#### Home > ... > H2020 >

A transcriptomic approach to understand the avian genetic susceptibility to West Nile Virus infection

HORIZON 2020

### A transcriptomic approach to understand the avian genetic susceptibility to West Nile Virus infection

#### Rendicontazione

Informazioni relative al progetto

TransWNV

ID dell'accordo di sovvenzione: 795537

Sito web del progetto 🔀

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Progetto chiuso

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Coordinato da AGENCIA ESTATAL CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS

#### Questo progetto è apparso in...

10-14

La quadratura del Circolo Polare Artico: proteggere e preservare l'Estremo Nord della Terra

# Periodic Reporting for period 1 - TransWNV (A transcriptomic approach to understand the avian genetic susceptibility to West Nile Virus infection)

Periodo di rendicontazione: 2018-10-15 al 2020-10-14

#### Sintesi del contesto e degli obiettivi generali del progetto

The rate of newly emerging infectious diseases has increased in recent years and poses one of the major global health challenges. Many of the pathogens causing this increase are wildlife pathogens and it has been estimated that around 80% of emerging infectious diseases in humans are zoonotic with a wildlife reservoir. One of the best examples illustrating this situation is the outbreaks caused by flaviviruses, which include among others the West Nile Virus (WNV). This virus is widely distributed throughout the world and has a considerable impact both on public and animal health. Since its discovery in 1937, WNV has propagated to a vast region of the globe leading to its current consideration as the most widespread mosquito-borne flavivirus and the most important causative agent of viral encephalitis worldwide. Only in Europe, from 2011 to 2019, 3549 human cases of WNV have been detected, with a peak of cases in 2018. The geographical distribution of WNV has also changed recently. Currently, it is expanding North with new cases described in Germany and the Netherlands and there has been an outbreak in Spain in 2020.

WNV is maintained in nature in a natural cycle involving mosquitos that are the transmission vector and mostly feed on birds. When infected mosquitos bite humans they can get infected with WNV and get sick, but humans do not transmit the virus. The main challenge when studying WNV is that the virus has a very complex eco-epidemiology. It can infect multiple vertebrate host species and use multiple mosquito species as vectors. Regarding birds, it has been estimated that the virus can infect over 300 species only in North America. However, there is a wide range of variation in the susceptibility both within and across different bird species. As a consequence, the role each species plays in viral transmission, amplification, spillover to humans, and outbreaks varies greatly. To develop effective intervention strategies, it is critical to understand the underlying mechanisms and factors that influence the variation in disease susceptibility to WNV across species. To fully understand why some hosts are affected by a pathogen while others are able to resist infections it is fundamental to understand the genetic basis of the immune response. The overarching goal of this project was to characterize how different bird species respond to WNV infections by looking at gene expression. This allowed us to gain insights into the avian immune response to the virus and uncover the genetic basis of susceptibility to WNV infection.

## Lavoro eseguito dall'inizio del progetto fino alla fine del periodo – – coperto dalla relazione e principali risultati finora ottenuti

To understand the differences in susceptibility to WNV among bird species we carried out experimental inoculations, i.e we infected a group of individuals with WNV. We compared the response to a West Nile Virus infection in three species, sparrows, European turtle dove, and common quail. The sparrows were the more susceptible, with individuals dying as a consequence of the infection. The dove and quail were less susceptible but there were no differences between them. Both were asymptomatic, but got infected and mounted an immune response that allowed them to develop antibodies. We then studied which genes were being expressed. To study gene expression, I used RNA extracted from two tissues. I designed probes to improve RNA library preparation and analyzed the results using bioinformatic tools. I was able to get gene expression results for the common quail and the European turtle dove. The results show that genes involved in the immune response that recognize RNA viruses. There was also gene expression of genes involved in the adaptive immune response like MHC (Major Histocompatibility Complex), a cluster of genes that codes for proteins on the cell surface that bind to antigens and present them to T cells to trigger the adaptive immune response. These results are consistent with the generation of antibodies in both species.

Work was conducted via 3 work packages that combined, scientific, training, and transfer of knowledge goals. During the fellowship, I have published 3 journal articles related to the research activity in this project (Ecosistemas 29:1969; Frontiers in Microbiology. 2020;11:3169; Environmental Research. 2021:110893) and one invited review (Molecular Ecology.29: 3809-3811). I expect to generate 2 additional publications from the data obtained in the last work package. In addition, I have also presented the project in a workshop. I have also carried out a number of outreach activities to communicate the results of the project beyond the scientific community. To this extend I have given 2 talks in elementary schools, I have presented a video, a talk, and an activity in the Night of European Researchers (2019 and 2020), I have given a talk at the Pint of Science 2019, and I have published one blog post on infectious diseases in the Blog of the Spanish Association of Terrestrial Ecology and a press article in the Diario de Sevilla. In addition, I have participated in the European Research Executive Agency #MyJobinResearch.

Progressi oltre lo stato dell'arte e potenziale impatto previsto (incluso l'impatto socioeconomico e le implicazioni sociali più ampie del progetto fino ad ora) Studying emerging infectious diseases is critical because of the important health and economic impacts on our society. Genomic tools offer an unprecedented opportunity not only to understand the mechanisms and factors that determine disease transmission but also to implement adequate prediction, surveillance, and control measures. This project represents one of the first projects to study WNV in birds using genomics. WNV has increasing importance in Europe, and at a regional level, the outbreak of 2020 in Spain represents the biggest outbreak of a mosquito-borne disease since the eradication of malaria in 1964. The genomic resources developed with this project provide basic information to understand the complex eco-epidemiology of WNV in its natural reservoir (birds) and may help to predict future outbreaks in humans. As such, this project makes an important direct contribution to the study of Emerging infectious diseases of zoonotic origin and increases the knowledge in one of Europe's Key Research areas. The recent outbreak of WNV in Andalusia has confirmed the relevance of two of the three study species of the TRANSWNV project given the high prevalence of antibodies detected both in doves and house sparrows living in the villages affected by the outbreak. This project has helped to identify some of the factors that determine the different contributions of each of these species to virus amplification and transmission to humans. The publications generated during the TRANSWNV project already highlight the relevance of considering the interspecific differences in the immune response to infection and how this may condition the amplification and transmission of zoonoses.

From a social perspective, with the development of multiple outreach activities, I have contributed to increasing awareness of the health problems associated with zoonotic diseases. In addition, the TRANSWNV project is the base for a future study led by the MSCA fellow which just received funding from the Spanish Ministry of Science and Innovation. In this project genomics and ecology will be integrated to improve prediction, surveillance, and control of WNV Outbreaks in Southern Spain. As such, the present MSCA project has made an important contribution to the local communities that suffered the outbreak in summer 2020.



West Nile Virus transmission cycle. Image created with Biorender.com

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Permalink: https://cordis.europa.eu/project/id/795537/reporting/it

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