Differences in prevalence of AMR in serovar 8 isolates of *Actinobacillus pleuropneumoniae* between the United Kingdom, Denmark and Norway

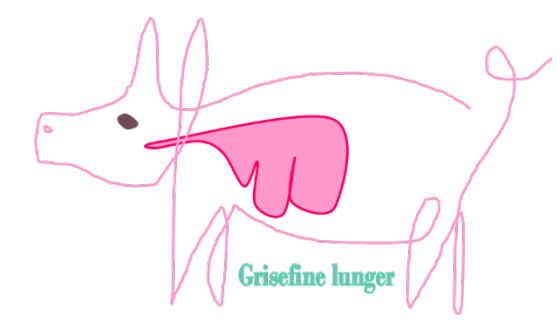Liza Miriam Cohen[1], Janine T. Bossé[2], Marc Stegger[3], Hülya Kaya[3], Paul R. Langford[2], Yanwen Li[2], Camilla Kielland[1], Thea B.B. Klem[4], Stine Margrethe Gulliksen[5], Birgit Ranheim[1], Carl Andreas Grøntvedt[4], Øystein Angen[3]

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Aim

The aim of this study was to compare prevalence of antimicrobial resistance (AMR) genes of isolates of *Actinobacillus (A.) pleuropneumoniae* serovar 8 (APP8) among isolates from the United Kingdom, Denmark and Norway.

Conclusion

Large differences in prevalence of AMR-genes and phenotypic resistance was found in APP8 between pig populations. It is possible that the treatment practices in the countries we studied has impacted the driving of AMR resistance in APP8 and highlights the importance of restricting contact between populations to safeguard low-resistance populations.

Background

Pleuropneumonia caused by *A. pleuropneumoniae* is a disease of great impact on pig health and productivity globally, and a common indication for use of antimicrobial drugs. Practices of treatment and prophylaxis varies between countries, antibiotic treatment has not been shown effective in eliminating the pathogen from all carrier animals (1). Monitoring antimicrobial resistance (AMR) in pathogenic bacteria is of value to make informed treatment choices and contributes to risk assessment of antimicrobial use.

Results and Discussion

Occurrence of AMR genes in the Norwegian isolates was overall low. Sulfonamide resistance gene, *sul2*, was the most common AMR gene occurring across countries, being present in 3.3% of the Norwegian and 67.2% of the UK isolates. The resistance profiles of a large collection of UK isolates has been described previously(2). The DK isolates were genetically distinct and formed two monophyletic groups except three of the isolates that clustered with the UK isolates and AMR profiles. The remaining 19 DK isolates were closer related to the Norwegian isolates and had an equally low prevalence of AMR-genes. In Norway benzylpenicillin-procaine is most commonly used to treat actinobacillosis, while in Denmark tilmicosin and tulathromycin are the most common drugs for this indication. Data on drugs used per indication is not available from the UK, but it is reported that Trimethoprim/sulfamethoxazole is the most common antibiotic used in pig medicine. Differences in prevalence of AMR genes among the three populations of APP8 isolates might be attributed to different treatment practices in the respective countries and contact between the populations that have led to bacterial transmission. It might also reflect inherent properties of the genetic lines.

The results are valuable in assessment of current AMR status of a common pig pathogen, and a reminder of the importance of restricting livestock exchange across populations. Introducing resistant bacteria, let alone pathogenic ones, into a population of a high health population like the Norwegian one can be detrimental.

Material and Methods

Clinical APP8 isolates from the United Kingdom (UK) (n=67), Denmark (DK) (n=22) and Norway (NO) (n=123) were collected between 1983 and 2019. For each isolate, genomic DNA was extracted, sequenced and assembly of reads into draft genomes. The isolates were all confirmed as serovar 8 by comparison of genes in the capsular polysaccharide locus to those found in the APP8 reference strain 405. SNPs in the core genome were inferred using NASP followed by purging of recombination and inference of relatedness using maximum likelihood as implemented in IQ-TREE. Antimicrobial resistance AMR genes were investigated using ARIBA against the ResFinder database found at http://www.genomicepidemiology.org.
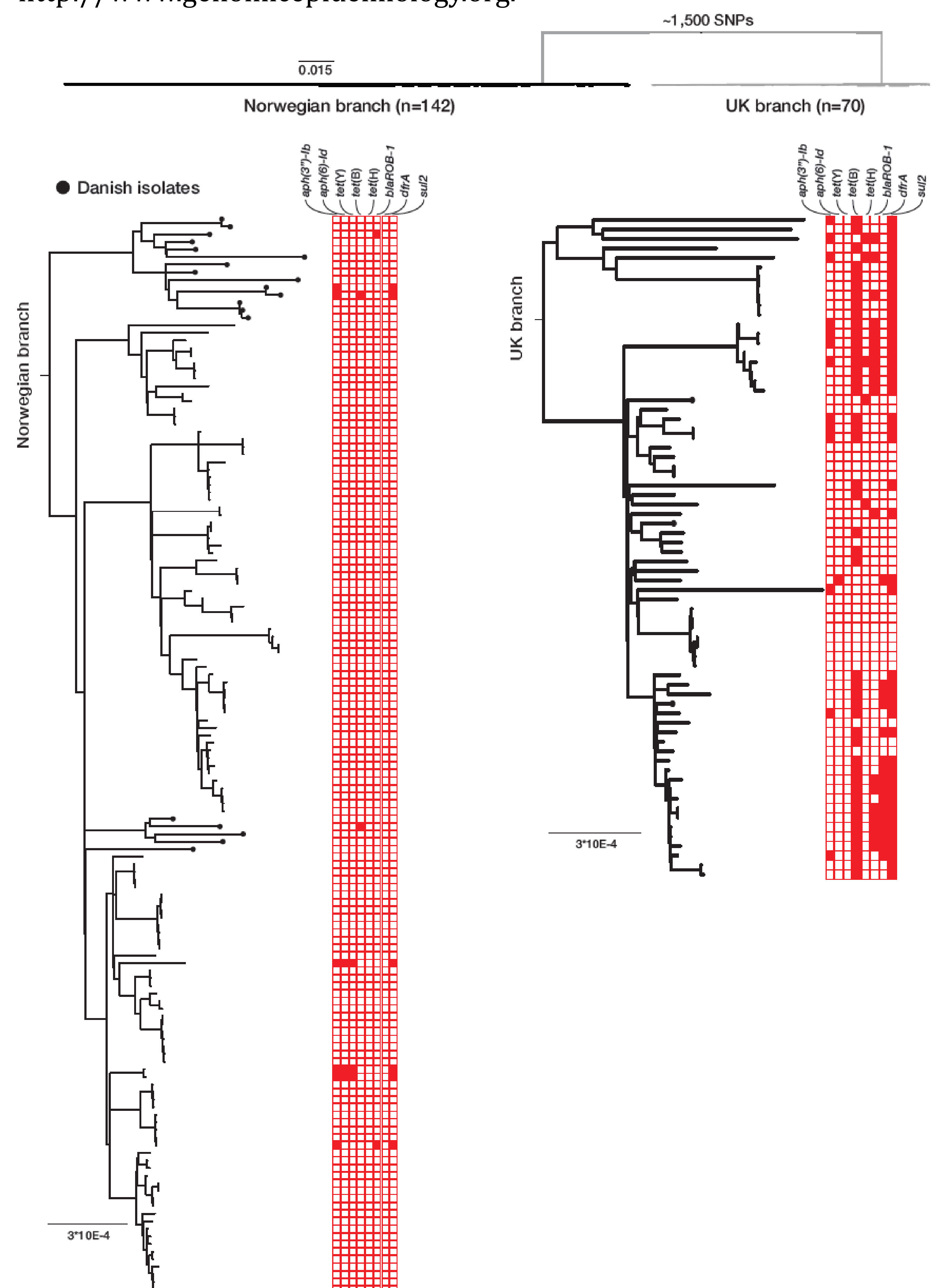

Figure 1 Top: A midpoint rooted phylogeny of isolates of *Actinobacillus pleuropneumoniae* serovar 8 (APP8) after removal of recombinant regions illustrating the two distinct branches of the APP collection. Left clade contains 19 Danish and 124 Norwegian isolates (n=143) whereas the right clade contain 3 Danish and 67 UK isolates (n=70) with ~1500 SNPs separating the clades. **Bottom:** Rooted phylogenies of Norwegian clade (left) and UK clade (right), including AMRgene plot for streptomycin resistance genes *aph(3'')-Ib* and *aph(6)*, tetracycline resistance genes *tet*(Y), *tet*(B) and *tet*(H), betalactame resistance gene *blaROB-1*, trimethoprim resistance gene *dfrA* and sulphonamide resistance gene *sul2*. Presence of gene is indicated by a colored box, while an empty box indicates absence of gene.

References

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