

Differences in IPS-1-Mediated Innate Immune Responses between Neurotrophic Flavivirus Infection

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Introduction

genus *Flavivirus* of the family *Flaviviridae* consists of more than 70 members and many of them are transmitted through arthropods [1]. viruses can cause severe diseases in humans and animals [2]. includes West Nile virus (WNV), Dengue virus (DENV), Japanese encephalitis virus (JEV), Yellow fever virus (YFV), Tick-borne encephalitis virus (TBEV), Murray Valley encephalitis virus (MVEV) and St. Louis encephalitis virus (SLEV) [1]. In most cases no vaccine is available and thousands of new infections are registered annually [3,4]. To date there is only symptomatic treatment available for infected patients [3,4].

Innate Recognition of Flaviviruses

Evidence indicates that innate immune responses play a crucial role in the control of TBEV infection [2]. Nucleic acids are the main pathogen-associated molecular pattern (PAMPs) recognized by the innate immune system [5]. Sensing of PAMPs results in the control of the wave of viral infection through the production of antiviral molecules and it contributes to the mobilization of the adaptive immune response [5]. Double-stranded RNA of TBEV is mainly sensed by Toll like receptors (TLRs) and Retinoic acid-inducible gene (RIG)-I like receptors (RLRs) [6,7]. RIG-I interacts with Interferon- promoter stimulator-1 (IPS-1) upon activation and triggers the activation of Interferon regulatory factor-3 (IRF-3), IRF-7 and Nuclear factor kappa-light-chain-enhancer of activated B-cells (NF- κ B), leading to the induction of type I interferons (IFNs) and

viral replication in parts of the brain [9]. For most viruses, IPS-1 dependent IFN- induction was shown to be distinct between analyzed cell types [9,11]. We have previously demonstrated that