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Human origin for avian pathogenic _Staphylococcus aureus_

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_S. aureus_ is a major human pathogen associated with nosocomial and community-acquired infections, and is also responsible for several economically important infections of livestock. However, the evolutionary origin of animal strains and the potential for cross-species transmission has not been well examined. We recently traced the origin of a common _S. aureus_ clone which is a significant cause of morbidity in the global broiler poultry industry. We provided evidence that it evolved from a single human to poultry host jump which was followed by extensive genetic diversification including acquisition of novel mobile genetic elements and loss of virulence gene function. The clone has since been disseminated widely to several different continents presumably through globalization of the poultry industry. In the current article, we summarise the findings of the paper, discuss their implications and speculate on the potential for other _S. aureus_ cross-species transfer events.

In recent years considerable attention has been paid to the potential for the zoonotic transfer of pathogens from animals to humans resulting in disease epidemics. For example, a global health alert has been triggered by the recent swine flu pandemic, and livestock-borne pathogens such as Campylobacter and _E. coli_ 0157:H7 continue to cause significant levels of morbidity among humans. The potential for _Staphylococcus aureus_ colonizing animals to cause infections of humans is unclear. However, the recent identification of strains of livestock-associated MRSA, such as the CC398 clone found in pigs, cows, poultry and horses, which have also been associated with disease of humans, is worrisome. Furthermore, the recent emergence of community-acquired MRSA as a major cause of disease in the USA and other countries, has led to speculation regarding the possible existence of an animal reservoir for newly emergent strains which are pathogenic for humans. In addition, the potential impact of industrialization and globalization of agriculture on the emergence and spread of new pathogens from livestock animals is an issue of public health concern. However, little attention has been paid to the possibility that humans could represent a source of new pathogens for animals which could have economic and food security implications. For example, infectious diseases are a major economic burden on the global poultry industry and _S. aureus_ is a common cause of broiler poultry infections such as dermatitis, subdermal abscesses (colloquially known as ‘bumble foot’), and bacterial chondronecrosis with osteomyelitis (BCO). In a recent paper, we used a combination of population genetics and comparative genome sequencing to investigate the evolutionary origin of _S. aureus_ strains from poultry.

Unexpectedly, we discovered that the majority of isolates examined belonged to a single clonal complex (CC5) defined by multilocus sequence typing which was widespread among both healthy and diseased birds. A recent study by Smyth et al. (2009) was the first report in the literature which identified CC5 isolates among poultry (on a farm in northern Ireland) which led the authors to speculate about the possibility of a cross-species transfer event. We demonstrated that the CC5 poultry isolates were widespread in countries in several different continents, but
that all isolates can be traced back to a single likely human to poultry host-jump which happened about 40 years ago and which originated in or near to Poland. This situation contrasts strongly with human strains of CC5 which demonstrated strong phylolgenetic clustering, indicating that the intercontinental spread of human CC5 strains and subsequent fixation in local populations is rare. We propose that the subsequent spread of the poultry ST5 clade has been facilitated by the globalized nature of the poultry industry whereby a small number of broiler breeding lines (and their resident normal flora) are distributed widely around the world.

Comparative genome sequencing of a representative poultry CC5 strain ED98 and the closely-related basal human strain MR1 allowed us to examine the genetic basis for the adaptation of S. aureus to an avian niche. A number of mutations leading to loss of gene function have occurred in the poultry strain ED98 since divergence from a common ancestor with the human strain MR1. For example, a nonsense mutation has occurred in the gene spa which encodes a major surface protein SpA involved in several aspects of human disease pathogenesis including the inhibition of phagocytosis by human neutrophils via the non-specific binding of IgG at the Fc fragment. Importantly, the Fc region of IgG which is the avian equivalent of IgG does not bind to SpA suggesting that SpA would not inhibit phagocytosis during infection of chickens. Of note, a poultry biotype of S. aureus was described previously which had a combination of unique phenotypic characteristics, including lack of expression of SpA, which differentiated it from human and other animal strains. In the genome of poultry S. aureus strain ED98 we discovered several novel mobile genetic elements which were not found in human or rumi-

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