

# The immunomodulatory role of flavivirus sNS1 protein on monocyte-derived dendritic cells

## Inhalt

Arthropod-borne flaviviruses cause important human diseases, including encephalitis and meningitis with long-term neurological sequelae. The flavivirus non-structural protein 1 (NS1) is secreted from cells in infected individuals and known to play a role in viral pathogenesis. We recently showed that sNS1 of different flaviviruses dampen the immune response of dendritic cells upon stimulation. However, the immunomodulatory role of sNS1 during flavivirus infection is less clear. Here, we examined the immune response of monocyte-derived dendritic cells (moDCs) during infection with Usutu virus (USUV) or stimulation with polyinosinic-polycytidylic acid (poly(I:C)). Pretreatment with recombinant USUV sNS1 was performed 16 hours prior to stimulation or infection. Cell lysates were used for western blot analysis of melanoma differentiation-associated protein 5 (MDA5) expression and supernatants for detection of pro-inflammatory cytokines interleukin 6 (IL-6) and tumor necrosis factor (TNF- $\alpha$ ) by ELISA. In poly(I:C) stimulated moDCs, cytokines and MDA5 expression were downregulated after pretreatment with USUV sNS1. Interestingly, cytokine production of moDCs was low after USUV infection, but upregulated in cells that were pre-treated with sNS1 prior to USUV infection. Our results suggest discordant effects of USUV sNS1 on uninfected bystander and actively infected moDCs. Unraveling the immune signaling in moDCs will advance our understanding of immunomodulation by flavivirus sNS1.

## Keywords

Flaviviruses, neurotropic infections, immunomodulation, arboviruses, astrocytes.

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## Professional Status of the Speaker

PhD Student

## Junior Scientist Status

No, I am not a Junior Scientist.

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