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Genetic basis of antimicrobial resistance in Pasteurellaceae of diseased cattle and pigs from Germany

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This study investigated the genetic basis of macrolide resistance and further antimicrobial resistance (AMR) properties in *Mannheimia haemolytica* and *Pasteurella multocida* from diseased cattle and pigs. Seventeen macrolide-resistant isolates from respiratory diseases included in GERM-Vet (*M. haemolytica*, cattle, 2008-2020, n=13/780; *P. multocida*, pigs, 2008-2021, n=4/1115) and eight bovine *P. multocida* from sporadic cases of mastitis (2021-2023) were investigated. Antimicrobial susceptibility testing was done according to CLSI recommendations. Closed whole genome sequences were generated via hybrid assembly of Illumina MiSeq and Oxford Nanopore MinION reads. Among the 25 isolates tested, resistance to several of the antimicrobial agents, including aminoglycosides, phenicols, penicillins, tetracyclines, macrolides and sulfonamides, was detected. In 19 isolates (respiratory disease n=12, mastitis n=7), integrative and conjugative elements (ICEs) were identified that conferred multidrug resistance. These ICEs, some of them novel, harbored the AMR genes *erm*(T), *lnu*(H), *est*T, *mef*(C), *mph*(G), *flo*R, *cat*A3, *aad*A31, *aad*(3'')(9), *aph*(3')-Ia, *aac*(3)-IIa, *str*A, *str*B, *tet*(H), *tet*(Y), and *sul*2 in varying combinations. Four *M. haemolytica* also carried a 4,613-bp plasmid with the β -lactamase gene *bla*ROB-1. Resistance-mediating ICEs or plasmids, as found here, can promote the rapid spread of AMR via horizontal gene transfer and co-selection events.

Keywords

Pasteurella multocida, *Mannheimia haemolytica*, cattle, pigs, respiratory infection, mastitis, resistance monitoring, whole-genome sequencing, mobile genetic elements

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Postdoc

Authors: KOSTOVA, Valeria (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany); JAHNEN, Johanna (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany)

Co-authors: HANKE, Dennis (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany); KASPAR, Heike (Federal Office of Consumer Protection and Food Safety (BVL), Berlin, Germany); FIEDLER, Stefan (Federal Office of Consumer Protection and Food Safety (BVL), Berlin, Germany); KADLEC, Kristina (Dairy Herd Consulting and Research Company (MBFG), Wunstorf, Germany); SCHWARZ,

Stefan (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany); KRÜGER-HAKER, Henrike (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany)

Presenter: KRÜGER-HAKER, Henrike (Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin, Germany)

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