Editorial: Streptococci in infectious diseases – pathogenic mechanisms and host immune responses

Simone Bergmann¹, Marcus Fulde² and Nikolai Siemens³*

¹Institute of Microbiology, Technische Universität Braunschweig, Braunschweig, Germany; ²Centre for Infection Medicine, Institute of Microbiology and Epizootics, Free University of Berlin, Berlin, Germany; ³Department of Molecular Genetics and Infection Biology, University of Greifswald, Greifswald, Germany

KEYWORDS
streptococci, pathogenesis, immune evasion, infection, diseases

The genus Streptococcus encompasses over fifty species which are classified into alphabetical groups based on cell surface antigens according to Lancefield (1928). Although the majority of them are commensal part of the human or animal microbiota, they also cause diseases (Krzysciak et al., 2013). Most streptococcal infections are of a mild nature. However, these bacterial species also cause highly invasive diseases. These include but are not limited to necrotizing skin and soft tissue infections (NSTIs; S. pyogenes) (Siemens et al., 2020), pneumonia, sepsis, and meningitis (S. pneumoniae, S. suis) (Votsch et al., 2018; Steinert et al., 2020; Palmer and Kimmey, 2022), neonatal sepsis (S. agalactiae) (Armistead et al., 2019), and endocarditis (S. anginosus) (Reissmann et al., 2010). The invasiveness is linked to a plethora of bacterial as well as host factors. Virulence factors help pathogens to escape the host immune response while uncontrolled and excessive activation of host factors can aggravate the disease progression (Doran et al., 2016; Siemens et al., 2020; Steinert et al., 2020). Consequently, all these actions can result in substantial host tissue damage, bacterial dissemination, and subsequent death of the host.

For this Research Topic we collected eight papers, including seven original research and one review articles. The review and two additional research papers describe epidemiology and virulence determinants of S. agalactiae (group B streptococcus [GBS]). Furuta et al. discuss the clinical impact of neonatal GBS invasive infections. The authors highlight key aspects of GBS maternal-infant transmission, pathogen acquisition, GBS pathogenesis, and suggest that it will be a key for future therapies to identify crucial pathogenic mechanisms of GBS in infants. GBS produce membrane vesicles (MV), which are implicated in disease pathogenesis (Armistead et al., 2021). McCutcheon et al. quantified MV production by different GBS isolates and examined protein composition.
The study revealed that MV production and composition is strain dependent. They contain virulence and immunomodulatory factors. The authors conclude that GBS MVs potentially have lineage specific functions in virulence. The study by Jones et al. presents important epidemiological results. One hundred GBS isolates, 50 obtained from rectovaginal screening swabs of pregnant women and 50 from blood cultures of invasive infections, were characterized. Capsular genotype Ia was predominant in colonizing strains while genotype V was predominant in invasive strains. All isolates were susceptible to penicillin. Of concern, two isolates showed reduced susceptibility to ceftriaxone and were found to have unique alleles at pbp2X and pbp1A. Several studies identified point mutations within pbp2x, which were associated with reduced or non-susceptibility to β-lactam antibiotics in streptococci (Southon et al., 2020; Mcgee et al., 2021; Beres et al., 2022). Therefore, emergence of such clones warrants ongoing monitoring.

Since S. pyogenes causes acute infections in humans, it was not considered a major biofilm forming species. A recent study identified biofilms in 32% of NSTI patients, which might be of concern for treatment of these infections (Siemens et al., 2016). Therefore, Skutlaberg et al. analyzed biofilm forming capacity of 57 S. pyogenes NSTI isolates of different emm-types and related them to patient demographics and clinical variables. The study shows that emm1 strains possess the best biofilm forming capacity compared to other emm types. However, the impact of biofilm formation on clinical outcomes remains uncertain and requires further studies.

Two research studies deal with cell wall associated components of S. suis. S. suis is a common swine pathogen. To escape immuno-clearance, streptococci modify LTA by incorporating D-alanine by the enzyme CAAX proteases. CAAX proteases are often accompanied by damaged endothelium (Steinert et al., 2020). Therefore, it is of crucial importance to establish experimental in vitro models that mimic flow conditions. The paper by Kopenhagen et al. presents an elegant approach to study endothelial cell migration and proliferation as two major prerequisites for tissue regeneration under shear stress. This technique provides a powerful tool to analyze the impact of pneumococcal infections in real time and should be considered for future studies of any type of bloodstream infections.

In conclusion, the eight articles provide new exciting insights into the kaleidoscope of streptococcal pathogenesis and offer fundamental news with regard to the various scientific topics. We sincerely thank all authors and reviewers for their contributions to this Research Topic.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Acknowledgments

We sincerely thank all authors and reviewers for their contributions to this Research Topic.

Conflict of interest

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

Publisher’s note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated institutions.
organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or
claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

Armistead, B., Oler, E., Adams Waldorf, K., and Rajagopal, L. (2019). The double life of group b Streptococcus: asymptomatic colonizer and potent pathogen. J. Mol. Biol. 431, 2914–2931. doi: 10.1016/j.jmb.2019.01.035

Armistead, B., Quach, P., Snyder, J. M., Santana-Ufret, V., Furuta, A., Brokaw, A., et al. (2021). Hemolytic membrane vesicles of group B Streptococcus promote infection. J. Infect. Dis. 223, 1488–1496. doi: 10.1093/infdis/jiaa548

Beres, S. B., Zhu, L., Pruitt, L., Olsen, R. J., Faili, A., Kayal, S., et al. (2022). Integrative reverse genetic analysis identifies polymorphisms contributing to decreased antimicrobial agent susceptibility in Streptococcus pyogenes. mBio13, e0361821. doi: 10.1128/mbio.03618-21

Commichau, F. M., and Stulke, J. (2018). Coping with an essential poison: a genetic suppressor analysis corroborates a key function of c-di-AMP in controlling potassium ion homeostasis in gram-positive bacteria. J. Bacteriol. 200, e00166-18. doi: 10.1128/JB.00166-18

Doran, K. S., Fulde, M., Gratz, N., Kim, B. J., Nau, R., Prasadaro, N., et al. (2016). Host-pathogen interactions in bacterial meningitis. Acta Neuropathol. 131, 185–209. doi: 10.1007/s00401-015-1531-9

Krysciaiak, W., Pluskva, K. K., Jurczak, A., and Koscieniak, D. (2013). The pathogenicity of the Streptococcus genus. Eur. J. Clin. Microbiol. Infect. Dis. 32, 1361–1376. doi: 10.1007/s10096-013-1914-9

Mcgee, L., Chochua, S., Li, Z., Mathis, S., Rivers, J., Metcalf, B., et al. (2021). Multistate, population-based distributions of candidate vaccine targets, clonal complexes, and resistance features of invasive group B Streptococci within the United States, 2015–2017. Clin. Infect. Dis. 72, 1004–1013. doi: 10.1093/cid/ciaa151

Palmer, C. S., and Kimmy, J. M. (2022). Neutrophil recruitment in Pneumococcal Pneumonia. Front. Cell. Infect. Microbiol. 12, 894644. doi: 10.3389/fcimb.2022.894644

Percy, M. G., and Grundling, A. (2014). Lipoteichoic acid synthesis and function in gram-positive bacteria. Annu. Rev. Microbiol. 68, 81–100. doi: 10.1146/annurev-micro-091213-112949

Reissmann, S., Friederichs, C., Rajkumari, R., Itzek, A., Fulde, M., Rodloff, A. C., et al. (2010). Contribution of Streptococcus anginosus to infections caused by groups C and G streptococci, southern India. Emerg. Infect. Dis. 16, 666–663. doi: 10.3201/eid1604.090448

Siemens, N., Chakrakodi, B., Shambat, S. M., Morgan, M., Bergsten, H., Hyldegaard, O., et al. (2016). Biofilm in group A streptococcal necrotizing soft tissue infections. JCI Insight 1, e87882. doi: 10.1172/jci.insight.87882

Siemens, N., Small, J., Svensson, M., and Norrby-Teglund, A. (2020). Pathogenic mechanisms of streptococcal necrotizing soft tissue infections. Adv. Exp. Med. Biol. 1294, 127–150. doi: 10.1007/978-3-030-57616-5_9

Southon, S. B., Beres, S. B., Kachroo, P., Saavedra, M. O., Erlandsdottir, H., Haraldsson, G., et al. (2020). Population genomic molecular epidemiological study of macrolide-resistant Streptococcus pyogenes in Iceland, 1995 to 2016: identification of a large clonal population with a pbp2x mutation conferring reduced in vitro beta-lactam susceptibility. J. Clin. Microbiol. 58. doi: 10.1128/JCM.00638-20

Steinert, M., Ramming, I., and Bergmann, S. (2020). Impact of von willebrand factor on bacterial pathogenesis. Front. Med. 7, 543. doi: 10.3389/fmed.2020.00543

Vogel, V., and Spellerberg, B. (2021). Bacteriocin production by beta-hemolytic streptococci. Pathogens 10, 867. doi: 10.3390/pathogens10070867

Votsch, D., Willenborg, M., Weldearegay, Y. B., and Valentín-Weigand, P. (2018). Streptococcus suis - The "Two Faces" of a pathobiont in the porcine respiratory tract. Front. Microbiol. 9, 480. doi: 10.3389/fmicb.2018.00480