frontiers | Frontiers in Bacteriology

TYPE Editorial
PUBLISHED 09 December 2024
DOI 10.3389/fbrio.2024.1530714

OPEN ACCESS

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RECEIVED 19 November 2024
ACCEPTED 28 November 2024
PUBLISHED 09 December 2024

CITATION
Christodoulides M (2024) Editorial: Editors' showcase: pathogenesis, vaccines, and immunity of bacterial infections.
Front. Bacteriol. 3:1530714.
doi: 10.3389/fbrio.2024.1530714

Editorial: Editors' showcase: pathogenesis, vaccines, and immunity of bacterial infections

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KEYWORDS

vaccine, pathogenesis, immunity, infection, bacteria

Editorial on the Research Topic
Editors' showcase: pathogenesis, vaccines, and immunity of bacterial infections

The premise of this specialty section is to present our readership with articles of the highest quality on the interconnected themes of bacterial pathogenesis and virulence, immunity to infection and vaccines. Our ethos is succinctly expressed in the Specialty Grand Challenge overview that opens this section (Christodoulides, 2022). The Research Topic features a broad diversity of articles from members of the editorial board, with a focus on important Gram-positive and Gram-negative bacterial pathogens causing human disease, namely *Legionella pneumophila, Burkholderia pseudomallei, Staphylococcus* spp., *Yersinia pestis, Pseudomonas aeruginosa* and *Neisseria gonorrhoeae*.

P. aeruginosa is a metabolically flexible Gram-negative organism that is a major opportunistic pathogen causing nosocomial infections (Dolan, 2020), and because of increased carbapenem resistance globally, it is ranked as a 'high priority' organism by the World Health Organisation for the development and introduction or new antibacterials and vaccines (World Health Orgainisation, 2024). *P. aeruginosa* is a formidable bacterium that can express a plethora of virulence factors, Type-secretion systems, quorum-sensing pathways and exopolysaccharides, and core resistance mechanisms such as drug permeability barriers, a chromosomally encoded AmpC enzyme and six superfamilies of multidrug efflux pumps (Miller and Arias, 2024). Efflux pumps play a major role in the pathogenesis of *P. aeruginosa* infection and resistance to treatment and clearance. In their mini-review, Fernandes and Jorth discuss the controversial and opposing roles of *P. aeruginosa* efflux pumps in virulence regulation. Efflux pumps function principally to eject antibiotics from the bacterial cell, although evidence is presented that these pumps may have alternative functions that can influence the virulence of *P. aeruginosa*. Efflux pumps are recognised targets for therapeutic interventions (Fernandes and Jorth) and they are potential antigens for vaccine development (Silva et al., 2024). The authors conclude that there may be unexpected consequences to targeting efflux pumps in the context of antimicrobial resistance and bacterial pathogenesis that must be considered when developing therapies.

Vaccine research was represented by papers on the Gram-negative bacteria *Yersinia pestis* and *Neisseria gonorrhoeae*. *Y. pestis* is a bacterium that has literally plagued humanity throughout our recorded history. It is a significant risk to public health and a potential

bioweapon, and outbreaks of the plague are still reported today, but certainly not at pandemic levels. *Y. pestis* vaccines have consisted of killed whole cells, but these lack efficacy and provide only short-term protection against bubonic plague (Wang et al., 2013). Various strategies have been used to develop alternative vaccines, and Biryukov et al. described a live attenuated vaccine (LAV) derived from *Y. pestis* CO92 or C12 strains with a deletion of a type 3 secretion-associated gene (Δ*yscN*) or the *pgm* pigmentation locus, and cured of the pPst (PCP1) plasmid (CO92 *pgm*– pPst–). The authors evaluated the LAVs alone or combined with a dose of a protein subunit vaccine (rF1V or rV) in a mouse model of vaccination and challenge with aerosol (pneumonic) or subcutaneous (bubonic) virulent *Y. pestis*. The study was important in showing that lethal infection with virulent, nonencapsulated *Y. pestis* could be prevented with flexible vaccination strategies using i) LAV and rF1V or rV protein subunit vaccine, and ii) vaccines with post-exposure streptomycin antibiotic treatment.

Infection with the obligate human pathogen *N. gonorrhoeae* causes the sexually transmitted disease gonorrhoea, and like *P. aeruginosa*, the gonococcus rests within the WHO 'high priority' list of pathogens, with antimicrobial resistance increasing globally. No vaccine exists to prevent gonorrhoea (Wetzler et al., 2016), and in recent years, research has focused on identifying putative vaccine candidates from microbiological–biochemical studies of the gonococcus and using technologies that exploit whole genome(s) information, e.g., proteomics, bioinformatics, and transcriptomics. The study from Dijokaite-Guraliuc et al. used an immuno-proteomics approach to examine the reactivity of a gonococcal proteome with sera from patients with uncomplicated gonorrhoea. Using a bio-informatics approach, the authors defined a final collection of 33 proteins that contained 24 OMPs/extracellular proteins never previously studied as vaccine antigens, 6 proteins with homologs in *Neisseria meningitidis* previously reported to generate functional immune responses, and 3 unknown proteins. The study is important in not only confirming the presence of candidate vaccine antigens reported using other 'omic' platforms, but also in presenting new antigens for further vaccine development.

The final collection of Research Topic papers detail certain aspects of the pathogenesis of *Burkholderia pseudomallei, Staphylococcus epidermidis* and *Legionella pneumophila*. *B. pseudomallei* is an environmental bacterium and causes melioidosis (Meumann et al., 2024), a complex, often fatal disease manifested by acute pneumonia, bacteraemia-sepsis and localised infection. In addition, patients can present with a chronic infection or a subclinical infection. The pathogen is also of concern as a potential Category B bioweapon (Rathjen and Shahbodaghi, 2021). The BALB/c mouse is useful for studying the pathogenesis of acute melioidosis and Klimko et al showed that low levels of transmission of *B. pseudomallei* were possible from clinically infected mice to naïve mice housed in the same cage(s). *S. epidermidis* is a common cause of biofilm formation and infection in cerebrospinal fluid shunt catheters inserted in infants with hydrocephalus (Simon et al., 2014). Adult mouse models are available that mimic *S. epidermidis* and *S. aureus* CNS catheter infections, and the study from Skar et al. described how a newly adapted infant mouse model of CNS catheter infection helped to identify key factors in the host immune response to staphylococcal infections in the CNS. In the infant mouse, *S. epidermidis* showed higher parenchymal spread and the absence of the elevated pro-inflammatory cytokines as seen in infected adult mice. Notably, an attenuated inflammatory response may contribute to the increased infection risk observed in neonates. *L. pneumophila* is an accidental pathogen that causes Legionnaire's disease (Fraser et al., 1977), which is a severe atypical pneumonia resulting from bacterial replication within lung alveolar macrophages. During its intracellular lifecycle, this bacterium establishes an endoplasmic reticulum-derived organelle within which it replicates. In the article from Wilkins et al. the authors examined the role of esterified fatty acids in bacterial replication in macrophages and concluded that intracellular replication of *L. pneumophila* was a function of lipid bilayer disorder and hydrophobic thickness. The final paper in our showcase from Reed et al. assessed the potentially different antibacterial properties of eumelanin-inspired derivatives and showed that a hydrophobic derivative EIPE-1 inhibited Gram-positive bacteria in a cytoplasmic membrane-directed manner, independent of oxygen.

In conclusion, the variety of articles included in the Research Topic merely touch on the breadth of research in bacterial pathogenesis, vaccines and immunity to bacterial infections, and we welcome submissions that increase our basic understanding of all three.

Author contributions

MC: Writing – original draft, Writing – review & editing.

Acknowledgments

The editor thanks all the authors who participated in this Research Topic, and the reviewers and staff of Frontiers for their time and assistance in the production of said articles.

Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Publisher's note

References

Christodoulides, M. (2022). Specialty grand challenge frontiers in bacteriology: Pathogenesis, vaccines, and immunity of bacterial infections. *Front. Bacteriol* 1. doi: 10.3389/fbrio.2022.1049307

Dolan, S. K. (2020). Current knowledge and future directions in developing strategies to combat pseudomonas aeruginosa infection. *J. Mol. Biol.* 432, 5509–5528. doi: 10.1016/j.jmb.2020.07.021

Fraser, D. W., Tsai, T. R., Orenstein, W., Parkin, W. E., Beecham, H. J., Sharrar, R. G., et al. (1977). Legionnaires' disease: description of an epidemic of pneumonia. *New Engl. J. Med.* 297, 1189–1197. doi: 10.1056/NEJM197712012972201

Meumann, E. M., Limmathurotsakul, D., Dunachie, S. J., Wiersinga, W. J., and Currie, B. J. (2024). Burkholderia pseudomallei and melioidosis. *Nat. Rev. Microbiol.* 22, 155–169. doi: 10.1038/s41579-023-00972-5

Miller, W. R., and Arias, C. A. (2024). ESKAPE pathogens: antimicrobial resistance, epidemiology, clinical impact and therapeutics. *Nat. Rev. Microbiol.* 22, 598–616. doi: 10.1038/s41579-024-01054-w

Rathjen, N. A., and Shahbodaghi, S. D. (2021). Bioterrorism. *Am. Fam Physician* 104, 376–385.

Silva, T. O., Bulla, A. C. S., Teixeira, B., Gomes, V. M. S., Raposo, T., Barbosa, L. S., et al. (2024). Bacterial efflux pump OMPs as vaccine candidates against Multidrug-Resistant Gram-negative bacteria. *J. Leukoc. Biol.* 116 (6), 1237–1253. doi: 10.1093/jleuko/qiae154

Simon, T. D., Pope, C. E., Browd, S. R., Ojemann, J. G., Riva-Cambrin, J., Mayer-Hamblett, N., et al. (2014). Evaluation of microbial bacterial and fungal diversity in cerebrospinal fluid shunt infection. *PloS One* 9, e83229. doi: 10.1371/journal.pone.0083229

Wang, X., Zhang, X., Zhou, D., and Yang, R. (2013). Live-attenuated Yersinia pestis vaccines. *Expert Rev. Vaccines* 12, 677–686. doi: 10.1586/erv.13.42

Wetzler, L. M., Feavers, I. M., Gray-Owen, S. D., Jerse, A. E., Rice, P. A., and Deal, C. D. (2016). Summary and recommendations from the national institute of allergy and infectious diseases (NIAID) workshop "Gonorrhea vaccines: the way forward. *Clin. Vacc Immunol.* 23, 656–663. doi: 10.1128/CVI.00230-16

World Health Orgainisation (2024). *WHO Bacterial Priority Pathogens List 2024: bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance* (Geneva: WHO).