A retrospective whole-genome-based study of *Salmonella* Dublin isolated from cattle and humans in 1996-2016

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The background. *Salmonella* Dublin is a cattle-adapted *S. enterica* serovar causing intestinal as well as systemic infection in its bovine host. *S*. Dublin may be transmitted to humans via contact to infected animals or consumption of contaminated milk or beef. Typically *S*. Dublin affects people with underlying diseases and is sometimes lethal. Despite the efforts to eradicate *S*. Dublin from the Danish cattle population since 2007, it remains present in around 7% of the dairy cattle herds, and clinical cases of human infection continue to be reported in Denmark. Investigation of transmission pathways is of interest to improve the prevention of spread of this loss-provoking infection.
The aim. To apply whole genome sequencing (WGS) for an improved understanding of the *S*. Dublin population in Danish cattle herds and human.
The methods. In total 196 isolates of *S*. Dublin from 58 cattle herds collected in different parts of Jutland from 1996 to 2016 were selected and whole genome sequenced with MiSeq (Illumina). All *S*. Dublin isolates from cattle have been classified into whether they originated from persistently and non-persistently infected farms according to a set of surveillance criteria. In addition, whole genome sequences of 46 clinical isolates from humans provided by SSI were analyzed.
Results. The comparison of the whole genomes of *S*. Dublin isolates from cattle based on the single nucleotide differences in the core genome resulted in their grouping into three major clusters: Cluster I – Northern and Southern Jutland, Cluster II – Northern and Mid-Jutland predominantly and Cluster III – Southern and Mid-Jutland predominantly. The persistence status and the year of isolation had no effect on the phylogeny of *S*. Dublin. However, the majority of the isolates collected from the same cattle herd, with a few exceptions, clustered together, possibly due to the existence of a local herd-restricted source of infection in the farm environment or persistence in the animals. Similarly, no genome content differences were found between the persistent and non-persistent isolates of *S*. Dublin, when the accessory genome of whole strain population was analyzed. Interestingly, a number of accessory genes were detected in isolates belonging to Cluster II, and these were found to represent two previously unreported plasmids of *S*. Dublin containing additional genes for antibiotic resistance and virulence. Finally, the comparison of cattle and human isolates resulted in human isolates clustering predominantly into Cluster II. The majority of human isolates within Cluster II also contained the two plasmids found in *S*. Dublin from cattle. Presumably, Cluster II may represent a more diverse, less host-restricted and more adaptive population of *S*. Dublin bacteria population in Denmark, which needs to be investigated in more detail.
Conclusion. The WGS of *S*. Dublin enabled better insight into its circulation in cattle herds over the years, the relationship between human and cattle isolates, and provided valuable data that can be further used for an improved *S*. Dublin control in Denmark.