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Abstract: Francisella tularensis genomes encode homologues of type IV pili. Though several F. tularensis genes required for Tfp expression are homologous to genes required for type II secretion (T2S), these gene clusters mainly bear structural signatures that are typical of Tfp.

With the biodefense initiative, there has been a major boost by the NIH to fund studies on bioterrorism agents, including Francisella, which is classified as a A bioterrorism agent. With the major interest in biodefense and the major threats of bioterrorism, Francisella tularensis has become a major interest for microbiologists, cell biologists, immunologists, and infectious disease experts. The volume explores the mechanisms of pathogenesis, genetics and genetic manipulations, genomics and metagenomics, identification of vaccine candidates, animal models to study the disease process, mechanisms of protective immunity, pathophysiology, vaccine development, genetic susceptibility, more effective therapies, clinical diagnosis, and routine and rapid microbiological diagnostic tools. Annals volumes are available for sale as individual books or as a journal. For information on institutional journal subscriptions, please visit www. Please contact the New York Academy of Sciences directly to place your order www. Members of the New York Academy of Science receive full-text access to the Annals online and discounts on print volumes. Molecular Ecology, Epidemiology and Evolution of Francisella: Genetics and Genetic Manipulations in Francisella Tularensis: Tom Zahrt and Dara Frank. Richard Titball and Joseph Petrosino. The Francisella Pathogenicity Island: Nano and Crystal Schmerk. Barker and Karl E. Daniel Clemens and Marcus A. Tina Guina and Ake Forsberg. John Gunn and Robert Ernst. Francisella Tularensis Activation of the Inflammasome: Weiss, Thomas Henry, and Denise M. Animal Models of Francisella Tularensis Infection: Rick Lyons and Terry Wu. Mucosal Immunopathogenesis of Francisella Tularensis: Innate and Adaptive Immunity to Francisella: Cowley, and Catharine M. Vaccines against Francisella Tularensis: Wayne Conlan and Petra C. Clinical, Epidemiologic and Ecological Characteristics: New Approaches to Diagnosis and Therapy of Tularemia: Arne Tarnvik and May Chu. Biosafety and Selectable Markers: Titball, Anders Sjostedt, Martin S.

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Chapter 2 : - NLM Catalog Result

The type II secretion pathway or the main terminal branch of the general secretion pathway, as it has also been referred to, is widely distributed among Proteobacteria, in which it is responsible.

Received Dec 2; Accepted Feb 4. This is an open-access article subject to an exclusive license agreement between the authors and Frontiers Media SA, which permits unrestricted use, distribution, and reproduction in any medium, provided the original authors and source are credited. This article has been cited by other articles in PMC. Abstract *Francisella tularensis* is a highly virulent intracellular human pathogen that is capable of rapid proliferation in the infected host. Mutants affected in intracellular survival and growth are highly attenuated which highlights the importance of the intracellular phase of the infection. Genomic analysis has revealed that *Francisella* encodes all genes required for expression of functional type IV pili Tfp, and in this focused review we summarize recent findings regarding this system in the pathogenesis of tularemia. Tfp are dynamic adhesive structures that have been identified as major virulence determinants in several human pathogens, but it is not obvious what role these structures could have in an intracellular pathogen like *Francisella*. In the human pathogenic strains, genes required for secretion and assembly of Tfp and one pilin, PilA, have shown to be required for full virulence. Importantly, specific genetic differences have been identified between the different *Francisella* subspecies where in the most pathogenic type A variants all genes are intact while several Tfp genes are pseudogenes in the less pathogenic type B strains. This suggests that there has been a selection for expression of Tfp with different properties in the different subspecies. There is also a possibility that the genetic differences reflect adaptation to different environmental niches of the subspecies and plays a role in transmission of tularemia. This is also in line with recent findings where Tfp pilins are found to be glycosylated which could reflect a role for Tfp in the environment to promote survival and transmission. We are still far from understanding the role of Tfp in virulence and transmission of tularemia, but with the genomic information and genetic tools available we are in a good position to address these issues in the future. *Francisella tularensis*, type IV pili, virulence, type II secretion

Introduction *Francisella tularensis*, the causative agent of tularemia, has attracted significant attention over the years. A major reason is that the most pathogenic variant, subspecies *tularensis* also known as type A, causes severe infections that without rapid therapeutic intervention shows high mortality rates. These strains have also been recognized to have potential for development of biological weapons. Type A strains are found exclusively in North America while the less pathogenic subspecies *holarctica*, also known as type B strains, is more broadly distributed in the Northern hemisphere Petersen and Schriefer, Still, *Francisella* remained an understudied pathogen and this did not really change until the first genome sequence became available and genetic systems were developed Golovliov et al. When the first genome sequence became accessible it was somewhat of a disappointment to note that the number of genes with homology to known virulence determinants in other pathogens were relatively few Larsson et al. One of the exceptions was the gene clusters predicted to encode a type IV pili Tfp system. Tfp have been identified as a major virulence determinant in many different pathogens even if it was not obvious what role a pilus adhesin could have for an intracellular pathogen like *Francisella*. In this focused review we summarize and discuss the main findings regarding the biological role of genes encoding the Tfp system in *F.* Type IV Pili – Dynamic Adhesive Surface Structures Type IV pili are multifunctional, flexible filamentous appendages that have been assigned specific virulence traits in several important pathogens. The nomenclature of the Tfp gene clusters have not been harmonized between systems and pathogens Craig and Li, , and also for *F.* Here we have chosen to mainly use the nomenclature adapted for *P.* Table 1 Nomenclature and presence of functional Tfp genes in different strains.

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Contents: Tularemia: history, epidemiology, pathogen physiology, and clinical manifestations / by Anders SjÅstедt -- Molecular epidemiology, evolution, and ecology of Francisella / by Paul Keim, Anders Johannson, and David M. Wagner -- Genetics and genetic manipulation in Francisella tularensis / by Dara W. Frank and Thomas C. Zahrt.