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EDITORIAL

The influence of two-partner secretion systems on the virulence of *Acinetobacter baumannii*

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Acinetobacter baumannii are a major cause of hospital outbreaks, particularly in intensive care units, accounting for about 80% of reported hospital infections in some countries (Centers of Disease Control (CDC)). Its increasing capacity to resist a broad range of antimicrobials has placed *A. baumannii* as a serious global health threat. In a hospital setting, this opportunistic pathogen is associated with bacteremia, pneumonia/ventilator-associated pneumonia (VAP), meningitis or urinary tract infection.[1] Patients that have undergone major surgery or present severe burns are at particular risk of infection.

The process of colonization requires the crucial step of bacterial adhesion to host cells. Previous studies on the capacity of *A. baumannii* to adhere to biotic surfaces identified some important bacterial factors. These include OmpA, a trimeric outer membrane porin,[2] the outer membrane protein Bap[3] and Ata, a surface exposed trimeric autotransporter, that is also able to bind to various types of collagen, an extracellular matrix/basal membrane protein.[4]

In this issue, work by Perez and colleagues highlights the role of a previously uncharacterized virulence factor of *A. baumannii* AbH12O-A2, a highly adhesive clinical strain isolated in a hospital outbreak in Madrid.[5] Analysis of the recently sequenced genome of this strain allowed identification of AbFhaB/AbFhaC as a potential two-partner secretion (TPS) system.[5] TPS systems, widespread among Gram-negative bacteria, are a subfamily of the Type V secretion system, composed of two proteins, TpsB, the outer membrane pore-forming transporter, and TpsA, the cognate secreted exoprotein.[6] TpsA have the characteristic of being large β-helical proteins ranging from 100 to more than 500 kDa that are surface associated and/or released in the extracellular media. Consistent with this, deletion of *AbfhaC*, the gene encoding the predicted transporter, resulted in absence of detectable AbFhaB, the TpsA protein, in outer membrane vesicles of *A. baumannii* AbH12O-A2.[5] Analysis of this mutant strain lacking AbFhaC showed decreased adhesion to human cultured lung epithelial cells as well as fibronectin directly implicating this AbFhaB/AbFhaC TPS system in bacterial adhesion.[5]

The diverse functions previously described for TpsA proteins include adhesins such as the prototypical filamentous hemagglutinin FHA of *Bordetella pertussis*[7] or HMW1 and HMW2, the high molecular weight adhesins of *Haemophilus influenza*.[8] Over the last 25 years, FHA and HMW1/2 adhesins have been used as models to study the mechanism of TPS systems, leading to considerable structural and functional characterization. *In vitro* studies have shown that *B. pertussis* uses the FHA in the first steps of whooping-cough infections in synergy with pertussis toxin to adhere specifically to human ciliated epithelial cells and macrophages.[7,9] Indeed, FHA is the primary component of acellular pertussis vaccines.[10] Altogether diverse studies have highlighted FHA and HMW1/2 adhesins as key virulence factors in pathogenicity of Gram-negative bacteria and illustrate the importance of expanding our understanding of TpsA-mediated adhesion. However, beside the prototypical FHA and HMW1/2 proteins, only a few TPS systems have been shown to be involved in adhesion to eukaryotic cells. HprA-HprB produced by *Neisseria meningitidis* contribute to the interaction of meningococci with epithelial cells[11] but also play a major role in intracellular growth/survival[12]. In the case of enterotoxigenic *Escherichia coli* (ETEC), EtpA binds to the tip of flagella to mediate adhesion to intestinal cells.[13]

Hence the importance of the work made by Perez *et al.*, which demonstrate that adhesion of whole *A. baumannii* AbH12O-A2 bacteria to epithelial cells and fibronectin involves AbFhaB, a TpsA adhesin.[5] While it is true that a TpsA adhesin was first described by Darvish and

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coworkers in *A. baumannii* ATCC19606(T),[16] this study was solely based on recombinant proteins produced in *E. coli* and the direct role of TPS systems in *A. baumannii* remained unexplored. Indeed, Perez *et al.* work went further by also showing that inactivation of the AbFhaB/AbFhaC in the AbH12O-A2 clinical strain negatively impacts virulence in *C. elegans* and a mouse model of infection following intra-peritoneal inoculation.[5]

The fact that FHA is a component of the acellular vaccine against the whopping-cought infection[10] highlights the importance of studying TPS systems in human pathogens. We believe that efforts toward discovering other TpsA and understanding their role in *A. baumannii* pathogenicity need to be made. TpsA adhesins could be considered as potential targets for eliciting protective immunity against *A. baumannii* infections. Antibodies against these factors would block adherence and therefore protect against cRolonization. Indeed, this could be a very promising approach supported by recent data showing vaccination of mice with *A. baumannii* ATCC19606(T) recombinant TpsA-TpsB proteins confers protection against *A. baumannii* infection.[16]

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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