Staphylococcus aureus CC398 - DTU Orbit (30/10/2017)

Staphylococcus aureus CC398: Host Adaptation and Emergence of Methicillin Resistance in Livestock

Since its discovery in the early 2000s, methicillin-resistant Staphylococcus aureus (MRSA) clonal complex 398 (CC398) has become a rapidly emerging cause of human infections, most often associated with livestock exposure. We applied whole-genome sequence typing to characterize a diverse collection of CC398 isolates (n = 89), including MRSA and methicillin-susceptible S. aureus (MSSA) from animals and humans spanning 19 countries and four continents. We identified 4,238 single nucleotide polymorphisms (SNPs) among the 89 core genomes. Minimal homoplasy (consistency index = 0.9591) was detected among parsimony-informative SNPs, allowing for the generation of a highly accurate phylogenetic reconstruction of the CC398 clonal lineage. Phylogenetic analyses revealed that MSSA from humans formed the most ancestral clades. The most derived lineages were composed predominantly of livestock-associated MRSA possessing three different staphylococcal cassette chromosome mec element (SCCmec) types (IV, V, and VII-like) including nine subtypes. The human-associated isolates from the basal clades carried phages encoding human innate immune modulators that were largely missing among the livestock-associated isolates. Our results strongly suggest that livestock-associated MRSA CC398 originated in humans as MSSA. The lineage appears to have undergone a rapid radiation in conjunction with the jump from humans to livestock, where it subsequently acquired tetracycline and methicillin resistance. Further analyses are required to estimate the number of independent genetic events leading to the methicillin-resistant sublineages, but the diversity of SCCmec subtypes is suggestive of strong and diverse antimicrobial selection associated with food animal production. IMPORTANCE Modern food animal production is characterized by densely concentrated animals and routine antibiotic use, which may facilitate the emergence of novel antibiotic-resistant zoonotic pathogens. Our findings strongly support the idea that livestock-associated MRSA CC398 originated as MSSA in humans. The jump of CC398 from humans to livestock was accompanied by the loss of phage-carried human virulence genes, which likely attenuated its zoonotic potential, but it was also accompanied by the acquisition of tetracycline and methicillin resistance. Our findings exemplify a bidirectional zoonotic exchange and underscore the potential public health risks of widespread antibiotic use in food animal production. IMPORTANCE: Modern food animal production is characterized by densely concentrated animals and routine antibiotic use, which may facilitate the emergence of novel antibiotic-resistant zoonotic pathogens. Our findings strongly support the idea that livestock-associated MRSA CC398 originated as MSSA in humans. The jump of CC398 from humans to livestock was accompanied by the loss of phage-carried human virulence genes, which likely attenuated its zoonotic potential, but it was also accompanied by the acquisition of tetracycline and methicillin resistance. Our findings exemplify a bidirectional zoonotic exchange and underscore the potential public health risks of widespread antibiotic use in food animal production.

General information
State: Published
Organisations: National Food Institute, Division of Microbiology and Risk Assessment, University Paris Diderot - Paris 7, Statens Serum Institut, Northern Arizona University, Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH, University of Ljubljana, Istituto Zooprofilattico Sperimentale delle Regioni Lazio e Toscana, National Veterinary Research Institute, Friedrich Loeffler Institute, Ghent University, Interdisciplinary Centre of Research in Animal Health, Universidad Complutense de Madrid, University of Iowa, University of Guelph, San Marcos Major National University, First Affiliated Hospital of Wenzhou Medical College, National Reference Center for Staphylococci, University of Mississippi, Translational Genomics Research Institute
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Pages: e00305
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: mBio
Volume: 3
Issue number: 1
ISSN (Print): 2150-7511
Ratings:
Web of Science (2017): Indexed Yes
Scopus rating (2016): CiteScore 5.79
Scopus rating (2015): CiteScore 4.93
Web of Science (2015): Indexed yes
Scopus rating (2014): CiteScore 4.23
Web of Science (2014): Indexed yes
Scopus rating (2013): CiteScore 4.26
