Comparative Immunology, Microbiology and Infectious Diseases 56 (2018) 30–33

Contents lists available at ScienceDirect

Comparative Immunology, Microbiology and Infectious Diseases

journal homepage: www.elsevier.com/locate/cimid

Absence of protection from West Nile virus disease and adverse effects in red legged partridges after non-structural NS1 protein administration

Belén Rebollo[a], Francisco Llorente[b], Elisa Pérez-Ramírez[b], Javier Sarraseca[a], Carmina Gallardo[b], María Ángeles Risalde[c], Úrsula Höfle[c], Jordi Figuerola[d,e], Ramón C. Soriguer[d,e], Ángel Venteo[a], Miguel Ángel Jiménez-Clavero[b,e,*]

[a] Inmunología y Genética Aplicada, S.A. (INGENASA), C/Hermanos García Noblejas 39, 28037, Madrid, Spain
[b] Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria – Centro de Investigación en Sanidad Animal (INIA-CISA), Ctra Algete-El Casar s/n, 208130, Valdeolmos, Madrid, Spain
[c] Instituto de Investigación en Recursos Cinegéticos, Universidad de Castilla-La Mancha, Ronda de Toledo, s/n, 13005, Ciudad Real, Spain
[d] Estación Biológica de Doñana CSIC, Calle Américo Vespucio, s/n, 41092, Seville, Spain
[e] Centro de Investigación Biomédica en Red de Epidemiologia y Salud Pública (CIBERESP), Spain

ARTICLE INFO

Keywords:
Flavivirus
West Nile virus
NS1
In-vivo
Adverse effects
Immunization
Red-legged partridge
Avian

ABSTRACT

The red-legged partridge (*Alectoris rufa*) is a competent host for West Nile virus (WNV) replication and highly susceptible to WNV disease. With the aim to assess in this species whether the inoculation of non-structural protein NS1 from WNV elicits a protective immune response against WNV infection, groups of partridges were inoculated with recombinant NS1 (NS1 group) or an unrelated recombinant protein (mock group), and challenged with infectious WNV. A third group received no inoculation prior to challenge (challenge group). The NS1 group failed to elicit detectable antibodies to NS1 while in the mock group a specific antibody response was observed. Moreover, no protection against WNV disease was observed in the NS1 group, but rather, it showed significantly higher viral RNA load and delayed neutralizing antibody response, and suffered a more severe clinical disease, which resulted in higher mortality. This adverse effect has not been observed before and warrants further investigations.

1. Introduction

West Nile virus (WNV, family *Flaviviridae*, genus *Flavivirus*) is a mosquito-borne virus with a broad vertebrate host range and different species of birds as reservoir hosts. WNV causes severe disease in horses, humans and some bird species [1]. The recent spread of this virus, remarkably in Europe and the Americas, is a matter of concern [2,3]. Effective vaccines are available for horses but not for humans or birds [4,5]. Hence, the development of new vaccines against WNV needs further efforts. For that, a better knowledge of the interaction between the host immune response and the different viral components might help identifying new targets for vaccine development.

WNV single-stranded RNA genome is translated as a single polyprotein that is cleaved to yield three structural (C, prM and E) and seven non-structural (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5) proteins. Host adaptive immunity against WNV mostly targets structural proteins [6]. However, NS1, which during infection is expressed as membrane and secreted forms, elicits an immune response in the host that has been involved in protection against WNV in mouse models [7]. Therefore, NS1 has been claimed as promising candidate for vaccine development [8]. The objective of this work was to assess the immune response elicited by the administration of NS1 in a natural avian host, the red-legged partridge [9] and if it conferred protection against a challenge with an infectious dose of a pathogenic WNV strain.

2. Materials and methods

2.1. Cloning and expression of recombinant proteins

Recombinant proteins used in this study were produced in the baculovirus expression system as described elsewhere [10]. Briefly, the NS1-coding region from WNV NY99 034EDV “crow” strain (obtained

* Corresponding author at: Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria – Centro de Investigación en Sanidad Animal (INIA-CISA), Valdeolmos, Madrid, Spain.
E-mail addresses: brebollo@ingenasa.com (B. Rebollo), dgracia@inia.es (F. Llorente), perez.elisa@inia.es (E. Pérez-Ramírez), investigacion2@ingenasa.com (J. Sarraseca), gallardo@inia.es (C. Gallardo), mariaA.risalde@uclm.es (M.Á. Risalde), ursula.hofle@uclm.es (Ú. Höfle), jordi@ebd.csic.es (J. Figuerola), soriguer@ebd.csic.es (R.C. Soriguer), aventeo@ingenasa.com (Á. Venteo), majimenez@inia.es (M.Á. Jiménez-Clavero).

https://doi.org/10.1016/j.cimid.2017.12.006
Received 16 November 2017; Received in revised form 29 December 2017; Accepted 29 December 2017