(1) Submission ID#1539641

Genotypic and phenotypic comparison of Neisseria meningitidis carriage and invasive disease isolates contemporaneously collected in the Netherlands

Author(s)

C. Hal Jones, PhD

Director

Pfizer Inc

Zhenghui Li, PhD

Principal Scientist

Pfizer Inc

Li Hao, PhD

Associate Research Fellow

Pfizer Inc

Arie van der Ende, PhD

Associate Professor and Head

Netherlands Reference Laboratory for Bacterial Meningitis

Paul Liberator, PhD

Senior Director

Pfizer Inc

Annaliesa S. Anderson, PhD

Vice President and Chief Science Officer

Pfizer Inc

Ashlesh K. Murthy, PhD

Director

Pfizer Inc

Background

Neisseria meningitidis, a commensal that colonizes the nasopharynx of 5%-24% of healthy humans, can cause invasive meningococcal disease (IMD) in a subset of individuals. We hypothesized that distinct genotypic and/or phenotypic signatures can be found in carriage versus invasive isolates.

Aim/Methods

Meningococcal carriage isolates were cultured from nasopharyngeal swabs (n=267) collected from healthy,

secondary school and university students (ages 13-21 years) during the 2013–2014 school years in the Netherlands. Invasive isolates (n=214) were cultured from all reported disease cases in the Netherlands between 2012 and 2014 and deposited at the Netherlands Reference Laboratory for Bacterial Meningitis. Whole core genome sequence was determined for all isolates, and comparison of selected genotypic markers and phylogenomic associations between carriage and disease isolates were analyzed. FHbp surface expression levels, determined using the flow cytometry-based MEASURE assay, were also captured for all isolates.

Results

30% of carriage isolates were non-groupable; genogroup was identified for all invasive isolates. Serogroup B (MenB) predominated, representing 27% of carriage and 75% of IMD isolates. Among MenB isolates, ST complex diversity was dominated by ST-41/44, ST-213, ST-32, and ST-269 in carriage (76%) and disease (86%). MenB FHbp subfamily A variants were prevalent in carriage (79%), whereas subfamily B variants were more frequent in disease (70%). Compared with carriage isolates, surface expression of FHbp was higher among IMD isolates. Carriage and IMD MenB isolates were broadly comparable based on phylogenomic clustering.

Conclusions

Carriage and IMD-causing Neisseria meningitidis strains, particularly MenB, display similar ST and phylogenomic profiles. Notable differences included the identification of non-groupable carriage isolates, and an increased FHbp subfamily B prevalence and enhanced level of FHbp surface expression in MenB disease–causing isolates. However, no unique signatures of IMD isolates were identified. These results indicate that (A) host susceptibility factors may also contribute to carriage versus IMD outcomes following colonization, and (B) vaccines that induce antibodies against the vast array of FHbp variants are likely most effective in preventing MenB IMD. Furthermore, the lack of clearly identifiable signatures suggests that preventive vaccination, as opposed to targeted interventions, remains the mainstay to protect against morbidity and mortality caused by IMD. Funded by Pfizer.