

Accepted Manuscript

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Lisa Miorin, Ana M. Maestre, Ana Fernandez-Sesma, Adolfo García-Sastre

PII: S0006-291X(17)31046-X

DOI: [10.1016/j.bbrc.2017.05.146](https://doi.org/10.1016/j.bbrc.2017.05.146)

Reference: YBBRC 37867

To appear in: *Biochemical and Biophysical Research Communications*

Received Date: 19 April 2017

Revised Date: 20 May 2017

Accepted Date: 24 May 2017

Please cite this article as: L. Miorin, A.M. Maestre, A. Fernandez-Sesma, A. García-Sastre, Antagonism of type I interferon by flaviviruses, *Biochemical and Biophysical Research Communications* (2017), doi: 10.1016/j.bbrc.2017.05.146.

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1 ANTAGONISM OF TYPE I INTERFERON BY FLAVIVIRUSES

2 Lisa Miorin^{1,2,*}, Ana M. Maestre^{1,*}, Ana Fernandez-Sesma^{1,3,#} and Adolfo García-
3 Sastre^{1,2,3,#}

4 Department of Microbiology¹, Global Health and Emerging Pathogens Institute²,
5 Department of Medicine, division of Infectious Diseases³, Icahn School of Medicine
6 at Mount Sinai, New York, NY 10029.

7 *Co-First authors

8 #Co-Corresponding authors

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10 HIGHLIGHTS:

- 11 • Flaviviruses are arthropod-borne viruses, many of which represent an
12 expanding threat to public health worldwide.
- 13 • Type I Interferons are key innate immune regulators for antiviral defense.
- 14 • Flaviviruses have evolved multiple strategies to overcome innate immune
15 detection and ensure viral replication and spread.
- 16 • This evolutionary struggle for survival results in a balance for coexistence of
17 both hosts and viruses.

18

19 KEYWORDS

20 Flaviviruses; innate immunity; type I interferon; viral innate immune evasion;
21 interferon antagonism.

22

23 ABSTRACT

24 The prompt and tightly controlled induction of type I interferon is a central event of
25 the immune defense against viral infection. Flaviviruses comprise a large family of
26 arthropod-borne positive-stranded RNA viruses, many of which represent a serious
27 threat to global human health due to their high rates of morbidity and mortality. All
28 flaviviruses studied so far have been shown to counteract the host's immune
29 response to establish a productive infection and facilitate viral spread. Here, we
30 review the current knowledge on the main strategies that human pathogenic
31 flaviviruses utilize to escape both type I IFN induction and effector pathways. A
32 better understanding of the specific mechanisms by which flaviviruses activate and

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