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Continuing genomic evolution of the urethritis-associated lineage 11.2 meningococcal clade NmUC

Author(s)

Emilio I. Rodriguez, Bachelor of Science

Graduate Student

Emory University

Yih-Ling Tzeng, Ph.D.

Research Associate Professor

Emory University School of Medicine

David Stephens, M.D.

Professor

Emory University School of Medicine

Background

Neisseria meningitidis (Nm) asymptomatically colonizes the nasopharynx in ~10% of adults, but occasionally causes invasive meningococcal diseases. Nm is rare as a urogenital pathogen; however, since 2013 cases, clusters, and outbreaks of meningococcal urethritis, originally presumed to be Neisseria gonorrhoeae (Ng), have been observed. Previously, 209 Nm urethritis isolates collected from 2013-2016 were sequenced and all isolates identified as clonal complex (cc)-11.2 lineage. This emerging group of urethral Nm was designated the Nm urethritis clade, NmUC. Genomic analysis revealed 1) an IS1301 element insertion in the capsule css operon resulting in a deletion of cssA/B/C and part of csc, encoding the serogroup C capsule polymerase, and the integrations of gonococcal DNA at multiple genomic sites, including 2) the gonococcal denitrification apparatus aniA-norB, 3) a partial gonococcal operon of 5 genes, and 4) argB encoding the acetylglutamate kinase.

Aim/Methods

The aim of this study was to understand the continuing genomic evolution of NmUC with 46 new NmUC isolates obtained globally from 2016-2021 and deposited in the PubMLST database. Genomic and phylogenetic analyses were performed on all 255 NmUC isolates to assess evolution of the clade over time and geographic distance.

Results

The analyses found that the four key genomic features noted above are maintained in the new clade isolates. Additionally, SNP-based phylogeny identified the emergence of a sub-clade, NmUC-B within NmUC, including 36 isolates collected in 2019-2021 from the U.S., the U.K., and Vietnam. This sub-clade is characterized by 5 regions of SNPs, 1.2-3.1 kb long, which are distinct from previous clade isolates (NmUC-A). These 5 regions cover 14 genes, and the regions appear to originate from Ng, non-clade Nm, and Neisseria cinerea. NmUC-B has genes associated with antibiotic resistance that are not present in NmUC-A; all 36 NmUC-B isolates contain a sulfonamide-resistant folP allele from N. cinerea, and 11 NmUC-B isolates contain gyrA alleles

associated with ciprofloxacin resistance.

Conclusions

The maintenance of previously established NmUC features indicate they are relevant to NmUC's role as a urogenital pathogen. The emergence of NmUC-B and its acquisition of additional gonococcal alleles and antimicrobial resistance genes suggest that the clade is continuing to evolve as a pathogen.