West Nile Virus Infections in (European) Birds

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Commentary

West Nile virus (WNV), a member of the *Flaviviridae* family is an important emerging pathogen transmitted by mosquitoes of the *Culex sp*. wild-and (peri) domesticated birds act as the natural hosts of WNV. Birds are not only susceptible to WNV, but also participate in maintaining the transmission cycle. WNV emerged in North America in 1999 and its emergence was associated with high numbers of neuroinvasive disease in humans and horses. In general, WNV outbreaks were preceded by mass mortality in birds, especially birds belonging to the family *Corvidae* proved to be particularly susceptible [1]. Today, crows serve as an important early warning system in the USA to monitor WNV activity [2]. WNV outbreaks have been reported in Europe since 1950s. T ese outbreaks were small and remained focal. In contrast to the USA, bird mortality has not been reported in Europe. T e emergence of a lineage 2 WNV coincided with increased reports of neuroinvasive disease in Europe. T e WNV strains that have been characterized in Europe are very heterogeneous (Figure 1). T is heterogeneity of WNV, at lineage level, together with the appearance of point mutations potentially a ecting virulence and/or transmissibility, and the co-circulation of other f aviviruses infecting birds and humans, have important consequences for understanding their ecology and pathogenicity.

A couple of hypotheses have been proposed and investigated to explain these observations: (1) European birds are not susceptible to natural WNV infection, (2) WNV strains in Europe are less virulent compared to the American viruses, (3) Culex mosquitoes in Europe are not competent to transmit WNV to birds, (4) T e feeding behavior of WNV infected Culex mosquitoes is di erent. T ese hypotheses have been addressed by our laboratory and others providing valuable answers, which allows for more tailored surveillance programs. Speci fcally, it has been shown that carrion crows are susceptible to experimental infection with certain WNV strains and therefore carrion crows could act as potential amplifying hosts in Europe [3,4]. In our laboratory, we have also shown that jackdaws can be productively infected and succumb to WNV infection. Although approximately 50% of this bird species is susceptible to lethal infection, jackdaws could function as sentinel to follow WNV activity in Europe [5]. Nevertheless, these experiments clearly showed that not all WNV strains that circulate in Europe can cause lethal infection in these birds [4,5]. Characterization of European WNV strains in mice has revealed little di erences in virulence between the di erent strains [6]. However, clear di erences in virulence were reported in birds, which do not correlate with virulence in mice and humans. Due to these di erences in virulence, we propose a surveillance system in birds, which is based on identifying antibodies to WNV, and when possible the genotype, since active surveillance may only reveal circulation of WNV strains that are virulent to birds.

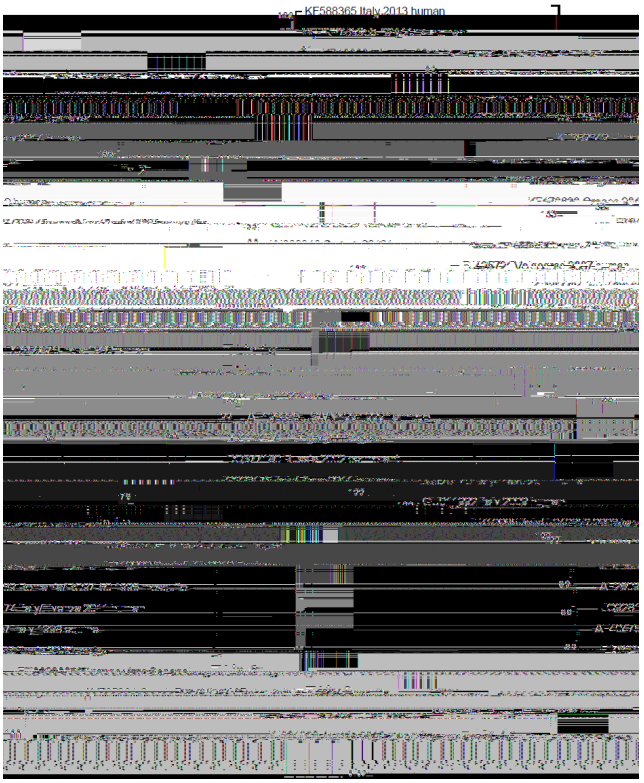

Figure 1: Phylogenetic tree of (European) WNV isolates depicting the di erent lineages of WNV as well as the phylogenetic di erences of virulent and avirulent European strains.

To date there is no specifc treatment of WNV neuroinvasive disease. Our limited knowledge of the pathogenesis at the cellular and molecular level still hampers the development of intervention strategies to reduce mortality and long-term functional defcits in survivors of WNV encephalitis. Understanding the correlates of virulence and pathogenesis of WNV neuroinvasive disease using state-