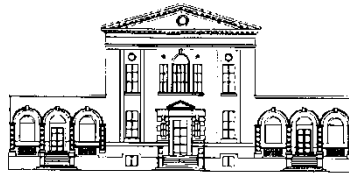


**First International  
Conference on Zika Virus**

**February 22-25, 2017 - Washington DC, USA**

# T-CELL PHENOTYPE AND FUNCTION DURING HUMAN ACUTE ZIKV INFECTION



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**WHO Collaborating Center for clinical care, diagnosis, response and training on  
Highly Infectious Diseases**

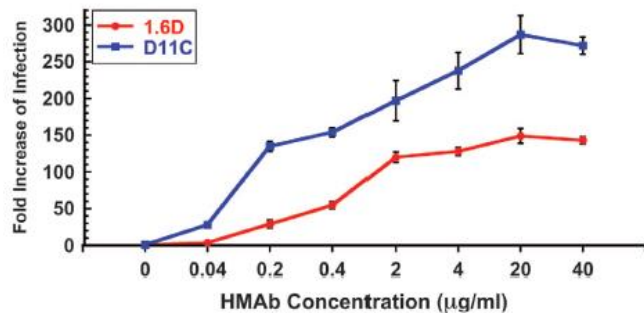
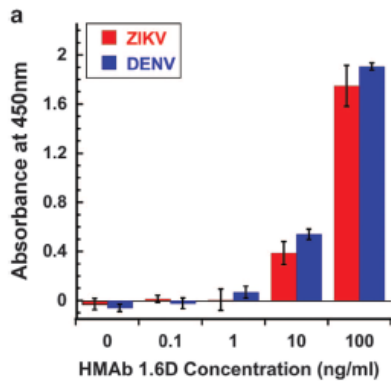
# What is known (1)

## Serological cross-reactivity

*Clin Trasl Immunol 2016*

### Dengue virus antibodies enhance Zika virus infection

Lauren M Paul, Eric R Carlin<sup>1</sup>, Meagan M Jenkins<sup>1</sup>, Amanda L Tan, Carolyn M Barcellona, Cindo O Nicholson<sup>2</sup>, Scott F Michael<sup>3</sup> and Sharon Isern<sup>3</sup>

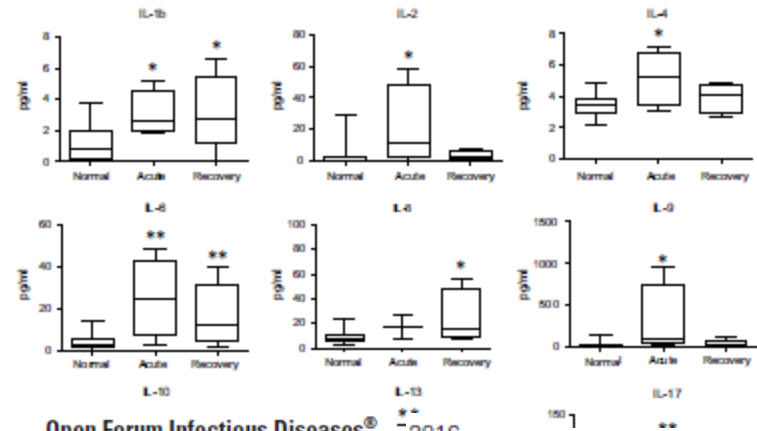


## Cytokines profile

*Med Microbiol Immunol (2016) 205:269–273*

### Cytokine kinetics of Zika virus-infected patients from acute to reconvalescent phase

Dennis Tappe<sup>1,2</sup>, José Vicente Pérez-Girón<sup>3</sup>, Lorenzo Zammarchi<sup>4</sup>, Jürgen Rissland<sup>5</sup>, Davis F. Ferreira<sup>6</sup>, Thomas Jaenisch<sup>7</sup>, Sergio Gómez-Medina<sup>3</sup>, Stephan Günther<sup>1,2</sup>, Alessandro Bartoloni<sup>4</sup>, César Muñoz-Fontela<sup>1,2,3</sup>, Jonas Schmidt-Chanait<sup>1,2</sup>



Open Forum Infectious Diseases® 2016.

### Zika Virus Causing Encephalomyelitis Associated With Immunoactivation

Rafael Mello Galliez,<sup>1,2</sup> Mariana Spitz,<sup>3,4</sup> Patricia Piazza Rafful,<sup>5,7</sup> Marcelo Cagy,<sup>3,4</sup> Claudia Escosteguy,<sup>5</sup> Caroline Spósito Brito Germano,<sup>3,4</sup> Elisa Sasse,<sup>3,4</sup> Alessandro Luis Gonçalves,<sup>8</sup> Paola Paz Silveira,<sup>8</sup> Paula Pezzuto,<sup>8</sup> Alice Maria de Magalhães Ornelas,<sup>8</sup> Amílcar Tanuri,<sup>8</sup> Renato Santana Aguiar,<sup>8</sup> and Fernanda Tovar Moll<sup>8,9</sup>



# What is known (2):

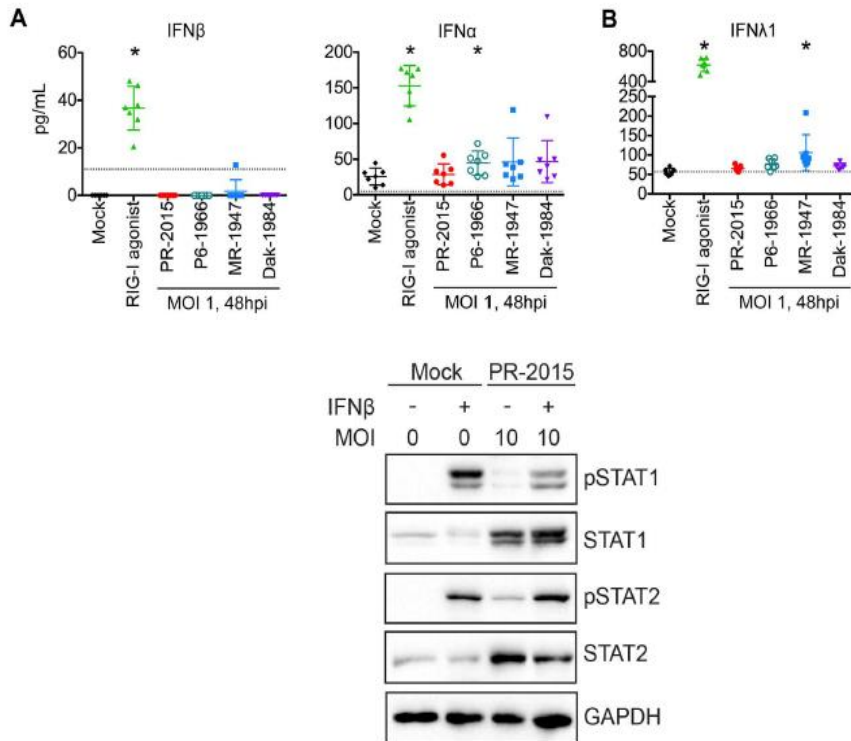
## Inhibition of type I IFNs

RESEARCH ARTICLE

### Zika Virus Antagonizes Type I Interferon Responses during Infection of Human Dendritic Cells

James R. Bowen<sup>1,2\*</sup>, Kendra M. Quicke<sup>1,2\*</sup>, Mohan S. Maddur<sup>2,3</sup>, Justin T. O'Neal<sup>1,2</sup>, Circe E. McDonald<sup>1,2</sup>, Nadia B. Fedorova<sup>4</sup>, Vinita Puri<sup>4</sup>, Reed S. Shabman<sup>4</sup>, Bali Pulendran<sup>2,3</sup>, Mehul S. Suthar<sup>1,2\*</sup>

PLOS Pathogens | DOI:10.1371/journal.ppat.1006164 February 2, 2017



## Cellular immune response

Cell Host & Microbe  
Article

### Mapping and Role of the CD8<sup>+</sup> T Cell Response During Primary Zika Virus Infection in Mice

Annie Elong Ngonu,<sup>1</sup> Edward A. Vizcarra,<sup>1</sup> William W. Tang,<sup>1</sup> Nicholas Sheets,<sup>1</sup> Yunichel Joo,<sup>1</sup> Kenneth Kim,<sup>1</sup> Matthew J. Gorman,<sup>2</sup> Michael S. Diamond,<sup>2</sup> and Sujan Shresta<sup>1,3\*</sup>

<sup>1</sup>Division of Inflammation Biology, La Jolla Institute for Allergy and Immunology, La Jolla, CA 92037, USA

<sup>2</sup>Department of Medicine, Molecular Microbiology, Pathology, and Immunology, Center for Human Immunology and Immunotherapy Programs, Washington University School of Medicine, St. Louis, MO 63110, USA

<sup>3</sup>Lead Contact

\*Correspondence: [sujan@lji.org](mailto:sujan@lji.org)

<http://dx.doi.org/10.1016/j.chom.2016.12.010>

✓ Adoptive transfer of ZIKV-immune CD8<sup>+</sup> T cells reduced viral burdens, whereas their depletion led to higher tissue burdens, ✓ *CD8*<sup>-/-</sup> mice displayed higher mortality with ZIKV infection. Collectively, these results demonstrate that CD8<sup>+</sup> T cells protect against ZIKV infection.



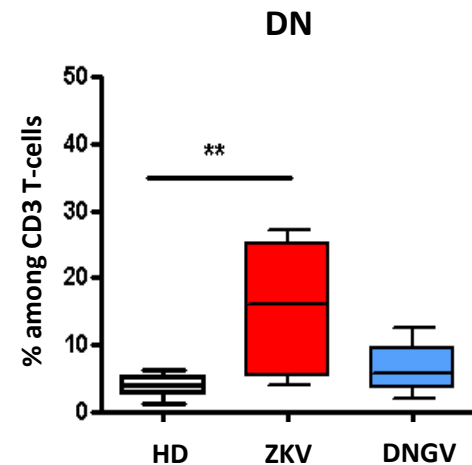
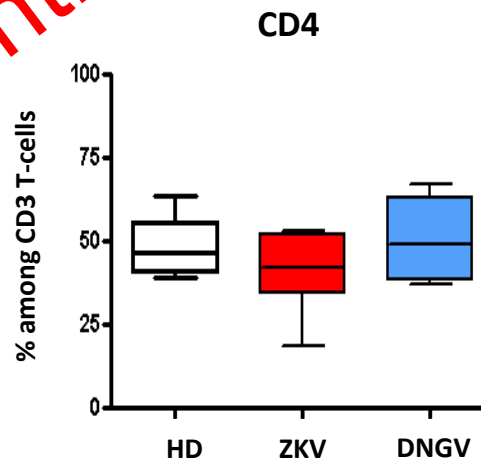
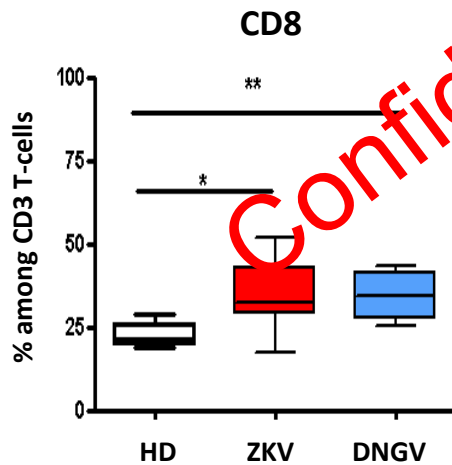
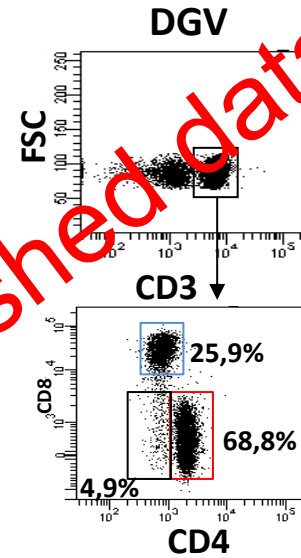
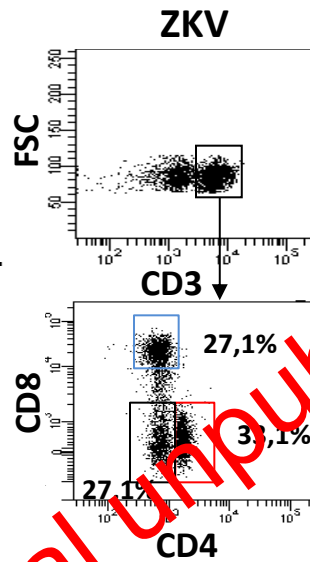
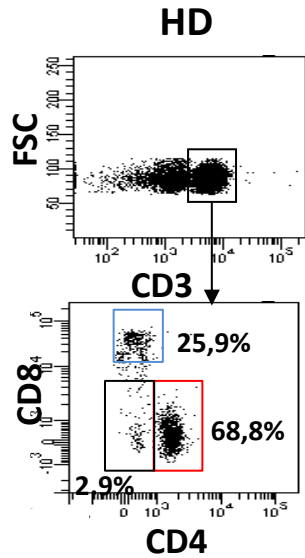
To compare the cellular immune response during Zika (ZIKV) and Dengue (DEGV) infection.

Patients	Age (Mean±SD)	M/F	Days after symptoms onset (min-max)
HD (n=10)	43 ± 13	5/3	n.a.
ZIKV (n=7)	37 ± 13	1/6	2-9
DEGV (n=4)	48 ± 15	2/2	2-9

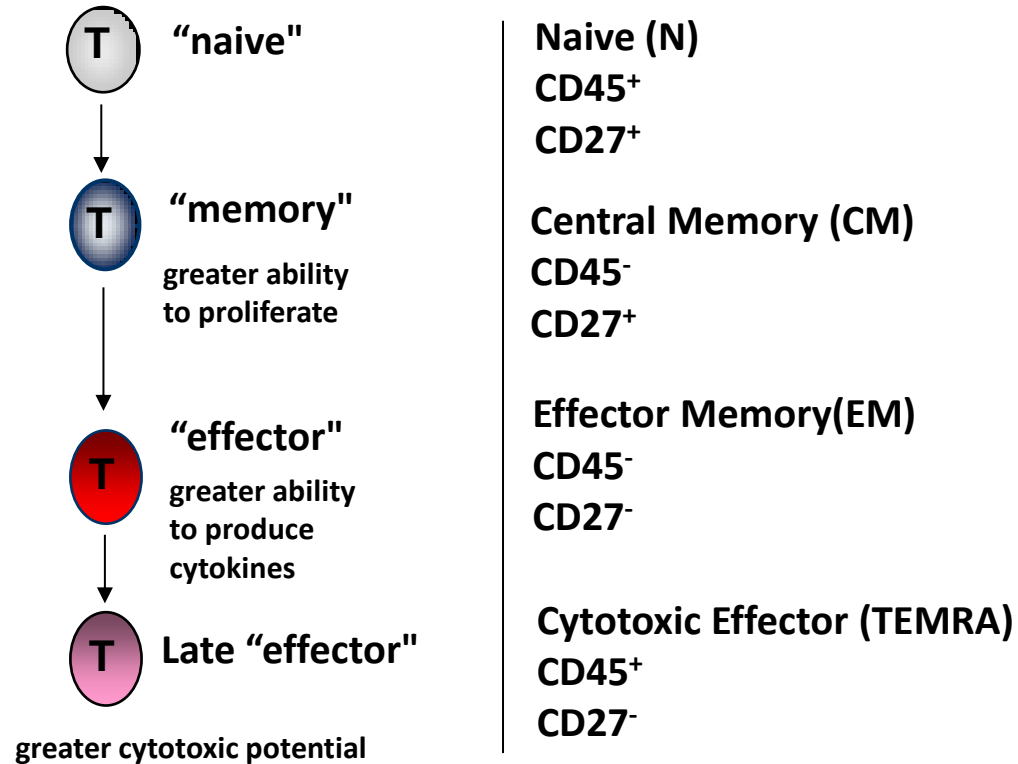
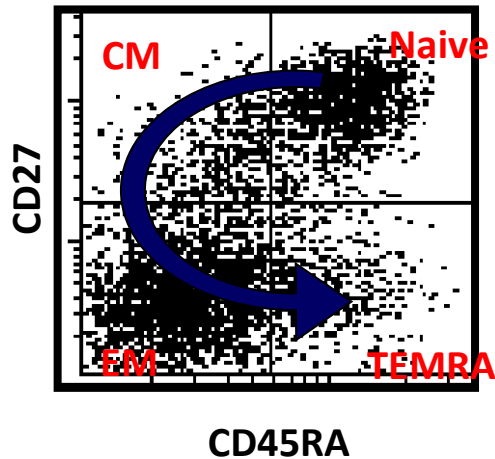
Patients and controls were enrolled at INMI L Spallanzani in Rome. The project was approved by INMI ethical committee



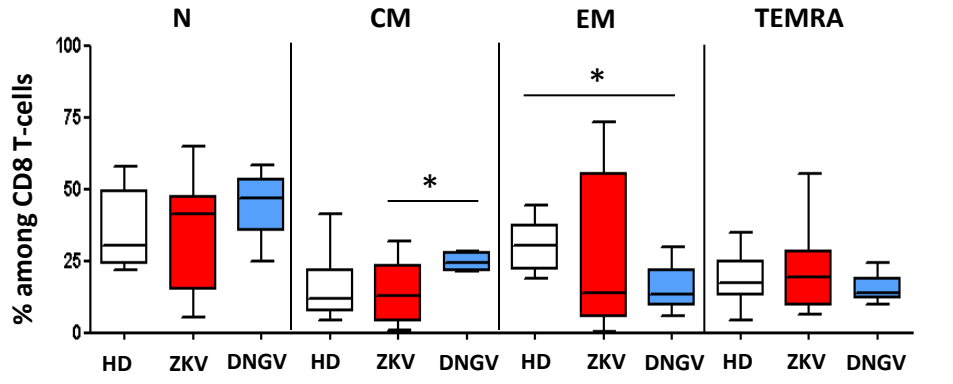
# T cell subsets



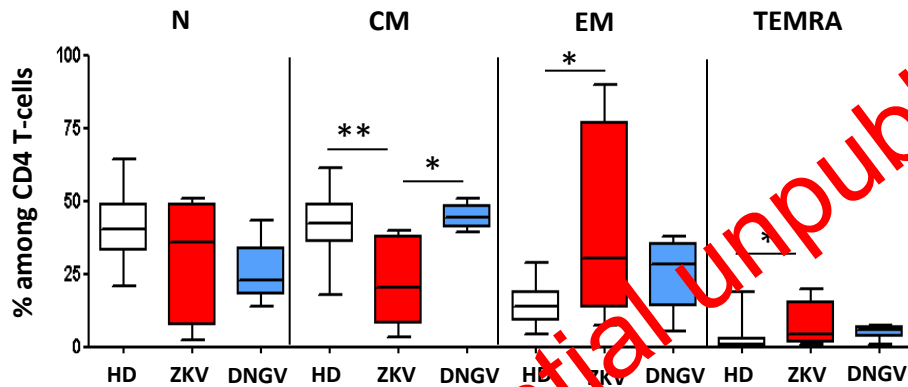
# T cell differentiation profile



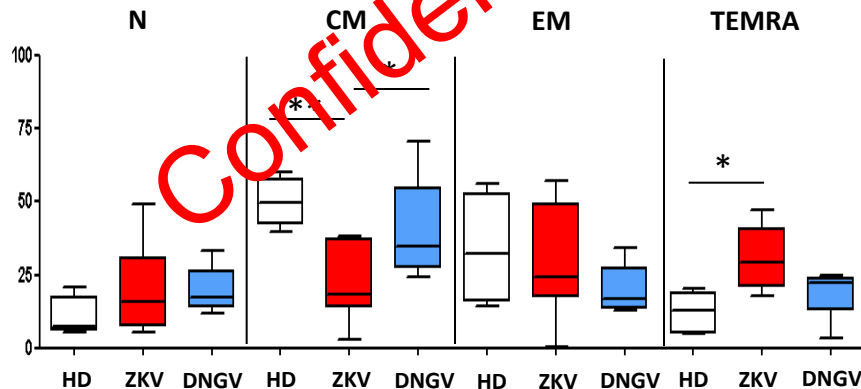
CD8



CD4



DN



- ZIKV induced CD4 T cell differentiation toward effector phenotype.

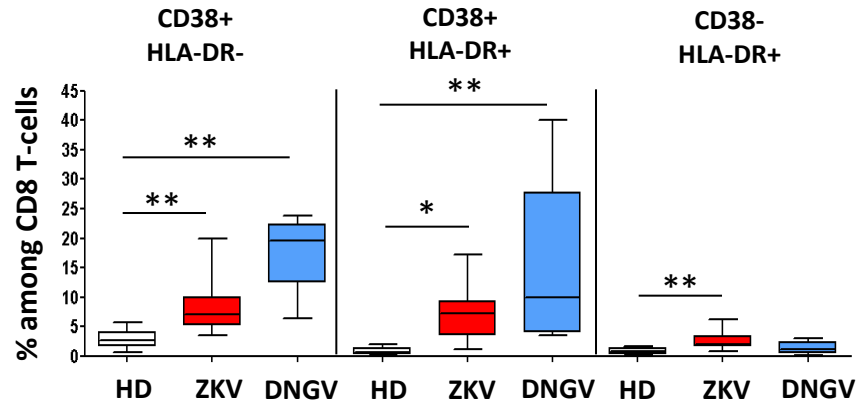
- ZIKV induced DN T cells differentiation toward terminally effector phenotype



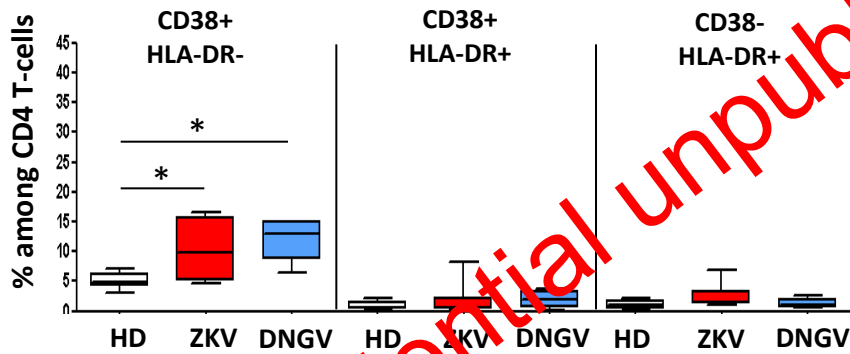


# T cell activation

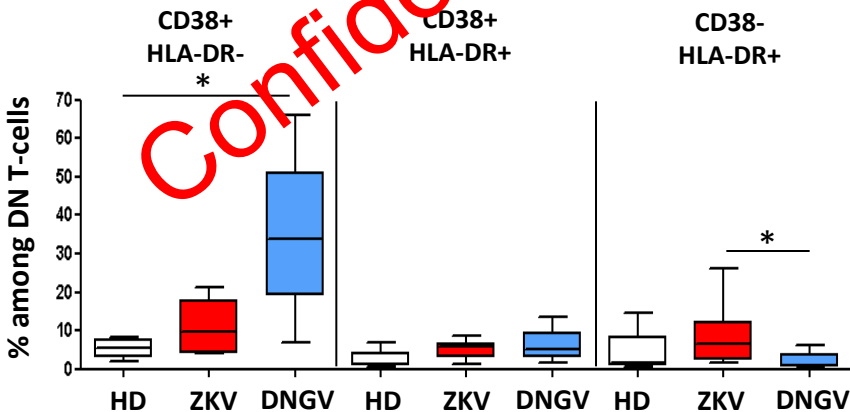
CD8



CD4



DN

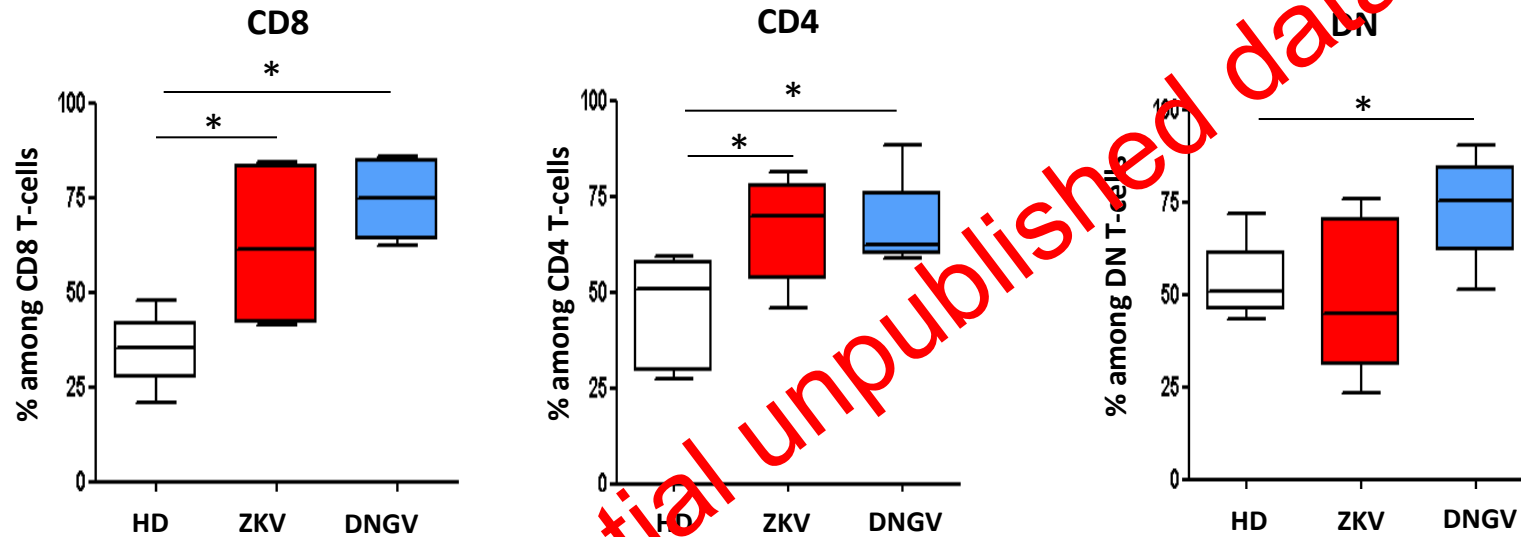


Both ZIKV and DEGV induced T cell activation

Confidential unpublished data



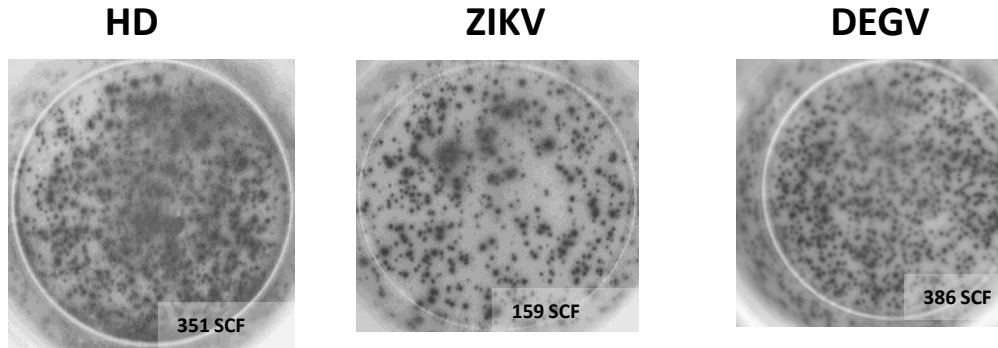
# CD95 expression on T cell subsets



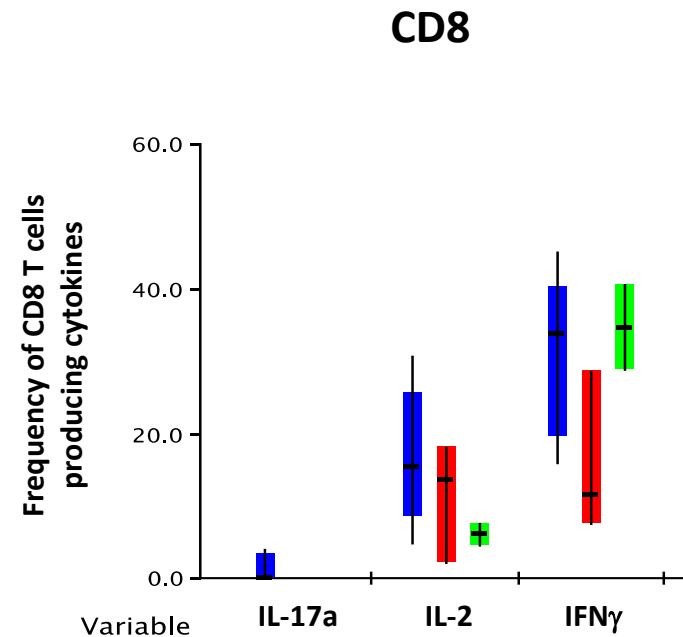
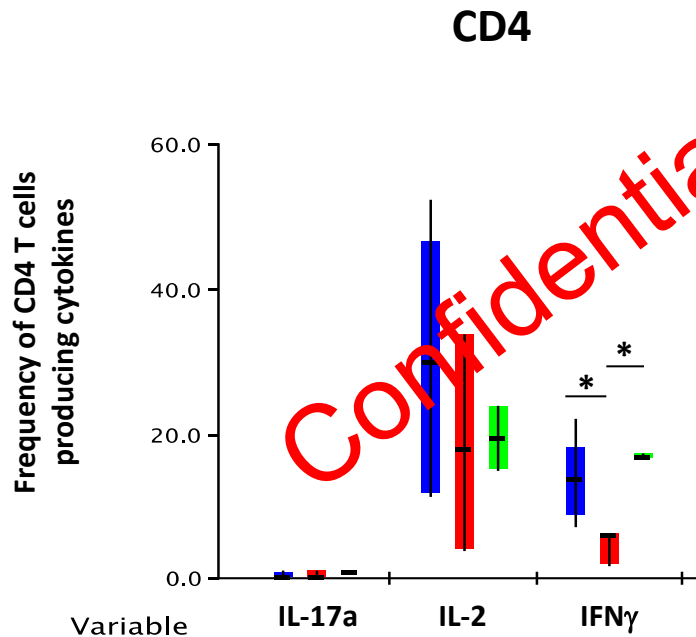
Confidential unpublished data



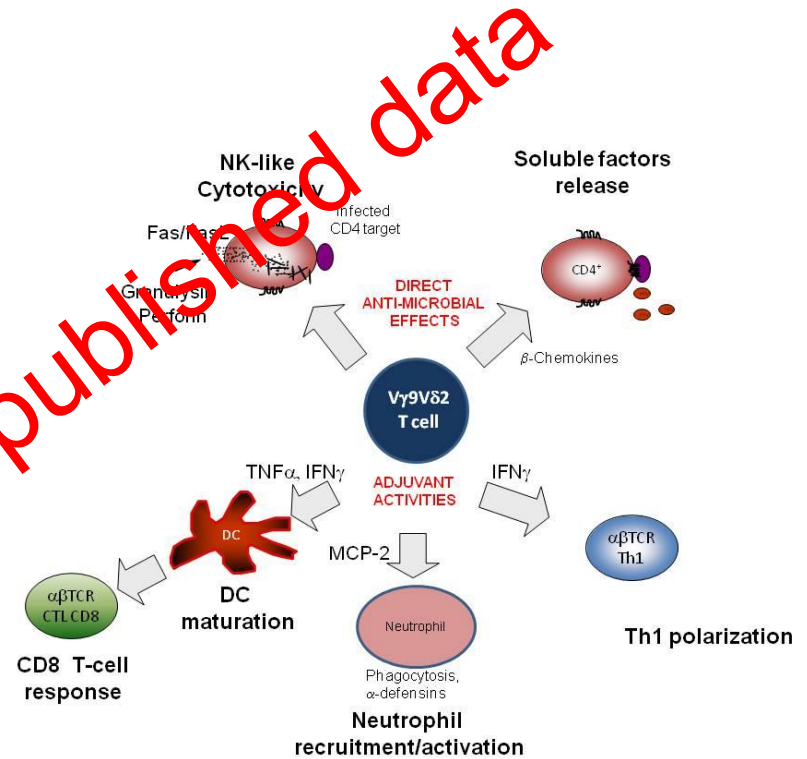
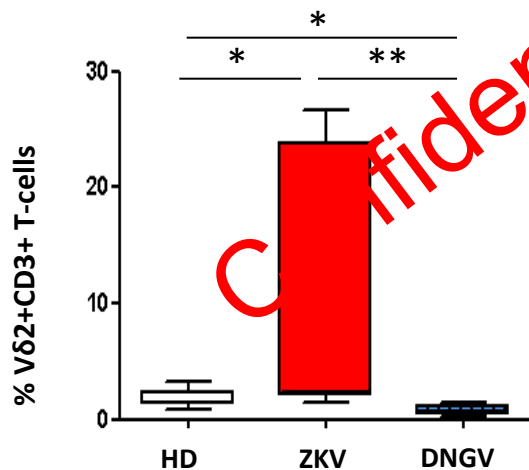
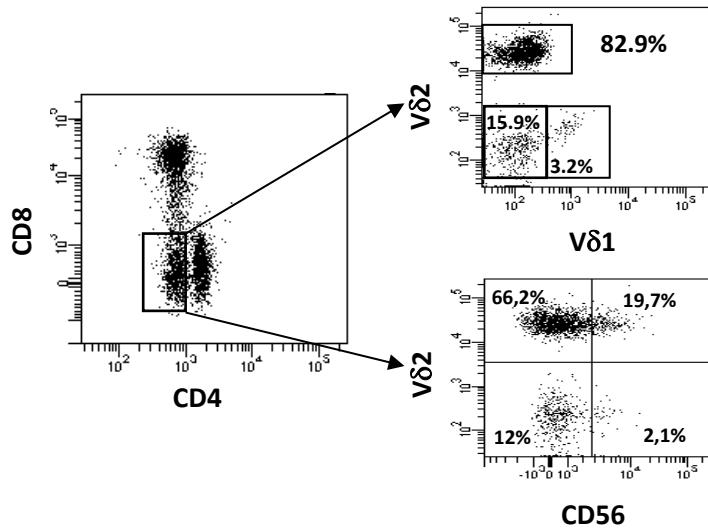
# Functional analysis of T cells



Significant reduction of IFN- $\gamma$  producing T cells during ZIKV infection

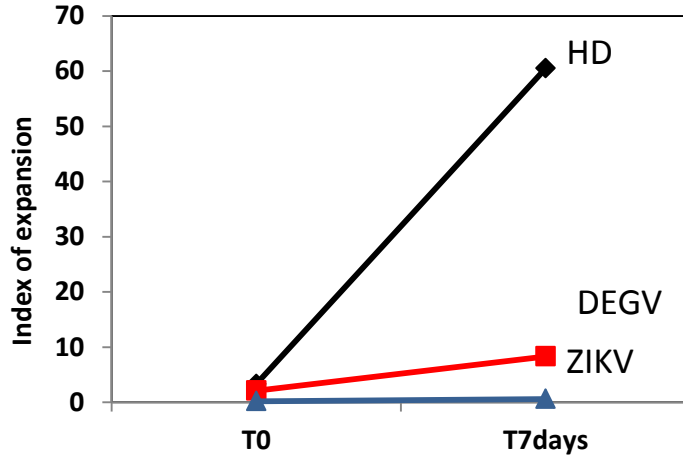


# V $\delta$ 2 T cells are the major subset of DN T cells



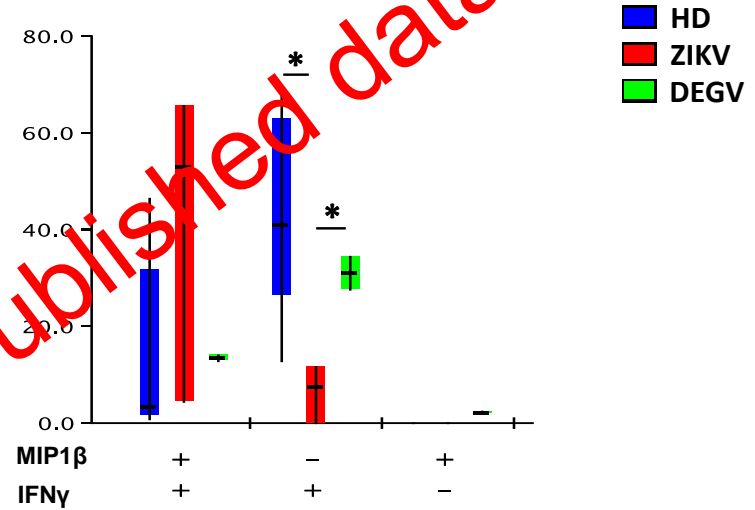
# Functional analysis of Vδ2 T cells

## Proliferation

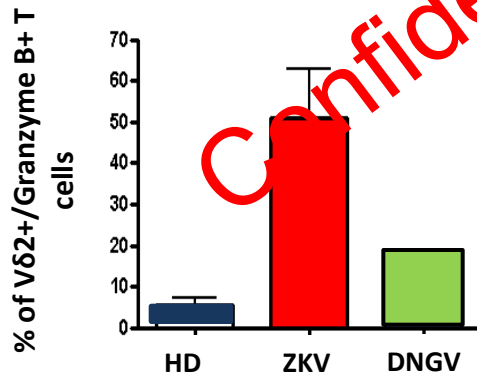


## Cytokine production

Frequency of Vδ2 T cells producing cytokines

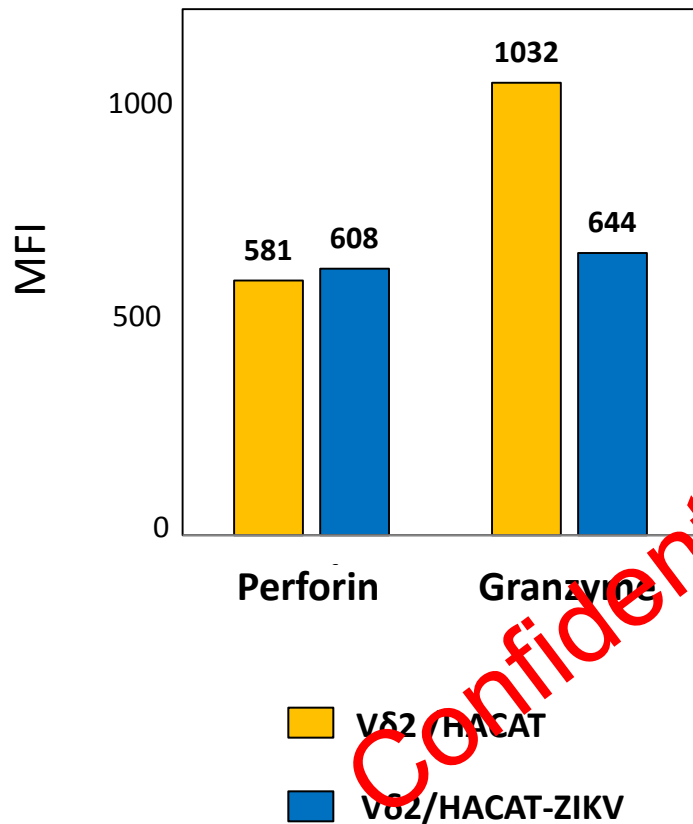


## Cytotoxic potential



Confidential unpublished data

# V $\delta$ 2 T cells recognize Zika-infected cells and release granzyme B



Ongoing experiments are focused to identify the recognition mechanisms and the cytotoxic activity.

Confidential unpublished data



# Conclusions

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**induced an increase of CD8 T cells and a general activation of T cells**



**ZIKV induced a significant increase of DN T cells expressing V $\delta$ 2 TCR and enriched of Granzyme B**

**ZIKV induced a significant decrease in IFN- $\gamma$  production by both  $\alpha\beta$  and  $\gamma\delta$  T cells**

**V $\delta$ 2 T cells recognize ZIKV infected cells and release granzyme B**



# Acknowledgements

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