IN VIVO PROTECTION AND IMMUNE RESPONSES INDUCED BY INTRAMUSCULAR AND INTRANASAL DELIVERY OF NON-LIVE SUBUNIT ROTAVIRUS VP6 VACCINE IN FORM OF TUBULAR STRUCTURES OR dI2/6-VLPs

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Development of non-live subunit RV – NoV combination vaccine

- Human RV VP6 protein + NoV GII-4 + GI-3 VLPs

→ Induction of broad heterologous immune responses to RV and NoV after parenteral delivery

Aim of the study

• Comparison of mucosal and parenteral immunization for induction of protective immunity against live RV challenge in mice

→ Does VP6 assembly have an effect on induction of protective immunity?
Determining of humoral and cell-mediated immune responses

Dose of trivalent vaccine: 10µg of VP6 (SGII)

1st Immunization IM or IN

Blood sample Fecal sample

2nd Immunization IM or IN

Whole blood Fecal sample Splenocytes

Termination

Wk 0 Wk 1 Wk 2 Wk 3 Wk 4 Wk 5

Female 7–9-week-old BALB/c mice (8-10 mice/group)
Induction of serum VP6-specific antibodies

Induction of serum IgA with IN immunization
Induction of fecal VP6-specific antibodies

→ Induction of similar levels of fecal IgA with IN immunizations
In vivo protection

Viral challenge orally with Murine RV strain EDIM\textsubscript{wt} (non SGI/SGII, G3P[16])

- Fecal samples collected daily
- Presence of RV antigen in fecal samples

→ Shedding curves for each animal
VP6-based vaccines protect mice from live EDIM challenge

Reduction in viral load by comparing mean areas under the curves
VP6-based vaccines protect mice from live EDIM challenge

>65% reduction in RV antigen shedding in feces of immunized mice

>50% reduction in virus shedding considered significant protection

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>Reduction in shedding</th>
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<tbody>
<tr>
<td>VP6 IM</td>
<td>66 ± 12%</td>
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<tr>
<td>dl2/6-VLP IM</td>
<td>81 ± 3%</td>
</tr>
<tr>
<td>VP6 IN</td>
<td>65 ± 18%</td>
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<tr>
<td>dl2/6-VLP IN</td>
<td>92 ± 3%</td>
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Days post-challenge:

Day 1  Day 2  Day 3  Day 4  Day 5  Day 6  Day 7  Day 8
Association of immune responses with protection

Increases in magnitudes of post-challenge serum IgA only
Conclusions

• Both IM and IN route induced protective VP6-specific immunity against live RV challenge

• No difference in protection levels between VP6 tubular structures or dl2/6-VLPs or delivery routes

→ Both VP6 tubules and dl2/6-VLPs are potential non-live RV candidate vaccines