Induction of Protective Antibodies Against Dengue Virus by Tetravalent DNA Immunization with Domain III of the Envelope Protein

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Dengue Virus
Flaviviridae
Den-1, Den-2, Den-3, Den-4

• World wide distribution
• 2 billion people at risk
• 100 millions of cases per year
• Co-circulation of 4 serotypes
• Increasing cases of FHD/SCD
• Mortality 5 %
Dengue Virus

- Esferic, nm
- Enveloped
- Positive strand RNA
- Multiple genotypes

Kuhn RJ. Cell, 2002
Dengue control strategies

• Prevention
• Vector control
• Vaccination

• Live attenuated vaccines
• Recombinant proteins
• Sub-viral particles
• Quimeric virus-based vaccines
• Live Vectors
• DNA-based vaccines
• Analyze and evaluate immune response against dengue virus in mice inoculated with plasmids that contains the domain III of the envelope protein
Experimental design

pcDNA3
5.4 kb

* There is an ATG upstream of the XbaI site.
Results

Cell transfection

pcDNA

D2
Results

Immunofluorescence  Den-2
Results

Immunizations

D1  D2  D2
D3  D4  pcDNA

[Diagram showing the process of immunizations with various stages and reactions depicted]
Results

ELISA

Mice immunized with Single pDIII constructs

**Den-1**

**Den-2**

**Den-3**

**Den-4**

Days post priming

- 100 µg DNA, i.m. route, dilution 1:100, n= 6-7 individuals
Results

ELISA
Mice immunized with tetravalent pDIII constructs

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<td>0.2</td>
<td>0.6</td>
<td>1.0</td>
<td>1.4</td>
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</tbody>
</table>

25 µg of each pDIII construct
50 µg of each pDIII construct
100 µg of each pDIII construct

i.m. route, dilution 1:100, n= 6-7 individuals
Results

Protection assays

[Diagram showing steps of protection assays with images and labels]

NO Protección

Protección
Den-2 Protection assays

Results

Neutralization titer by CPE

Survival (%) vs Days post challenge

pcDNA3
T50 (1:10)
T100 (1:10)
pDIII-D2 (1:10)
D III is expressed in transfected cells

Immunization with DIII plasmids induce specific antibodies against dengue virus

Antibody titer is dose-dependent

Immunization with DIII constructs induce neutralization antibodies

Tetravalent immunization also induce a dose-dependent antibody response

Antibodies induced with DIII constructs protects mice