Medical countermeasures against Rift Valley fever

Jonas Näslund

RVF research in Umeå

• Kinetics of RVFV infection in mice
Quantitative real-time PCR

- Detect and quantify the RVFV (genomes)
- Primers that target the S-segment

Kinetics of RVFV infection

RVF research in Umeå

• Kinetics of RVFV infection in mice
• RVFV vaccination in mice

Treatment and Vaccines

Anti viral
→ No specific for RVFV exist

Vaccines
→ Animals
  → Smithburn vaccine strain – attenuated through neuroadaption
  → Formalin inactivated RVFV
→ Humans (only for high risk personnel)
  → TSI-GSD-200
Vaccine Candidates

- Clone 13 - natural isolate
- MP12 - chemically induced attenuation
- R556 - reassortant of Clone 13 and MP12
- Genetically engineered RVFV
- Viral vectors – Adenovirus, Alphavirus, Newcastle disease virus
- DNA vaccine
- Virus-like particles

VLP vaccination against RVFV

- Intra peritoneal immunised mice (C57Bl/6).
- 2 different doses.
- Challenged with wild type RVFV.
RVF VLPs are immunogenic in mice

Vaccination with RVF VLPs induce virus neutralizing antibodies

VLP vaccination against RVFV

Outcome

Control 1x10⁵ VLPs/dose 1x10⁶ VLPs/dose

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Vaccinations with RVF VLPs suppress viral replication after challenge

VLP vaccination against RVFV
Näslund et al., Virology, 2009

RVF research in Umeå
• Kinetics of RVFV infection in mice
• RVFV vaccination in mice
• Field sampling

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Field sampling

- Nobuto filter strips
- Dried in blood samples with known amounts of virus
- Measure RNA load and infectivity

RVFV RNA was not detected
Blood stored on filter paper less than 48h may contain viable RVFV particles
RVF research platform in Umeå

- Animal model
- Mosquito transmission facilities
- BSL-3 lab
- RVFV with reporter genes (BSL 2)
- VLPs with marker dyes
- Small inhibitory compound screening platform
- Cell line library
- qRT-PCR, antibodies (serology)
- Collaboration with scientists in endemic countries

RVFV in Umeå

Magnus Evander, Umeå University
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Nina Lagerkvist, Umeå University and Karolinska Inst.
Maria Baudin, Umeå University

Collaboration
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Åke Lundkvist, Karolinska Institute
Osama Ahmed Hassan, Sudan

Thank you for your attention!!
Rift Valley Fever Virus
*Bunyaviridae, Phlebovirus*

- **S segment**
  - N protein
  - NSs protein

- **M segment**
  - Gn, Gc proteins
  - NSm protein

- **L segment**
  - L protein

**RNP** = Ribonucleoprotein
Vector competence for RVFV Viruses in Swedish mosquitoes

47 different blood-feeding mosquitoes in Sweden
Competent for RVFV transmission?
RVFV infection kinetics in mosquitoes

Virus surveillance in Swedish mosquitoes
### Advantages and disadvantages of animal models for RVF virus

<table>
<thead>
<tr>
<th>Model</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Mouse</td>
<td>Highly susceptible to RVF</td>
<td>No hemorrhagic fever</td>
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<td>Infected most usually die in 3–5 weeks, and are suitable for viral challenge studies</td>
<td>No severe disease</td>
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<td>Rodent</td>
<td>Slightly susceptible, non-pathological in nature</td>
<td>Suitable for studying host genes responsible for RVF viral propagation</td>
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<td>Vehicle pathogenic challenge to the animal</td>
<td>Slightly susceptible, non-pathological in nature</td>
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<td>Useful for the study of RVF replication</td>
<td>The use of different animal models can be affected by different factors such as RVF virus</td>
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<tr>
<td></td>
<td>Minireplicon constructs</td>
<td>Reproducibility differences in susceptibility</td>
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<tr>
<td>Hamster</td>
<td>Slightly susceptible to RVF</td>
<td>No hemorrhagic fever</td>
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<tr>
<td></td>
<td>Ideal animal for viral challenge studies by inoculation</td>
<td>No severe disease</td>
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<tr>
<td></td>
<td>Useful for studying viral transmission by inoculation</td>
<td>Limited research resources</td>
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<td>Octid</td>
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<td>Guinea pig</td>
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### RVF Virus–Like–Particles (VLP)

- **L**: Viral polymerase
- **M**: Viral glycoproteins Gc and Gn
- **N**: Nucleocapsid protein
- **Ren**: Minireplicon construct
- **FF**: Firefly luciferase

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