O031
Oral Session
Epidemiology based on whole genome sequencing

WHOLE-GENOME MOLECULAR EPIDEMIOLOGY OF ISOLATES CAUSING INCREASE IN NEISSERIA MENINGITIDIS SEROGROUP Y DISEASE

B. Tˆrˆs[1], S. Thulin Hedberg[1], M. Unemo[1], S. Jacobsson[1], D. Hill[2], H. Fredlund[1], H. Bratcher[2], K. Jolley[2], M. Maiden[2], P. Mˆlling[1]

[1]Laboratory Medicine Clinical Microbiology, Orebro University Hospital, Örebro, Sweden ; [2]Zoology, University of Oxford, Oxford, United Kingdom

Objectives: The human commensal and facultatively pathogenic *Neisseria meningitidis* is primarily classified into a number of serogroups. For decades serogroups B and C caused the majority of invasive meningococcal disease (IMD) in North and South America, Australia and Europe; however, a significant increase in serogroup Y disease occurred during the mid 1990's in the US, and at the end of the 2000's this increase was also noted in Europe, mainly in Scandinavia. In Sweden, the serogroup Y incidence increased tenfold from 0.05 to 0.46/100,000 population from 2006 to 2012. Previous genetic characterization has identified one specific strain type, which was mainly responsible for the observed increase of meningococcal serogroup Y disease (representing 59% of all Swedish serogroup Y isolates in 2010). The aim of the present study was to describe the genome-based molecular epidemiology of the emerging serogroup Y. Serogroup Y isolates from the UK were used for comparison to a country with comparatively low incidence of serogroup Y disease.

Methods: The genomes of all invasive Swedish serogroup Y isolates from 1995 to 2012 (n=186) were sequenced on the HiSeq (Illumina). The draft genomes were analyzed using the Bacterial Isolate Genome Sequence Database (BIGSdb) on pubmlst.org/neisseria/. Other serogroup Y genomes included in the data analysis for comparison were the two strains which represent the early and late strain type which predominated in the United States during the 1990's and the genomes from the Meningitis Research Foundation Meningococcus Genome Library, including isolates causing meningitis or septicaemia collected in England, Wales and Northern Ireland in 2010 to 2012 (serogroup Y isolates, n=146).

Results: Neighbor-Net graphs of the Swedish isolates using the 1600 *N. meningitidis* 'core genes' (Figure 1 A), showed that the previously characterized most common strain type was distinct from the second and third most common strain types. In addition, it revealed a fourth possible strain type related to the predominant one. The clusters recovered, were similar to those obtained with UK and US isolates (Figure 1 B). A Neighbor-Net graph with isolates belonging to the Swedish predominant strain type exclusively, revealed two groupings, one of which contained only isolates collected from after the year 2006.

Conclusion: MLST and the genes *porA*, *fetA*, *'porB*, *fHbp* and *penA* previously used for the genetic characterization provided results generally concordant with the results from the whole-genome analysis. The genomes of the serogroup Y population in Sweden are similar to those of other serogroup Y populations with lower serogroup Y disease incidence. However, Sweden has one unique strain type from which the whole-genome analysis found one subvariant which is primarily responsible for the serogroup Y incidence increase. Future genome-wide association studies may elucidate which genomic alterations could explain the increase of serogroup Y disease.

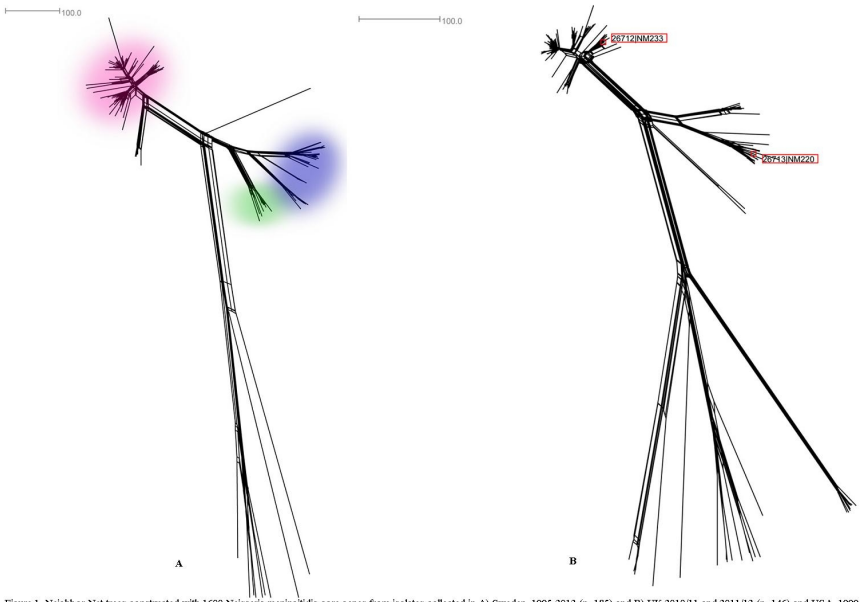

Figure 1. Neighbor-Net trees constructed with 1600 Neisseria meningitidis core genes from isolates collected in A) Sweden, 1995-2012 (n=185) and B) UK 2010/11 and 2011/12 (n=146) and USA, 1999 (n=2, marked in red). The three most common invasive N. meningitidis serogroup Y strain types in Sweden are distributed among the isolates in the pink, blue and green circles, respectively.