ROLE OF CAPRINE *HERPESVIRUS*–1 (CPHV-1) IN THE INNATE IMMUNO-EVASION INTERFERON MEDIATE

Giuseppe Pisanelli, Rosa Loponte, Valentina Iovane, Ugo Pagnini, Giuseppe Iovane

Department of Veterinary Medicine and Animal Production, University of Napoli Federico II, Napoli, Italy

Caprine Herpesvirus-1 (CpHV-1) is a member of *Varicellovirus* genus within *Herpesvirus* family. CpHV-1 is the responsible of a disease that causes respiratory symptoms, balanopostitis, vulvovaginitis and abortion in adult goats. It also affects young goats with a systemic disease [1]. Type I (IFN-a/ß) and type II (IFN g) interferons, are the first weapons of the host to fight against viral infections. Type I IFNs induce the expression of more than 100 Interferon Stimulated Genes (ISGs) to establish an antiviral state that limits viral replication and dissemination. [2] Type II IFN is produced by activated immune cells and leads to the production of a different subset of ISGs via a distinct signaling pathway. Many viruses are able to subvert both type I and type II IFN-mediated antiviral responses. *Herpesviruses* are able to evade the IFN response by targeting different transcriptions factors of the interferon (IFN) signaling pathway [3]. There are no reports in literature about the role of CpHV-1 in IFN antagonism. Aim of the work: Herein, we describe a work to address the possible role of CpHV-1 as modulator of the innate immune response interferon mediate. Materials and methods. To investigate whether CpHV-1 interferes with type I interferon production, we performed an IFN-ß reporter assay, using a reporter plasmid that carries the IFN-ß promoter driving the expression of a firefly luciferase gene. A renilla-luciferase reporter plasmid was used as control. For the activation of the pathway we used the constitutively active N-terminal (2CARD) domain of RIG-I. To evaluate the potential CpHV-1-mediated inhibition of IFN a/ß signaling, we performed an ISRE54 reporter assay using a construct having an ISRE54 promoter driving the expression of firefly luciferase. A renilla-luciferase reporter plasmid was used as internal control. Results. Our results show that CpHV-1 infection strongly suppressed the activation of IFN-β promoter induced by RIGI 2 CARD domain. Moreover cells mock infected and treated with type I IFN showed a significant increase in luciferase expression, as expected compared with the cells that were not treated with type I IFN and were not infected. The cells infected with CpHV-1 and treated with type I IFN showed significantly reduced luciferase expression driven by the ISRE54 promoter.

These results showed that CpHV-1 is a strong inhibitor of type I Interferon production and signaling pathways.

[1] Tempesta M, Pratelli A, Greco G, Martella V, Buonavoglia C, 1999. Detection of caprine herpes virus 1 in the sacral ganglia of latently infected goats by polimerasi chain reactionj J Clin Microbiol 37, 1598-99.

[2] Garcia-Sastre A, Biron CA (2006) Type 1 interferons and the virus-host relationship: a lesson in detente. Science 312: 879-882. [3] Afroz S, Brownlie R, Fodje M, van Drunen Littel-van den Hurk S. VP8, the Major Tegument Protein of Bovine Herpesvirus 1, Interacts with Cellular STAT1 and Inhibits Interferon Beta Signaling. J Virol. 2016 Apr 29; 90(10): 4889-904.