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Proceeding Paper

Neurodegerative Role of West Nile Virus Non-Structural Protein 1: Effect on Tlr3 and Amyloid Beta Expression †

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Abstract: A single paragraph of about 100 words to give a brief introduction to your work.

Keywords: keyword 1; keyword 2; keyword 3 (List three to ten pertinent keywords specific to the article yet reasonably common within the subject discipline.)

1. Introduction

In the last years, the North-Est region of Italy, in particular Veneto and Emilia-Romagna [1], has been characterized by a significant increase of West Nile Virus (WNV) infection rate. Neuroinvasive WNV viral infection may be linked epidemiologically and mechanistically to neurodegeneration, which have been associated with a significant prevalence of sequelae such as memory loss, confusion, and fatigue years later.

Non-structural protein 1 (NS1) is a highly conserved protein among Flaviviruses, which is actively secreted by infected cells and detected in the serum between days 3 and 8 post-infection, peaking on day 5, the day prior to the onset of clinical disease. Extracellular forms of NS1 are implicated in immune modulation and in promoting endothelial dysfunction at blood-tissue barriers, facilitating WNV dissemination to the brain and affecting disease outcomes. Moreover, it has been reported a possible crucial role of Toll-like Receptor 3 (TLR3), an endosomal Pathogen Pattern Receptors (PPRs) involved in RNA viruses sensing, in WNV immune evasion and cell entry.

2. Aim

Focusing on the recently discovered antimicrobial roles of amyloid beta [2], we connected WNV late pathology to overlapping features encountered in neurodegenerative diseases such as Alzheimer's disease. We aimed to investigate the possible effect of soluble NS1 on neurodegenerative and dysfunctional biomarkers (e.g., amyloid beta (Aβ), amyloid precursor protein (APP), glial fibrillary acidic protein (GFAP), β-III tubulin and TLR3 signaling pathway), to clarify the mechanism underlying the CNS sequelae associated to WNV infection.

3. Methods

2D cultures and 3D neuronal model were obtained with on human glial model (T98G cells) and iPS (Induced Pluripotent Stem) cells and treated with purified WNV NS1. Gene expression and proteomic profiles were evaluated by RT real-time PCR, ELISA and immunofluorescence analysis.

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4. Results

We observed the ability of soluble NS1 to affect the expression of neurodegenerative and dysfunctional biomarkers. In particular, NS1 induced Aβ altered expression via TLR3, an endosomal Pathogen Pattern Receptors (PPRs) involved in RNA viruses sensing [3]. We reported an increase in Aβ 1-42 isoform in association with increased glial activation and decreased β-III tubulin, suggesting a role of glial cells in Aβ accumulation and consequent neuronal death due to NS1 stimulation.

5. Conclusions

Our preliminary results suggest a possible role of soluble NS1 on CNS damage associated to WNV infection. Interestingly, TLR3 increased expression has been found associated to Aβ plaque in AD brains [4] and Aβ itself stimulates TLRs expression, prompting the neurodegeneration [5]. NS1 released by WNV infected cells might participate in CNS neurodegenerative process by altering TLR3 signaling and Aβ expression, suggesting a novel pathogenetic role.

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