First International
Conference on Zika Virus

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T-CELL PHENOTYPE AND FUNCTION DURING HUMAN ACUTE ZIKV INFECTION

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**What is known (1)**

**Serological cross-reactivity**

*Clin Trasl Immunol 2016*

**Dengue virus antibodies enhance Zika virus infection**

Lauren M Paul, Eric R Carlin³, Meagan M Jenkins³, Amanda I Tan, Carolyn M Barcellona, Cindy O Nicholson³, Scott F Michael³ and Sharon Isem³

**Cytokines profile**


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

Dennis Tappe¹,², José Vicente Pérez-Girón³, Lorenzo Zammarchi⁴, Jürgen Risland⁵, Davis F. Ferreira⁵, Thomas Jaensch⁷, Sergio Gómez-Medina³, Stephan Günther¹,², Alessandro Bartoloni⁴, Cesar Muñoz-Fontela¹,²,³, and Jonas Schmidt-Chanasit¹,²

**Zika Virus Causing Encephalomyelitis Associated With Immunoactivation**

Rafael Mello Galiano¹,², Mariana Spitz³, Patricia Piazza Rafful⁶,⁷, Marcelo Cayg³,⁴, Claudia Escosteguy⁵, Caroline Spósito Brito Germano,³,⁴ Elisa Sasset³,⁴, Alessandro Luis Gonçalves³, Paula Paz Silveira⁵, Paula Pezzuto³, Alice Maria de Magalhães Ornelas⁴, Amilcar Tanuri⁵, Renato Santana Aguiar⁶, and Fernanda Tobar Molf¹
What is known (2):

- Adoptive transfer of ZIKV-immune CD8+ T cells reduced viral burdens, whereas their depletion led to higher tissue burdens.
- CD8−/− mice displayed higher mortality with ZIKV infection.

Collectively, these results demonstrate that CD8+ T cells protect against ZIKV infection.
AIM

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

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

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

Confidential unpublished data
T cell differentiation profile

- **Naive (N)**
  - CD45^+ CD27^+
  - Greater ability to proliferate
  - More "naive"

- **Central Memory (CM)**
  - CD45^- CD27^+
  - "Memory"
  - Greater ability to produce cytokines

- **Effector Memory (EM)**
  - CD45^- CD27^-
  - "Effector"

- **Cytotoxic Effector (TEMRA)**
  - CD45^+ CD27^-
  - Late "Effector"
  - Greater cytotoxic potential
- ZIKV induced CD4 T cell differentiation toward effector phenotype.

- ZIKV induced DN T cells differentiation toward terminally effector phenotype
Both ZIKV and DENV induced T cell activation
CD95 expression on T cell subsets

Confidential unpublished data
Functional analysis of T cells

Significant reduction of IFN-γ producing T cells during ZIKV infection
Vδ2 T cells are the major subset of DN T cells
Functional analysis of Vδ2 T cells

Cytotoxic potential

% of Vδ2+/Granzyme B+ T cells

HD
ZIKV
DENV

Cytotoxic potential

Frequency of Vδ2 T cells producing cytokines

Cytokine production

IFNγ
MIP1β

Unpublished data

Confidential
Vδ2 T cells recognize Zika-infected cells and release granzyme B

Ongoing experiments are focused to identify the recognition mechanisms and the cytotoxic activity.
ZIKV induced a significant increase of DN T cells expressing Vδ2 TCR and enriched of Granzyme B.

ZIKV induced a significant decrease in IFN-γ production by both αβ and γδ T cells.

Vδ2 T cells recognize ZIKV infected cells and release granzyme B.
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