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Within-host evolution of *Staphylococcus pseudintermedius* in dogs with skin disease

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This study assessed within-host phenotypic and genotypic evolution amongst methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) isolates from two dogs with chronic skin disease and recurrent pyoderma. Phenotypic antimicrobial susceptibility was determined by broth microdilution. Isolates underwent genome sequencing using both short read and long read platforms. Genome short reads were assessed for the accumulation of core genome single nucleotide polymorphisms (SNPs). Assembled genomes were interrogated for variations in accessory genome content. Phylogenetic, phenotypic and genotypic variation in antimicrobial resistance was evident in longitudinally isolated *S. pseudintermedius* from both dogs. Dog 1 had three infections with the same MRSP clone (ST316) and one infection with an unrelated methicillin-susceptible (MSSP) clone. Dog 2 had three different clones over five infection episodes: two infections were due to ST64 MRSP, two ST257 MSSP and one ST2814 MSSP. Non-synonymous SNPs accumulated in genes relating biofilm formation, rifampicin resistance, metabolism and cell wall synthesis. Sequential ST316 MRSP isolates from Dog 1 developed a mutated *rpoB* gene which conferred phenotypic rifampicin resistance, making the isolate extensively drug resistant. Within clonal types, plasmid content was stable while prophage content was variable. These findings provide evidence for the emergence of extensive drug resistance during recurrent *S. pseudintermedius* infection.

Keywords

Staphylococcus, antimicrobial resistance, bacterial evolution, pyoderma

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