope integrity By targeting highly conserved processes the T6SS has the capacity to mediate antagonism between highly disparate organisms The cost of such versatility is that bacteria are susceptible to their own T6SS effectors In order to overcome this hurdle antibacterial effectors are invariably associated with cognate immunity proteins that prevent their toxicity protecting the producing cell Beyond initial biochemical characterization of antibacterial effector proteins this work describes informatic efforts to identify substrates secreted by the interbacterial T6SS throughout sequenced bacterial genomes This strategy uncovered highly divergent effector sequences comprising distinct families within superfamilies defined by a common enzymatic target These divergent effectors not only exhibit distinct substrate specificities but also vary in their capacity to be neutralized by different sets of immunity proteins Lastly our informatic efforts led to the discovery of antibacterial effector proteins in a phylum of Gram negative bacteria not predicted to encode a T6SS the Bacteroidetes My work on this abundant environmental and human associated phylum of bacteria has found that they possess a highly divergent T6S like pathway one that like its Proteobacterial homolog takes part in interbacterial antagonism Together these findings represent a significant advancement in the field of interbacterial T6S and serve as a platform for further work defining the in situ benefit of this antagonistic pathway

**Characterization of Type VI Secretion System in *Acinetobacter Baylyi* ADP1** Di Hu, 2015

*Functional and Mechanistic Studies of Type VI Secretion Systems in *Azorhizobium* and *Agrobacterium** □□□, 2020

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