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# The pathogenic *Yersiniae*—advances in the understanding of physiology and virulence

Matthew S. Francis\*

Department of Molecular Biology and Umeå Centre for Microbial Research, Umeå University, Umeå, Sweden

\*Correspondence: matthew.francis@molbiol.umu.se

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Yousef A. Kwaik, University of Louisville School of Medicine, USA

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Of the ~16 *Yersinia* species, only *Y. pestis*, *Y. pseudotuberculosis*, and *Y. enterocolitica* are pathogenic to humans (Koornhof et al., 1999; Smego et al., 1999). The zoonotic obligate pathogen *Y. pestis* is the causal agent of plague, a systemic disease that is usually fatal if left untreated. Free-living *Y. enterocolitica* and *Y. pseudotuberculosis* are the agents of yersiniosis, a rarely systemic gastrointestinal disease. At the forefront of *Yersinia* research are studies of host cell contact, protein secretion, pathogenesis, immunity and the host response, nutrient sensing and sequestration and the control of gene expression. In this special research topic on the pathogenic *Yersiniae* is a compilation of reviews and research articles that highlight current knowledge and new developments in these areas of *Yersinia* pathophysiology.

## BACTERIA–HOST CELL CONTACT

*Yersinia* is armored with diverse membrane anchored surface adhesins that each contribute to pathogen–host interactions. Mikula et al. (2013) explore the structure and virulence function of the most prominent of these adhesins. They describe salient roles of select adhesins in intestinal pathogenesis by enteric *Yersinia* and give insight on how altered adhesive potential through specific gene loss or gain may have contributed to *Y. pestis* lifestyle changes. Complementing this is Kolodziejek et al. (2012) that dissects specific physical properties and functional contributions of the esoteric Ail adhesin to *Y. pestis* infections.

## PROTEIN SECRETION

The Ysc-Yop type III secretion system (T3SS) is encoded on a virulence plasmid common to all human pathogenic *Yersinia* (Cornelis et al., 1998). This injectisome is believed to provide a conduit through which Yop effector toxins can be delivered from the bacterial cytoplasm into the eukaryotic cell cytosol in one step or two (Edgren et al., 2012). Dewoody et al. (2013) provide insight into the regulatory mechanisms controlling injectisome assembly and the hierarchal coordination of substrate secretion. One important regulatory mechanism is the YopN secretion plug, and this is the focus of a study by Joseph and Plano (2013) that demonstrate a stretch of sequence within YopN - corresponding to a site for chaperone binding - is also required for environmental control of Ysc-Yop secretion.

While *Yersinia* pathogenicity is correlated mostly to the plasmid encoded Ysc-Yop T3SS, von Tils et al. (2012) discuss the impact of type II secretion systems (T2SS)—found in the genomes of all pathogenic and non-pathogenic *Yersinia* alike—to bacterial survival in the environment and in the host.

## IMMUNITY AND PATHOGENESIS

Of the six known Ysc-Yop T3SS translocated effector toxins, YopM function remains enigmatic. As a consequence, Uittenbogaard et al. (2012) performed an exhaustive characterization of early host cell responsiveness to YopM of *Y. pestis*. This revealed exciting new molecular pathways potentially targeted by YopM. Early host responsiveness was also the focus of Vagima et al. (2012), which presents a role for bone marrow derived cells in the early sensing of lung infections by *Y. pestis*. Moreover, recognizing that cell death is a critical attribute of host immunity and microbial pathogenicity, Philip and Brodsky (2012) report on how cell death programs serve as both a *Yersinia* virulence strategy via T3SS-translocated YopJ effector function, as well as an elicitor of innate and adaptive immune responses designed to counteract *Yersinia* infections.

Critical in the evolution of *Y. pestis* has been the acquisition of the gene *pla* encoding an omptin-like outer membrane plasminogen activator protease (Pla). Korhonen et al. (2013) discuss this by summarizing features of controlled Pla protease activation, and its subsequent complex repertoire of interactions with host coagulation and fibrinolysis factors.

## NUTRIENT SENSING AND SEQUESTRATION

A growing theme in infection biology research is the link between carbon metabolism and virulence (Poncet et al., 2009; Rohmer et al., 2011). Heroven et al. (2012) explore this concept in *Yersinia* pathogenicity using global omics-based profiling. They establish that the carbon storage regulator (Csr) system is controlled by the cAMP receptor protein (Crp), and together customize virulence gene expression according to the prevailing nutrient availability during *Yersinia* infections.

A critical nutrient for growth of all life forms is iron. Rakin et al. (2012) describe an array of independent siderophore-mediated iron sequestration systems encoded by *Y. pestis* and the enteric *Yersinia*. They propose that by acquiring multiple alternative endogenous siderophore systems with unique physiological properties, *Yersinia* has gained the capacity to adapt and thrive in diverse environmental niches.

## GENE EXPRESSION CONTROL

Defining roles for small non-coding RNAs (ncRNAs) in regulation of gene expression dominates the infection biology landscape. Schiano and Lathem (2012) provide examples of small ncRNAs and various other post-transcriptional mechanisms in the regulation of virulence gene expression in *Yersinia*. They even propose that subtle sequence and/or regulatory differences found

in certain small ncRNAs could account for some of the acquired lifestyle changes of *Y. pestis*.

Conditions that threaten the integrity of the bacterial envelope are collectively termed extracytoplasmic stresses (ECS). Bacteria encode distinct regulatory pathways designed to maintain bacterial envelope integrity when challenged by ECS. Flores-Kim and Darwin (2012) describe how these ECS responsive pathways are also important for the control of *Yersinia* virulence determinants; particularly those embedded in the bacterial envelope such as integral membrane-spanning T3SSs and the well-known surface adhesin invasins. The environmental control of invasins gene expression in *Y. enterocolitica* is further explored by Brzostkowska et al. (2012). They demonstrate that OmpR, a response regulator of the EnvZ/OmpR two-component regulatory system, binds the *inv* promoter to directly negatively influence invasins expression.

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## NEW FRONTIERS

The systems biology era has revolutionized infectious biology research. Yang et al. (2012) illustrate the power of omics-based explorations in dissecting *Yersinia*-host cell interplay. In so doing, they provide a perspective on the future of omics-based research in benefitting our understanding of *Yersinia* cellular physiology and metabolism as well as host cellular responsiveness and immunity.

Finally, manned space exploration demands an evaluation into the effect of such conditions on microbial virulence and infectious disease communicability. Rosenzweig and Chopra (2012) explain that low shear force conditions reduce the virulence capacity of *Y. pestis*. Thus, knowledge of the mechanisms behind these repressive effects could benefit understanding of *Y. pestis* pathogenicity both in space and on earth.