REVIEW

Yersinia virulence factors - a sophisticated arsenal for combating host defences [version 1; peer review: 2 approved]

Steve Atkinson, Paul Williams

Centre for Biomolecular Sciences, School of Life Sciences, University of Nottingham, Nottingham, UK

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Abstract

The human pathogens *Yersinia pseudotuberculosis* and *Yersinia enterocolitica* cause enterocolitis, while *Yersinia pestis* is responsible for pneumonic, bubonic, and septicemic plague. All three share an infection strategy that relies on a virulence factor arsenal to enable them to enter, adhere to, and colonise the host while evading host defences to avoid untimely clearance. Their arsenal includes a number of adhesins that allow the invading pathogens to establish a foothold in the host and to adhere to specific tissues later during infection. When the host innate immune system has been activated, all three pathogens produce a structure analogous to a hypodermic needle. In conjunction with the translocon, which forms a pore in the host membrane, the channel that is formed enables the transfer of six 'effector' proteins into the host cell cytoplasm. These proteins mimic host cell proteins but are more efficient than their native counterparts at modifying the host cell cytoskeleton, triggering the host cell suicide response. Such a sophisticated arsenal ensures that yersiniae maintain the upper hand despite the best efforts of the host to counteract the infecting pathogen.

Keywords

Yersinia pestis , yersiniae , ail locus , pH6 antigen , virulence factors

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1. **James Bliska**, Stony Brook University, Stony Brook, USA
2. **Andrew Roe**, University of Glasgow, Glasgow, UK

Any comments on the article can be found at the end of the article.

Corresponding authors: Steve Atkinson (steve.atkinson@nottingham.ac.uk), Paul Williams (paul.williams@nottingham.ac.uk)

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Introduction

Across an infection timeline, the host and invading bacterial pathogen each vie for supremacy. At any given time, either may have the upper hand, but the final outcome of this battle ultimately determines the fate of the host. The triggered host response will aim to reduce the infectivity of the pathogen, but in order to stay one step ahead many bacterial species have evolved sophisticated strategies to ensure they can successfully cause infection following colonisation.

The three human pathogens belonging to the genus *Yersinia* employ a range of virulence factors that confer efficient adherence to host cells/tissues and subvert host cell functions. This mini-review highlights the key virulence factors that constitute the virulence arsenal of *Yersinia* spp. and how such a sophisticated suite of biological weapons enables these pathogens to combat host defences.

Yersinia pseudotuberculosis, *Yersinia pestis*, and *Yersinia enterocolitica* are highly adaptable psychrotrophic primary human pathogens. *Y. pseudotuberculosis* and *Y. enterocolitica* cause self-limiting gastric infections. *Y. pestis* is a recently evolved near-identical subclone of *Y. pseudotuberculosis*^{1,2} with approximately 98% identity at the DNA level. Its strategy for transmission relies on the colonisation of rat fleas, which then carry *Y. pestis* between the rodent host and humans³. Once inside the human host, *Y. pestis* can cause bubonic, pneumonic, and septicemic plague with mortality rates approaching 100% without antibiotic treatment⁴. The World Health Organisation considers *Y. pestis* a 're-emerging' pathogen that, worryingly, is capable of acquiring resistance to multiple antibiotics⁵ and is also a serious potential bioterrorism threat. The differences in lifestyle and virulence between *Y. pseudotuberculosis* and *Y. pestis* are mostly attributable to minor genomic differences on the respective chromosomes and the presence of two additional virulence plasmids that *Y. pestis* possesses.

The *Yersinia* type three secretion system

The key *Yersinia* virulence determinants and certainly the most comprehensively studied are those secreted via a type three secretion system (T3SS). To evade host innate immunity and to enable the pathogen to replicate and propagate extracellularly, all human pathogenic *Yersinia* species harbour an approximately 70 kb virulence plasmid. Located on this plasmid is a set of genes whose transcription is activated by temperatures of 37°C in the presence of millimolar concentrations of calcium, conditions representing the mammalian host. These genes code for the T3SS 'nanomachine', a hypodermic needle-like structure (the injectisome) and the translocon, which forms a pore across the host cell membrane (Figure 1). Along with a combination of regulators and chaperones, the T3SS's primary function is to inject multiple toxic *Yersinia* effector proteins (Yops) directly into the eukaryotic host cell cytosol. Once inside, they subvert host cell signalling pathways and trigger a pre-programmed metabolic chain reaction that results in apoptosis^{6,7}. Yops also inhibit phagocytosis and block cytokine production.

The structure of the T3SS needle and translocon

Structurally, the base of the injectisome is composed of a number of proteins that adopt a cylindrical architecture similar to that of the

flagellar basal body⁸ that are directed to the membrane by the secretion (Sec)-dependent pathway⁹. The injectisome incorporates two membrane rings termed the MS (membrane and supramembrane) and OM (outer membrane) rings. These are connected to five integral membrane proteins that play a role in exporting proteins^{10,11} (Figure 1). The export apparatus itself is flanked by YscQ, which facilitates the binding of the ATPase YscN and the secretion substrate-chaperone complexes¹². YscN provides the proton motive force necessary for driving the secretion of the Yop effectors^{9,13,14}.

Protruding into the extracellular space from the basal body is a hollow needle formed by the helical polymerisation of YscF protein subunits^{9,15,16}. YscF is exported and polymerised in a T3SS-dependent manner along with YscP, a protein akin to a molecular ruler that determines the length of the needle and limits its size^{17–19}. It has recently been shown that fully formed T3SS needles form clusters on the bacterial cell surface and new needles appear to localise to these clusters rather than being randomly distributed²⁰ (Figure 2). The needle tip is capped with LcrV^{21,22}, a protein that directs the formation of a pore or 'translocon'²³. The translocon consists of a tripartite protein pore, which is inserted into host cell membranes and drives the translocation of Yop effectors into the host target cell cytoplasm. The pore is composed of the transmembrane proteins YopB and YopD²³ and the injectisome tip complex LcrV^{24–26}. Bacteria lacking the tip and translocon proteins are able to secrete effectors into the extracellular environment but are defective in translocating Yops into host cells^{27–29}.

Chaperones facilitate the formation and operation of the T3SS

Given the complexity of the T3SS, part of its sophistication relates to its in-built ability to discriminate between structural and secretion substrates, providing strict order to ensure the needle is assembled and polymerised before translocon and Yop effector secretion³⁰. Such ordering requires specific chaperones, typically small protein dimers that protect the target T3SS protein from degradation^{31,32} and prevent premature oligomerisation²⁴ and also ushering into the injectisome. These T3SS chaperones are usually subdivided into three classes: class I chaperones bind the Yop effector proteins and often share high structural conservation, class II chaperones associate with the translocon proteins YopB, YopD, and LcrV, and class III chaperones tend to form heterodimers and associate with structural components of the injectisome.

The Yop effectors

The Yop effector proteins are virulence factors synthesised in the bacterial cytoplasm and secreted through the T3SS needle and translocon into eukaryotic target cells (Figure 1). Four of these (YopE, YopT, YpkA, and YopH) are involved in disrupting the normal activities of the cytoskeleton and, apart from YopH, also target an important group of eukaryotic cell signalling components, the RhoA family of small GTPases that direct cytoskeletal rearrangements necessary for phagocytosis. YopE is a functional mimic of eukaryotic GTPase-activating proteins (GAPs)³³ and disrupts the actin cytoskeleton^{34–36}, resulting in the inhibition of phagocytosis by macrophages. YopT suppresses RhoA-mediated signalling by cleaving the post-translationally modified Rho GTPases³⁷, which ultimately prevents the formation of the phagocytic cup for bacterial internalisation, and inhibits the assembly

Figure 1. Assembly of the type three secretion system (T3SS) needle. The needle is fixed into the bacterial inner and outer membrane and protrudes from the surface to penetrate the host membrane. The translocon forms a channel through the host membrane and the Yop effectors are transferred into the host from the bacterial cytoplasm via the needle and translocon (**a**). The needle protrudes from the bacterial surface prior to host cell penetration (**b**, **c** arrowed). *Salmonella typhimurium* T3SS needles isolated from the bacterial membrane (**d**). (**a**) adapted from 133, (**b**) reproduced with permission and taken from reference 56, (**c**) reproduced with permission and taken from reference 16, and (**d**) reproduced from reference 134.

of focal adhesion complexes required for the development of pseudopodia and macrophage migration^{38,39}. YpkA (YopO in *Y. enterocolitica*) associates with RhoA family proteins^{40,41} and inhibits phagocytosis^{42,43} by binding to and phosphorylating actin that is used as bait by *Y. enterocolitica* to titrate out host regulators responsible for actin polymerisation⁴⁴. YopH is multi-functional and disrupts pathways involved in both innate and adaptive immunity and is essential for the virulence of *Y. pestis*, *Y. pseudotuberculosis*, and

Y. enterocolitica in mice^{45–47}. YopH inhibits autophagy following binding of invasins or YadA (see next section) to β 1-integrins⁴⁸ and also blocks phagocytosis in macrophages^{49,50} by dephosphorylating focal adhesion complex proteins, which disrupts the link to the actin cytoskeleton^{51,52}.

The remaining two effectors (YopJ and YopM) down-regulate elements of the immune system, such as inflammation and leukocyte

Figure 2. Type 3 secretion system (T3SS) needles (circled) appear to cluster together as they form at the cell surface. Reproduced from reference 20.

recruitment^{53–57}. YopJ (YopP in *Y. enterocolitica*) is a serine/threonine/lysine acetyltransferase that catalyses the acylation of kinases, inhibiting their ability to activate the release of NF- κ B, which would otherwise induce pro-inflammatory cytokine production^{58–62}. Recently, YopJ was also shown to play an important role in inhibiting caspase-1 in activated macrophages⁶³.

YopM is translocated into macrophages⁶⁴ and may also be able to self-deliver into some human cells⁶⁵, yet it has no known enzymatic activity⁶⁶ and its true function has yet to be elucidated. Inside eukaryotic cells, YopM may interact with and stimulate cellular kinases⁶⁷ and is thought to localise to the nucleus^{68–70}, where it may influence the expression of a range of genes, down-regulating many pro-inflammatory cytokines^{65,71}, counteract the innate immune system by promoting depletion of natural killer cells in the liver, spleen, and blood⁷², and also prevent pyroptosis by binding to caspase-1, inhibiting its activity^{73,74}.

Yersinia surface adhesins

For yersiniae to efficiently deliver Yops into the host, it is essential that they adhere to the host cell surface and remain in close association during the delivery process. To ensure that this is possible, the yersiniae produce virulence factors in addition to the T3SS. An active T3SS can deliver effector proteins into the host cell cytosol only if the bacterial cells make direct contact with, and bind tightly to, the host cell surface. Over the last 30 years, several chromosomally or plasmid-encoded protein virulence

factors have been identified that play a variety of roles in host cell attachment prior to effector protein injection. In each case, attachment is not their exclusive function and not all are present or active in all three of the human pathogens. However, a combination of these proteins confers the ability to adhere to and invade host cells or bind sufficiently to ensure successful T3SS delivery of Yops.

Invasin

Invasin is a chromosomally encoded protein that mediates attachment to and entry into host cells by *Y. pseudotuberculosis* and *Y. enterocolitica*⁷⁵, although in *Y. pestis* it is a pseudogene and therefore inactive⁷⁶ (Figure 3). Invasin promotes small intestine epithelial cell internalisation by binding to host cell target receptors known as β 1-integrins⁷⁷ that present on the host cell surface. Integrins form clusters upon invasin binding, and the result is the rearrangement of the host cell cytoskeleton. This promotes phagocytosis and ultimately internalisation of the bacteria into the epithelial cells. In fact, invasin has a significantly greater (up to 100 times) affinity for some integrins than its natural ligand, fibronectin⁷⁸, and such strong associations are believed to be major contributing factors to the efficiency of internalisation and Yop delivery into host cells.

Invasin expression is regulated by both temperature and pH in *Y. enterocolitica*^{79,80}. The invasin gene is maximally expressed at 26°C, peaking during late exponential/early stationary phase with lower expression levels observed at 37°C. This apparent contradiction, since invasin is required for infection at 37°C, was resolved when Pepe *et al.* revealed that the expression of invasin at 37°C was restored to levels seen at 26°C when the pH was reduced to 5.5. It has been suggested that rather than an experimental artefact, the expression of invasin at ambient temperatures could prepare the bacteria for infection following ingestion and promote rapid transcytosis through the epithelia^{81,82}. The pH effect is not evident in *Y. pseudotuberculosis*, suggesting that the mechanisms of regulation of invasin expression may differ between the two species⁸³. Two regulators have been found to be important for invasin expression: RovA, required for the positive regulation of invasin, and YmoA, required for negative regulation^{83–85}. Both RovA and YmoA recognise the promoter region of invasin and compete for binding. Once RovA is bound, it appears to prevent YmoA from binding, thus inhibiting negative regulation of invasin^{86,87}. The expression of rovA is itself regulated by temperature via RovM, which acts as a repressor of rovA expression under inducing growth conditions⁸⁸.

YadA

After crossing the intestinal epithelium, the major adhesin responsible for Yersinia contact with cells of the submucosa is the virulence plasmid-encoded protein YadA (recently reviewed by Mühlenkamp *et al.*⁸⁹) (Figure 3). YadA expression is induced at or above 37°C^{90,91}, and under these conditions it is so abundant that it can virtually coat the entire outer surface of the bacterial cell⁹². Interestingly, despite YadA's utility and abundance, *Y. pestis* possesses an inactive yadA pseudogene due to a single nucleotide deletion that results in a frame-shift mutation⁹³ (Figure 3). Although *Y. pestis* does not produce a functional YadA protein, the chromosome carries two orthologues, YadB and YadC. Also found in *Y. pseudotuberculosis*, these two proteins are not thought to play

Figure 3. Virulence factors found on the surface of *Yersinia pseudotuberculosis*, *Yersinia enterocolitica* (a), and *Yersinia pestis* (b). Ail, YadB, and YadC are shared by all three pathogens – YadB and YadC are absent from panel (a) for clarity – while Pla is unique to *Y. pestis*. YadA and invasin are important adhesins in *Y. pseudotuberculosis* and *Y. enterocolitica* but are not expressed by *Y. pestis*. Reproduced from reference 95.

a role in adherence but may contribute to host cell invasion. They may also be required for full virulence and lethality in bubonic but not pneumonic plague in mouse infection models⁹⁴.

YadA is a non-fimbrial adhesin⁹⁵ belonging to the trimeric autotransporter adhesin family members, which are usually referred to as obligate homotrimeric proteins. The protein is shaped like a lollipop, with an N-terminal globular head domain connected by a coiled-coil stalk to a C-terminal anchor domain embedded in the outer membrane⁹². YadA has multiple functions but as an adhesin may act as a docking system, allowing the injectisome of the T3SS to come into contact with the target cell membrane to deliver the Yop effector proteins⁹⁶.

Until recently, it was thought that YadA bound only to the large proteins of the extracellular matrix – collagen, fibronectin, and laminin – which in turn bind $\beta 1$ -integrins^{97–99}. However, Keller *et al.*¹⁰⁰ recently discovered that YadA-mediated adhesion may be facilitated by a broad range of host cell receptors and in the absence of $\beta 1$ -integrins may facilitate Yop injection via αV integrins as well as other unidentified cofactors. *Y. enterocolitica* YadA also binds leukocytes in a $\beta 1$ -integrin-independent manner during systemic infection¹⁰¹, all of which suggests that YadA has the potential to target a broad range of cell types to ensure efficient Yop delivery.

The collagen-binding activity of YadA in *Y. enterocolitica* is an absolute requirement for pathogenicity; however, YadA is not essential for virulence in *Y. pseudotuberculosis*⁹⁷. YadA mediates adhesion to a number of cell types, including epithelial cells and macrophages, and can act as a haemagglutinin⁹⁷. In *Y. pseudotuberculosis*, YadA promotes the invasion of epithelial cells and is interchangeable with the activity of invasin¹⁰², although *Y. enterocolitica* YadA is not as efficient an invasin as that of

*Y. pseudotuberculosis*¹⁰³. YadA also mediates bacteria-bacteria autoagglutination, since the head domain has an affinity for itself⁹². This self-affinity also promotes the formation of densely packed microcolonies that may promote antiphagocytic activity in *Y. enterocolitica*. YadA also binds to intestinal mucus¹⁰⁴ and plays a major role in conferring serum resistance^{105–107}.

Ail

The ail locus is chromosomally located and encodes a 17 kDa surface-associated protein (Figure 3) that is thermally regulated, being maximally expressed at 37°C^{108,109}. In *Y. enterocolitica*, Ail-directed adhesion to host cells shows more specificity than invasin, as it allows invasion of some cell lines, such as human laryngeal epithelial type 2 (HEp-2), human endometrial (HEC-1B), and Chinese hamster ovary (CHO) cells, but no invasion of Madin-Darby canine kidney (MDCK) cells¹¹⁰. Both laminin and fibronectin are known targets for *Y. pestis* Ail binding¹¹¹ and vitronectin is actively recruited to the *Y. pestis* surface through the activities of Ail¹¹². Interestingly, *Y. pseudotuberculosis* Ail is unable to promote the attachment and invasion phenotypes when expressed in *Escherichia coli*¹¹³. As with invasin, Ail-mediated tight attachment to host cells presumably ensures that Yop delivery is rapid and efficient¹¹⁴. Aside from its adhesive properties, Ail also confers resistance to serum killing¹¹⁵ in all three human pathogenic yersiniae. It is apparent that Ail plays a more prominent role in the virulence of *Y. pestis*, which is presumably owing to the fact that the other prominent virulence factors contributing many of the Ail functions in *Y. pseudotuberculosis* and *Y. enterocolitica* are dysfunctional.

Psa – the pH6 antigen

The chromosomally encoded pH6 antigen (Psa) was originally identified in *Y. pestis* as a surface antigen expressed at mammalian body temperatures at pH values similar to those found in

phagolysosomes¹¹⁶. It was subsequently found to cause the agglutination of erythrocytes^{113,117}. Further investigation revealed a cell surface complex composed of aggregates of a 15 kDa protein (PsaA) that requires two regulators, PsaE and PsaF, for maximal induction^{118,119}. PsaA possesses a flexible fimbrial structure that is highly expressed during macrophage infection¹²⁰. Biochemical examination of Psa reveals that it binds to β 1-linked galactosyl residues in glycosphingolipids¹²¹, mainly of the type found in apolipoprotein-B-containing lipoproteins in human plasma, such as low-density lipoprotein (LDL) and in lipid rafts in macrophage membranes¹²². Furthermore, Psa acts as a bacterial Fc receptor, binding human immunoglobulin (IgG) but not reacting with rabbit, mouse, or sheep IgG¹²³. As with the other adhesins, the activities of Psa appear to mediate Yop secretion. *Y. pseudotuberculosis* and *Y. enterocolitica* both produce a surface protein analogous to Psa but it is referred to as MyfA. Both Psa and MyfA coat the bacterial surface with a fibrillar matrix^{120,124} and in *Y. pseudotuberculosis* MyfA promotes attachment to tissue culture cells and haemagglutination¹¹³.

Y. pestis plasmid-specific virulence factors

Apart from the T3SS virulence plasmid, two other plasmids, pPCP and pMT (sometimes referred to as pFra) that are unique to *Y. pestis*, possess additional virulence factors. pPCP encodes the plasminogen activator Pla protease/adhesin (Figure 3). Pla converts plasminogen to plasmin^{125,126}, which then degrades extracellular matrices and confers on *Y. pestis* the ability to rapidly invade the host and migrate to lymphatic tissues^{127,128}. The over-activation of plasmin results in laminin and fibrin clot degradation, exacerbating migration across host barriers¹²⁹, which is further compounded by the activities of Pla as an adhesin and an invasin^{130,131}. pMT is

responsible for the production of a murine toxin that is required during the colonisation of fleas¹³².

Concluding remarks

Over the last three decades, a considerable amount of detailed knowledge has accumulated that has enabled us to understand how the yersiniae colonise tissues and combat host defences during infection. While the Yersinia T3SS is perhaps the best understood system of its kind, many questions remain unanswered. For example, fully elucidating the function of YopM will offer an important step change, as will understanding more clearly the global molecular mechanisms that underpin the regulatory relationships that must exist between the T3SS system and the adhesins. It is also important to try to understand the relationships that exist between the different adhesins, how they compensate for each other, and which environmental signals dictate their site-specific expression. Finally, although the structures of many of the adhesins have been elucidated, there is certainly a need to better understand how they interact with different host ligands. While significant progress has been made in defining this sophisticated and finely tuned arsenal of virulence determinants, much more work is required to fully appreciate the success of the yersiniae as pathogens.

Competing interests

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References

- Achtman M, Zurth K, Morelli G, *et al.*: ***Yersinia pestis*, the cause of plague, is a recently emerged clone of *Yersinia pseudotuberculosis*.** *Proc Natl Acad Sci U S A*. 1999; **96**(24): 14043–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Achtman M, Morelli G, Zhu P, *et al.*: **Microevolution and history of the plague bacillus, *Yersinia pestis*.** *Proc Natl Acad Sci U S A*. 2004; **101**(51): 17837–42.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
- Prentice MB, Rahallison L: **Plague.** *Lancet*. 2007; **369**(9568): 1196–207.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Stenseth NC, Atshabar BB, Begon M, *et al.*: **Plague: past, present, and future.** *PLoS Med*. 2008; **5**(1): e3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Guiyoule A, Gerbaud G, Buchrieser C, *et al.*: **Transferable plasmid-mediated resistance to streptomycin in a clinical isolate of *Yersinia pestis*.** *Emerg Infect Dis*. 2001; **7**(1): 43–8.
[PubMed Abstract](#) | [Free Full Text](#)
- Wren BW: **The yersiniae—a model genus to study the rapid evolution of bacterial pathogens.** *Nat Rev Microbiol*. 2003; **1**(1): 55–64.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Trosky JE, Liverman AD, Orth K: ***Yersinia* outer proteins: Yops.** *Cell Microbiol*. 2008; **10**(3): 557–65.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Diepold A, Armitage JP: **Type III secretion systems: the bacterial flagellum and the injectisome.** *Philos Trans R Soc Lond, B Biol Sci*. 2015; **370**(1679): pii: 20150020.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
- Diepold A, Amstutz M, Abel S, *et al.*: **Deciphering the assembly of the *Yersinia* type III secretion injectisome.** *EMBO J*. 2010; **29**(11): 1928–40.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
- Edqvist PJ, Olsson J, Lavander M, *et al.*: **YscP and YscU regulate substrate specificity of the *Yersinia* type III secretion system.** *J Bacteriol*. 2003; **185**(7): 2259–66.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Sorg I, Wagner S, Amstutz M, *et al.*: **YscU recognizes translocators as export substrates of the *Yersinia* injectisome.** *EMBO J*. 2007; **26**(12): 3015–24.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
- Jackson MW, Plano GV: **Interactions between type III secretion apparatus components from *Yersinia pestis* detected using the yeast two-hybrid system.** *FEMS Microbiol Lett*. 2000; **186**(1): 85–90.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Zarivach R, Vuckovic M, Deng W, *et al.*: **Structural analysis of a prototypical ATPase from the type III secretion system.** *Nat Struct Mol Biol*. 2007; **14**(2): 131–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Woestyn S, Allaoui A, Wattiau P, *et al.*: **YscN, the putative energizer of the *Yersinia* Yop secretion machinery.** *J Bacteriol*. 1994; **176**(6): 1561–9.
[PubMed Abstract](#) | [Free Full Text](#)
- Hoiczky E, Blobel G: **Polymerization of a single protein of the pathogen *Yersinia enterocolitica* into needles punctures eukaryotic cells.** *Proc Natl Acad Sci U S A*. 2001; **98**(8): 4669–74.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | **F1000 Recommendation**
- Cornelis GR: **The type III secretion injectisome.** *Nat Rev Microbiol*. 2006; **4**(11):

- 811–25.
[PubMed Abstract](#) | [Publisher Full Text](#)
17. Stainier I, Bleves S, Josenhans C, *et al.*: **YscP, a *Yersinia* protein required for Yop secretion that is surface exposed, and released in low Ca²⁺.** *Mol Microbiol.* 2000; 37(5): 1005–18.
[PubMed Abstract](#) | [Publisher Full Text](#)
 18. Wagner S, Sorg I, Degiacomi M, *et al.*: **The helical content of the YscP molecular ruler determines the length of the *Yersinia* injectisome.** *Mol Microbiol.* 2009; 71(3): 692–701.
[PubMed Abstract](#) | [Publisher Full Text](#)
 19. Payne PL, Straley SC: **YscP of *Yersinia pestis* is a secreted component of the Yop secretion system.** *J Bacteriol.* 1999; 181(9): 2852–62.
[PubMed Abstract](#) | [Free Full Text](#)
 20. Kudryashev M, Diepold A, Amstutz M, *et al.*: ***Yersinia enterocolitica* type III secretion injectisomes form regularly spaced clusters, which incorporate new machines upon activation.** *Mol Microbiol.* 2015; 95(5): 875–84.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 21. Broz P, Mueller CA, Müller SA, *et al.*: **Function and molecular architecture of the *Yersinia* injectisome tip complex.** *Mol Microbiol.* 2007; 65(5): 1311–20.
[PubMed Abstract](#) | [Publisher Full Text](#)
 22. Mueller CA, Broz P, Müller SA, *et al.*: **The V-antigen of *Yersinia* forms a distinct structure at the tip of injectisome needles.** *Science.* 2005; 310(5748): 674–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 23. Håkansson S, Bergman T, Vanooteghem JC, *et al.*: **YopB and YopD constitute a novel class of *Yersinia* Yop proteins.** *Infect Immun.* 1993; 61(1): 71–80.
[PubMed Abstract](#) | [Free Full Text](#)
 24. Neyt C, Cornelis GR: **Role of SycD, the chaperone of the *Yersinia* Yop translocators YopB and YopD.** *Mol Microbiol.* 1999; 31(1): 143–56.
[PubMed Abstract](#) | [Publisher Full Text](#)
 25. Bröms JE, Forslund AL, Forsberg A, *et al.*: **Dissection of homologous translocon operons reveals a distinct role for YopD in type III secretion by *Yersinia pseudotuberculosis*.** *Microbiology.* 2003; 149(Pt 9): 2615–26.
[PubMed Abstract](#) | [Publisher Full Text](#)
 26. Holmström A, Olsson J, Cherepanov P, *et al.*: **LcrV is a channel size-determining component of the Yop effector translocon of *Yersinia*.** *Mol Microbiol.* 2001; 39(3): 620–32.
[PubMed Abstract](#) | [Publisher Full Text](#)
 27. DeBord KL, Lee VT, Schneewind O: **Roles of LcrG and LcrV during type III targeting of effector Yops by *Yersinia enterocolitica*.** *J Bacteriol.* 2001; 183(15): 4588–98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 28. Lee VT, Schneewind O: **Type III machines of pathogenic *Yersinia* secrete virulence factors into the extracellular milieu.** *Mol Microbiol.* 1999; 31(6): 1619–29.
[PubMed Abstract](#) | [Publisher Full Text](#)
 29. Cheng LW, Schneewind O: ***Yersinia enterocolitica* TyeA, an intracellular regulator of the type III machinery, is required for specific targeting of YopE, YopH, YopM, and YopN into the cytosol of eukaryotic cells.** *J Bacteriol.* 2000; 182(11): 3183–90.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 30. Cornelis GR, Wolf-Watz H: **The *Yersinia* Yop virulon: a bacterial system for subverting eukaryotic cells.** *Mol Microbiol.* 1997; 23(5): 861–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 31. Woestyn S, Sory MP, Boland A, *et al.*: **The cytosolic SycE and SycH chaperones of *Yersinia* protect the region of YopE and YopH involved in translocation across eukaryotic cell membranes.** *Mol Microbiol.* 1996; 20(6): 1261–71.
[PubMed Abstract](#) | [Publisher Full Text](#)
 32. Cheng LW, Schneewind O: ***Yersinia enterocolitica* type III secretion. On the role of SycE in targeting YopE into HeLa cells.** *J Biol Chem.* 1999; 274(31): 22102–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 33. Evdokimov AG, Tropea JE, Routzahn KM, *et al.*: **Crystal structure of the *Yersinia pestis* GTPase activator YopE.** *Protein Sci.* 2002; 11(2): 401–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 34. Black DS, Bliska JB: **The RhoGAP activity of the *Yersinia pseudotuberculosis* cytotoxin YopE is required for antiphagocytic function and virulence.** *Mol Microbiol.* 2000; 37(3): 515–27.
[PubMed Abstract](#) | [Publisher Full Text](#)
 35. Aili M, Isaksson EL, Hallberg B, *et al.*: **Functional analysis of the YopE GTPase-activating protein (GAP) activity of *Yersinia pseudotuberculosis*.** *Cell Microbiol.* 2006; 8(6): 1020–33.
[PubMed Abstract](#) | [Publisher Full Text](#)
 36. Andor A, Trülsch K, Essler M, *et al.*: **YopE of *Yersinia*, a GAP for Rho GTPases, selectively modulates Rac-dependent actin structures in endothelial cells.** *Cell Microbiol.* 2001; 3(5): 301–10.
[PubMed Abstract](#) | [Publisher Full Text](#)
 37. Shao F, Merritt PM, Bao Z, *et al.*: **A *Yersinia* effector and a *Pseudomonas* virulence protein define a family of cysteine proteases functioning in bacterial pathogenesis.** *Cell.* 2002; 109(5): 575–88.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 38. Aepfelbacher M, Trasak C, Wiedemann A, *et al.*: **Rho-GTP binding proteins in *Yersinia* target cell interaction.** *Adv Exp Med Biol.* 2003; 529: 65–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
 39. Schmidt G: ***Yersinia enterocolitica* outer protein T (YopT).** *Eur J Cell Biol.* 2011; 90(11): 955–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 40. Barz C, Abahji TN, Trülsch K, *et al.*: **The *Yersinia* Ser/Thr protein kinase YpkA/YopO directly interacts with the small GTPases RhoA and Rac-1.** *FEBS Lett.* 2000; 482(1–2): 139–43.
[PubMed Abstract](#) | [Publisher Full Text](#)
 41. Groves E, Rittinger K, Amstutz M, *et al.*: **Sequestering of Rac by the *Yersinia* effector YopO blocks Fcγ receptor-mediated phagocytosis.** *J Biol Chem.* 2010; 285(6): 4087–98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 42. Navarro L, Koller A, Nordfelth R, *et al.*: **Identification of a molecular target for the *Yersinia* protein kinase A.** *Mol Cell.* 2007; 26(4): 465–77.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 43. Juris SJ, Rudolph AE, Huddler D, *et al.*: **A distinctive role for the *Yersinia* protein kinase: actin binding, kinase activation, and cytoskeleton disruption.** *Proc Natl Acad Sci U S A.* 2000; 97(17): 9431–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 44. Lee WL, Grimes JM, Robinson RC: ***Yersinia* effector YopO uses actin as bait to phosphorylate proteins that regulate actin polymerization.** *Nat Struct Mol Biol.* 2015; 22(3): 248–55.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 45. Cantwell AM, Bubeck SS, Dube PH: **YopH inhibits early pro-inflammatory cytokine responses during plague pneumonia.** *BMC Immunol.* 2010; 11: 29.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 46. Logsdon LK, Meccas J: **Requirement of the *Yersinia pseudotuberculosis* effectors YopH and YopE in colonization and persistence in intestinal and lymph tissues.** *Infect Immun.* 2003; 71(8): 4595–607.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 47. Trülsch K, Sporleder T, Igwe EI, *et al.*: **Contribution of the major secreted yops of *Yersinia enterocolitica* O:8 to pathogenicity in the mouse infection model.** *Infect Immun.* 2004; 72(9): 5227–34.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 48. Deuretzbacher A, Czymmek N, Reimer R, *et al.*: **Beta1 integrin-dependent engulfment of *Yersinia enterocolitica* by macrophages is coupled to the activation of autophagy and suppressed by type III protein secretion.** *J Immunol.* 2009; 183(9): 5847–60.
[PubMed Abstract](#) | [Publisher Full Text](#)
 49. Rosqvist R, Skurnik M, Wolf-Watz H: **Increased virulence of *Yersinia pseudotuberculosis* by two independent mutations.** *Nature.* 1988; 334(6182): 522–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
 50. Bölin I, Wolf-Watz H: **The plasmid-encoded Yop2b protein of *Yersinia pseudotuberculosis* is a virulence determinant regulated by calcium and temperature at the level of transcription.** *Mol Microbiol.* 1988; 2(2): 237–45.
[PubMed Abstract](#) | [Publisher Full Text](#)
 51. Bliska JB, Guan KL, Dixon JE, *et al.*: **Tyrosine phosphate hydrolysis of host proteins by an essential *Yersinia* virulence determinant.** *Proc Natl Acad Sci U S A.* 1991; 88(4): 1187–91.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 52. Navarro L, Alto NM, Dixon JE: **Functions of the *Yersinia* effector proteins in inhibiting host immune responses.** *Curr Opin Microbiol.* 2005; 8(1): 21–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 53. Grosdent N, Maridonneau-Parini I, Sory MP, *et al.*: **Role of Yops and adhesins in resistance of *Yersinia enterocolitica* to phagocytosis.** *Infect Immun.* 2002; 70(8): 4165–76.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 54. Shao F: **Biochemical functions of *Yersinia* type III effectors.** *Curr Opin Microbiol.* 2008; 11(1): 21–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 55. Matsumoto H, Young GM: **Translocated effectors of *Yersinia*.** *Curr Opin Microbiol.* 2009; 12(1): 94–100.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 56. Cornelis GR: **The *Yersinia* Ysc-Yop ‘type III’ weaponry.** *Nat Rev Mol Cell Biol.* 2002; 3(10): 742–52.
[PubMed Abstract](#) | [Publisher Full Text](#)
 57. Cornelis GR: ***Yersinia* type III secretion: send in the effectors.** *J Cell Biol.* 2002; 158(3): 401–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 58. Mukherjee S, Keitany G, Li Y, *et al.*: ***Yersinia* YopJ acetylates and inhibits kinase activation by blocking phosphorylation.** *Science.* 2006; 312(5777): 1211–4.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 59. Orth K, Xu Z, Mudgett MB, *et al.*: **Disruption of signaling by *Yersinia* effector YopJ, a ubiquitin-like protein protease.** *Science.* 2000; 290(5496): 1594–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 60. Mittal R, Peak-Chew SY, McMahon HT: **Acetylation of MEK2 and I kappa B kinase (IKK) activation loop residues by YopJ inhibits signaling.** *Proc Natl Acad Sci U S A.* 2006; 103(49): 18574–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)

61. Ruckdeschel K, Harb S, Roggenkamp A, *et al.*: ***Yersinia enterocolitica* impairs activation of transcription factor NF-kappaB: involvement in the induction of programmed cell death and in the suppression of the macrophage tumor necrosis factor alpha production.** *J Exp Med.* 1998; 187(7): 1069–79.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
62. Boland A, Cornelis GR: **Role of YopP in suppression of tumor necrosis factor alpha release by macrophages during *Yersinia* infection.** *Infect Immun.* 1998; 66(5): 1878–84.
[PubMed Abstract](#) | [Free Full Text](#)
63. Schoberle TJ, Chung LK, McPhee JB, *et al.*: **Uncovering an Important Role for YopJ in the Inhibition of Caspase-1 in Activated Macrophages and Promoting *Yersinia pseudotuberculosis* Virulence.** *Infect Immun.* 2016; 84(4): 1062–72.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
64. Boland A, Sory MP, Iriarte M, *et al.*: **Status of YopM and YopN in the *Yersinia* Yop virulon: YopM of *Y. enterocolitica* is internalized inside the cytosol of PU5-1.8 macrophages by the YopB, D, N delivery apparatus.** *EMBO J.* 1996; 15(19): 5191–201.
[PubMed Abstract](#) | [Free Full Text](#)
65. Bertrand J, Ruther C, Scharnert J, *et al.*: **The bacterial effector protein YopM is a selfdelivering immune therapeutic agent that reduces inflammation in rheumatoid arthritis.** *Ann Rheum Dis.* 2010; 69: A47.
[Publisher Full Text](#) | [F1000 Recommendation](#)
66. Höfling S, Grabowski B, Norkowski S, *et al.*: **Current activities of the *Yersinia* effector protein YopM.** *Int J Med Microbiol.* 2015; 305(3): 424–32.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
67. Hentschke M, Berneking L, Belmar Campos C, *et al.*: ***Yersinia* virulence factor YopM induces sustained RSK activation by interfering with dephosphorylation.** *PLoS One.* 2010; 5(10): pii: e13165.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
68. Benabdillah R, Mota LJ, Lützelshwab S, *et al.*: **Identification of a nuclear targeting signal in YopM from *Yersinia* spp.** *Microb Pathog.* 2004; 36(5): 247–61.
[PubMed Abstract](#) | [Publisher Full Text](#)
69. Skrzypek E, Myers-Morales T, Whiteheart SW, *et al.*: **Application of a *Saccharomyces cerevisiae* model to study requirements for trafficking of *Yersinia pestis* YopM in eucaryotic cells.** *Infect Immun.* 2003; 71(2): 937–47.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
70. Skrzypek E, Cowan C, Straley SC: **Targeting of the *Yersinia pestis* YopM protein into HeLa cells and intracellular trafficking to the nucleus.** *Mol Microbiol.* 1998; 30(5): 1051–65.
[PubMed Abstract](#) | [Publisher Full Text](#)
71. Ye Z, Kerschen EJ, Cohen DA, *et al.*: **Gr1⁺ cells control growth of YopM-negative *Yersinia pestis* during systemic plague.** *Infect Immun.* 2009; 77(9): 3791–806.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
72. Kerschen EJ, Cohen DA, Kaplan AM, *et al.*: **The plague virulence protein YopM targets the innate immune response by causing a global depletion of NK cells.** *Infect Immun.* 2004; 72(8): 4589–602.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
73. LaRock CN, Cookson BT: **The *Yersinia* virulence effector YopM binds caspase-1 to arrest inflammasome assembly and processing.** *Cell Host Microbe.* 2012; 12(6): 799–805.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
74. Chung LK, Philip NH, Schmidt VA, *et al.*: **IQGAP1 is important for activation of caspase-1 in macrophages and is targeted by *Yersinia pestis* type III effector YopM.** *MBio.* 2014; 5(4): e01402–14.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
75. Isberg RR, Voorhis DL, Falkow S: **Identification of invasins: a protein that allows enteric bacteria to penetrate cultured mammalian cells.** *Cell.* 1987; 50(5): 769–78.
[PubMed Abstract](#) | [Publisher Full Text](#)
76. Parkhill J, Wren BW, Thomson NR, *et al.*: **Genome sequence of *Yersinia pestis*, the causative agent of plague.** *Nature.* 2001; 413(6855): 523–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
77. Clark MA, Hirst BH, Jepson MA: **M-cell surface beta1 integrin expression and invasin-mediated targeting of *Yersinia pseudotuberculosis* to mouse Peyer's patch M cells.** *Infect Immun.* 1998; 66(3): 1237–43.
[PubMed Abstract](#) | [Free Full Text](#)
78. Hamburger ZA, Brown MS, Isberg RR, *et al.*: **Crystal structure of invasin: a bacterial integrin-binding protein.** *Science.* 1999; 286(5438): 291–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
79. Isberg RR, Swain A, Falkow S: **Analysis of expression and thermoregulation of the *Yersinia pseudotuberculosis* inv gene with hybrid proteins.** *Infect Immun.* 1988; 56(8): 2133–8.
[PubMed Abstract](#) | [Free Full Text](#)
80. Pepe JC, Badger JL, Miller VL: **Growth phase and low pH affect the thermal regulation of the *Yersinia enterocolitica* inv gene.** *Mol Microbiol.* 1994; 11(1): 123–35.
[PubMed Abstract](#) | [Publisher Full Text](#)
81. Grassl GA, Bohn E, Müller Y, *et al.*: **Interaction of *Yersinia enterocolitica* with epithelial cells: invasin beyond invasion.** *Int J Med Microbiol.* 2003; 293(1): 41–54.
[PubMed Abstract](#) | [Publisher Full Text](#)
82. Uliczka F, Pisano F, Kochut A, *et al.*: **Monitoring of gene expression in bacteria during infections using an adaptable set of bioluminescent, fluorescent and colorigenic fusion vectors.** *PLoS One.* 2011; 6(6): e20425.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
83. Nagel G, Lahrz A, Dersch P: **Environmental control of invasin expression in *Yersinia pseudotuberculosis* is mediated by regulation of RovA, a transcriptional activator of the SlyA/Hor family.** *Mol Microbiol.* 2001; 41(6): 1249–6.
[PubMed Abstract](#) | [Publisher Full Text](#)
84. Revell PA, Miller VL: **A chromosomally encoded regulator is required for expression of the *Yersinia enterocolitica* inv gene and for virulence.** *Mol Microbiol.* 2000; 35(3): 677–85.
[PubMed Abstract](#) | [Publisher Full Text](#)
85. Ellison DW, Young B, Nelson K, *et al.*: **YmoA negatively regulates expression of invasin from *Yersinia enterocolitica*.** *J Bacteriol.* 2003; 185(24): 7153–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
86. Heroven AK, Nagel G, Tran HJ, *et al.*: **RovA is autoregulated and antagonizes H-NS-mediated silencing of invasin and rovA expression in *Yersinia pseudotuberculosis*.** *Mol Microbiol.* 2004; 53(3): 871–88.
[PubMed Abstract](#) | [Publisher Full Text](#)
87. Ellison DW, Miller VL: **H-NS represses inv transcription in *Yersinia enterocolitica* through competition with RovA and interaction with YmoA.** *J Bacteriol.* 2006; 188(14): 5101–12.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
88. Heroven AK, Dersch P: **RovM, a novel LysR-type regulator of the virulence activator gene rovA, controls cell invasion, virulence and motility of *Yersinia pseudotuberculosis*.** *Mol Microbiol.* 2006; 62(5): 1469–83.
[PubMed Abstract](#) | [Publisher Full Text](#)
89. Mühlenkamp M, Oberhettinger P, Leo JC, *et al.*: ***Yersinia* adhesin A (YadA)—beauty & beast.** *Int J Med Microbiol.* 2015; 305(2): 252–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
90. Skurnik M, Toivanen P: **LcrF is the temperature-regulated activator of the yadA gene of *Yersinia enterocolitica* and *Yersinia pseudotuberculosis*.** *J Bacteriol.* 1992; 174(6): 2047–51.
[PubMed Abstract](#) | [Free Full Text](#)
91. Zaleska M, Lounatmaa K, Nurminen M, *et al.*: **A novel virulence-associated cell surface structure composed of 47-kd protein subunits in *Yersinia enterocolitica*.** *EMBO J.* 1985; 4(4): 1013–8.
[PubMed Abstract](#) | [Free Full Text](#)
92. Hoiczky E, Roggenkamp A, Reichenbecher M, *et al.*: **Structure and sequence analysis of *Yersinia* YadA and *Moraxella* UspAs reveal a novel class of adhesins.** *EMBO J.* 2000; 19(22): 5989–99.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
93. Skurnik M, Wolf-Watz H: **Analysis of the yopA gene encoding the Yop1 virulence determinants of *Yersinia* spp.** *Mol Microbiol.* 1989; 3(4): 517–29.
[PubMed Abstract](#) | [Publisher Full Text](#)
94. Forman S, Wulff CR, Myers-Morales T, *et al.*: **yadBC of *Yersinia pestis*, a new virulence determinant for bubonic plague.** *Infect Immun.* 2008; 76(2): 578–87.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
95. Mikula KM, Kolodziejczyk R, Goldman A: ***Yersinia* infection tools—characterization of structure and function of adhesins.** *Front Cell Infect Microbiol.* 2013; 2: 169.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
96. Visser LG, Annema A, van Furth R: **Role of Yops in inhibition of phagocytosis and killing of opsonized *Yersinia enterocolitica* by human granulocytes.** *Infect Immun.* 1995; 63(7): 2570–5.
[PubMed Abstract](#) | [Free Full Text](#)
97. El Tahir Y, Skurnik M: **YadA, the multifaceted *Yersinia* adhesin.** *Int J Med Microbiol.* 2001; 291(3): 209–18.
[PubMed Abstract](#) | [Publisher Full Text](#)
98. Terti R, Skurnik M, Vartio T, *et al.*: **Adhesion protein YadA of *Yersinia* species mediates binding of bacteria to fibronectin.** *Infect Immun.* 1992; 60(7): 3021–4.
[PubMed Abstract](#) | [Free Full Text](#)
99. Flügel A, Schulze-Koops H, Heesemann J, *et al.*: **Interaction of enteropathogenic *Yersinia enterocolitica* with complex basement membranes and the extracellular matrix proteins collagen type IV, laminin-1 and -2, and nidogen/entactin.** *J Biol Chem.* 1994; 269(47): 29732–8.
[PubMed Abstract](#)
100. Keller B, Mühlenkamp M, Deuschle E, *et al.*: ***Yersinia enterocolitica* exploits different pathways to accomplish adhesion and toxin injection into host cells.** *Cell Microbiol.* 2015; 17(8): 1179–204.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
101. Deuschle E, Keller B, Siegfried A, *et al.*: **Role of β 1 integrins and bacterial adhesins for Yop injection into leukocytes in *Yersinia enterocolitica* systemic mouse infection.** *Int J Med Microbiol.* 2016; 306(2): 77–88.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
102. Eitel J, Dersch P: **The YadA protein of *Yersinia pseudotuberculosis* mediates high-efficiency uptake into human cells under environmental conditions in which invasin is repressed.** *Infect Immun.* 2002; 70(9): 4880–91.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
103. Heise T, Dersch P: **Identification of a domain in *Yersinia* virulence factor YadA that is crucial for extracellular matrix-specific cell adhesion and uptake.**

- Proc Natl Acad Sci U S A.* 2006; **103**(9): 3375–80.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
104. Mantle M, Husar SD: **Binding of *Yersinia enterocolitica* to purified, native small intestinal mucins from rabbits and humans involves interactions with the mucin carbohydrate moiety.** *Infect Immun.* 1994; **62**(4): 1219–27.
[PubMed Abstract](#) | [Free Full Text](#)
 105. Biedzka-Sarek M, Jarva H, Hyytiäinen H, *et al.*: **Characterization of complement factor H binding to *Yersinia enterocolitica* serotype O:3.** *Infect Immun.* 2008; **76**(9): 4100–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 106. Biedzka-Sarek M, Salmenlinna S, Gruber M, *et al.*: **Functional mapping of YdaA- and Ail-mediated binding of human factor H to *Yersinia enterocolitica* serotype O:3.** *Infect Immun.* 2008; **76**(11): 5016–27.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 107. Kirjavainen V, Jarva H, Biedzka-Sarek M, *et al.*: ***Yersinia enterocolitica* serum resistance proteins YdaA and ail bind the complement regulator C4b-binding protein.** *PLoS Pathog.* 2008; **4**(8): e1000140.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 108. Miller VL, Falkow S: **Evidence for two genetic loci in *Yersinia enterocolitica* that can promote invasion of epithelial cells.** *Infect Immun.* 1988; **56**(5): 1242–8.
[PubMed Abstract](#) | [Free Full Text](#)
 109. Miller VL, Bliska JB, Falkow S: **Nucleotide sequence of the *Yersinia enterocolitica* ail gene and characterization of the Ail protein product.** *J Bacteriol.* 1990; **172**(2): 1062–9.
[PubMed Abstract](#) | [Free Full Text](#)
 110. Miller VL, Mekalanos JJ: **A novel suicide vector and its use in construction of insertion mutations: osmoregulation of outer membrane proteins and virulence determinants in *Vibrio cholerae* requires toxR.** *J Bacteriol.* 1988; **170**(6): 2575–83.
[PubMed Abstract](#) | [Free Full Text](#)
 111. **F** Yamashita S, Lukacik P, Barnard TJ, *et al.*: **Structural insights into Ail-mediated adhesion in *Yersinia pestis*.** *Structure.* 2011; **19**(11): 1672–82.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 112. **F** Bartra SS, Ding Y, Fujimoto LM, *et al.*: ***Yersinia pestis* uses the Ail outer membrane protein to recruit vitronectin.** *Microbiology.* 2015; **161**(11): 2174–83.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 113. Yang Y, Merriam JJ, Mueller JP, *et al.*: **The psa locus is responsible for thermotolerant binding of *Yersinia pseudotuberculosis* to cultured cells.** *Infect Immun.* 1996; **64**(7): 2483–9.
[PubMed Abstract](#) | [Free Full Text](#)
 114. **F** Felek S, Muszyński A, Carlson RW, *et al.*: **Phosphoglucosyltransferase of *Yersinia pestis* is required for autoaggregation and polymyxin B resistance.** *Infect Immun.* 2010; **78**(3): 1163–75.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 115. Pierson DE, Falkow S: **The ail gene of *Yersinia enterocolitica* has a role in the ability of the organism to survive serum killing.** *Infect Immun.* 1993; **61**(5): 1846–52.
[PubMed Abstract](#) | [Free Full Text](#)
 116. Ben-Efraim S, Aronson M, Bichowsky-Slomnicki L: **New antigenic component of *Pasteurella pestis* formed under specified conditions of pH and temperature.** *J Bacteriol.* 1961; **81**(5): 704–14.
[PubMed Abstract](#) | [Free Full Text](#)
 117. Bichowsky-Slomnicki L, Ben-Efraim S: **Biological activities in extracts of *Pasteurella pestis* and their relation to the “pH 6 antigen”.** *J Bacteriol.* 1963; **86**(1): 101–11.
[PubMed Abstract](#) | [Free Full Text](#)
 118. Lindler LE, Klempner MS, Straley SC: ***Yersinia pestis* pH 6 antigen: genetic, biochemical, and virulence characterization of a protein involved in the pathogenesis of bubonic plague.** *Infect Immun.* 1990; **58**(8): 2569–77.
[PubMed Abstract](#) | [Free Full Text](#)
 119. Yang Y, Isberg RR: **Transcriptional regulation of the *Yersinia pseudotuberculosis* pH6 antigen adhesin by two envelope-associated components.** *Mol Microbiol.* 1997; **24**(3): 499–510.
[PubMed Abstract](#) | [Publisher Full Text](#)
 120. Lindler LE, Tall BD: ***Yersinia pestis* pH 6 antigen forms fimbriae and is induced by intracellular association with macrophages.** *Mol Microbiol.* 1993; **8**(2): 311–24.
[PubMed Abstract](#) | [Publisher Full Text](#)
 121. Payne D, Tatham D, Williamson ED, *et al.*: **The pH 6 antigen of *Yersinia pestis* binds to beta1-linked galactosyl residues in glycosphingolipids.** *Infect Immun.* 1998; **66**(9): 4545–8.
[PubMed Abstract](#) | [Free Full Text](#)
 122. Makoveichuk E, Cherepanov P, Lundberg S, *et al.*: **pH6 antigen of *Yersinia pestis* interacts with plasma lipoproteins and cell membranes.** *J Lipid Res.* 2003; **44**(2): 320–30.
[PubMed Abstract](#) | [Publisher Full Text](#)
 123. Zav'yalov VP, Abramov VM, Cherepanov PG, *et al.*: **pH6 antigen (PsaA protein) of *Yersinia pestis*, a novel bacterial Fc-receptor.** *FEMS Immunol Med Microbiol.* 1996; **14**(1): 53–7.
[PubMed Abstract](#) | [Publisher Full Text](#)
 124. Iriarte M, Vanooteghem JC, Delor I, *et al.*: **The Myf fibrillae of *Yersinia enterocolitica*.** *Mol Microbiol.* 1993; **9**(3): 507–20.
[PubMed Abstract](#) | [Publisher Full Text](#)
 125. Beesley ED, Brubaker RR, Janssen WA, *et al.*: **Pesticins. 3. Expression of coagulase and mechanism of fibrinolysis.** *J Bacteriol.* 1967; **94**(1): 19–26.
[PubMed Abstract](#) | [Free Full Text](#)
 126. Degen JL, Bugge TH, Goguen JD: **Fibrin and fibrinolysis in infection and host defense.** *J Thromb Haemost.* 2007; **5**(Suppl 1): 24–31.
[PubMed Abstract](#) | [Publisher Full Text](#)
 127. Plow EF, Ploplis VA, Carmeliet P, *et al.*: **Plasminogen and cell migration *in vivo*.** *Fibrinolysis Proteol.* 1999; **13**(2): 49–53.
[Publisher Full Text](#)
 128. **F** Sebbane F, Jarrett CO, Gardner D, *et al.*: **Role of the *Yersinia pestis* plasminogen activator in the incidence of distinct septicemic and bubonic forms of flea-borne plague.** *Proc Natl Acad Sci U S A.* 2006; **103**(14): 5526–30.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 129. Haiko J, Kukkonen M, Ravaniti JJ, *et al.*: **The single substitution I259T, conserved in the plasminogen activator Pla of pandemic *Yersinia pestis* branches, enhances fibrinolytic activity.** *J Bacteriol.* 2009; **191**(15): 4758–66.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 130. Kienle Z, Emödy L, Svanborg C, *et al.*: **Adhesive properties conferred by the plasminogen activator of *Yersinia pestis*.** *J Gen Microbiol.* 1992; **138**(Pt 8): 1679–87.
[PubMed Abstract](#) | [Publisher Full Text](#)
 131. Lähteenmäki K, Kukkonen M, Korhonen TK: **The Pla surface protease/adhesin of *Yersinia pestis* mediates bacterial invasion into human endothelial cells.** *FEBS Lett.* 2001; **504**(1–2): 69–72.
[PubMed Abstract](#) | [Publisher Full Text](#)
 132. **F** Hinnebusch BJ, Rudolph AE, Cherepanov P, *et al.*: **Role of *Yersinia* murine toxin in survival of *Yersinia pestis* in the midgut of the flea vector.** *Science.* 2002; **296**(5568): 733–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 133. Wiechmann A: **Quorum sensing and the regulation of multicellular behaviour in *Yersinia pseudotuberculosis*.** (PhD Thesis. The University of Nottingham).
 134. Schraidt O, Lefebvre MD, Brunner MJ, *et al.*: **Topology and organization of the *Salmonella typhimurium* type III secretion needle complex components.** *PLoS Pathog.* 2010; **6**(4): e1000824.
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Institute of Infection, Immunity and Inflammation, and Institute of Molecular, Cell and Systems Biology, University of Glasgow, Glasgow, UK

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2. James Bliska

Center for Infectious Diseases and Department of Molecular Genetics and Microbiology, Stony Brook University, Stony Brook, NY, USA

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