Oral Vaccines for Tick Borne Diseases: an example for Lyme Borreliosis

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IPM
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• Replacing sensitive Information
Background

• Fikrig et al work 1990-1997 : OspA

• Steere 1998 human OspA vaccine clinical trial (76% efficacy after 3 doses)

• In Feb 2002 Glaxo-SK pulled LYMErix from the market =>

• Feb 2002-2006: Repurpose the OspA vaccine for indirect applications to reduce exposure to Lyme disease risk : develop the Bb transmission blocking vaccine (Can we vaccinate mice to protect humans from Lyme?)
Bb Transmission Blocking Vaccines: How does it work?

The Enzootic Cycle Of The Lyme Disease Spirochete
The Hypothesis

- Egg mass
- Larvae
- Nymph
- Molting
- Adult

- Uninfected
- Infected with *B. burgdorferi*

- RTV
- RTV Immunized

**EM** *E. migrans*
Testing the hypothesis

1/9 = 11% mice infected/~90% protected

10% of the ticks contained Bb/90% ticks not infected after feeding on vaccinated mice

Oral vaccine that breaks the transmission cycle of the Lyme disease spirochete can be delivered via bait.

2007 In Lab: optimized OspA-RTV schedule of immuniz in wfm, RTV dose, testing RTV resistance under natural field conditions.

Reservoir targeted vaccine for lyme borreliosis induces a yearlong, neutralizing antibody response to OspA in white-footed mice.

Meirelles Richer L, Arosa M, Contente-Cuomo T, Ivanova L, Gomes-Solecki M.
Testing the Ec-OspA RTV in the Field (2007-2012)

- In 2007 in collaboration with Rick Ostfeld (IES, NY) and Dustin Brisson (UPenn) we started a field study to trap and orally immunize *P. leucopus* with our Ec-OspA RTV bait vaccine in 7 field sites in Millbrook, NY.

Spring and Summer:
- Deploy ~15,000 RTV/year
- No RTV: Ctrl1, Ctrl2, Ctrl3 2007-2011

- Blood  Anti-OspA Ab
- PCR for B. b. FlaB
Anti-OspA antibody distribution in plots that received > 3 yrs of treatment (NY1 & NY2)
Anti-OspA antibody distribution in plots that received 3 years of treatment (NY3 & NY4)

<table>
<thead>
<tr>
<th></th>
<th>Ctrl’09-11</th>
<th>NY3’09-11</th>
<th>NY4’09-11</th>
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</thead>
<tbody>
<tr>
<td>n</td>
<td>78</td>
<td>101</td>
<td>113</td>
</tr>
<tr>
<td>OD₄₅₀</td>
<td>0.220 (0.174)</td>
<td>0.337 (0.261)</td>
<td>0.387 (0.333)</td>
</tr>
<tr>
<td>pTukey</td>
<td></td>
<td>0.30</td>
<td>0.02</td>
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<tr>
<td>% Seroprevalence (SP)</td>
<td>27</td>
<td>48</td>
<td>41</td>
</tr>
<tr>
<td>% Protective SP (Nr OD1/Nr Pos.)</td>
<td>5</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>pχ²</td>
<td></td>
<td>0.39</td>
<td>&lt;0.01</td>
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Ec-OspA RTV field trial

Summary of Imnz Schedule

$\alpha$-OspA Seroprevalence data

We deployed >35 RTV/mouse

Mice were captured repeatedly w avrg of ~6 recaptures/mouse

51% mice consumed 5-60 units RTV; 49 % consumed 0-4

Prevalence of mice w protective levels of anti-OspA abs ($OD_{450}>1$) was higher in **NY1 (28%)**, **NY2 (33%)** and **NY4 (21%)**
Nymphal Infection Prevalence (NIP) 4 yrs (NY2) and 5 yrs (NY1) treatment

ny2 = 37 ticks/yr  
nctrl = 106 ticks/yr

ny1 = 36 ticks/yr  
nctrl = 95 ticks/yr
Nymphal Infection Prevalence (NIP) 
3 yrs treatment (NY3 & NY4)

\[ n_{NY3} = 35 \text{ ticks/yr} \]
\[ n_{Ctrl} = 96 \text{ ticks/yr} \]

\[ n_{NY4} = 54 \text{ ticks/yr} \]
\[ n_{Ctrl} = 96 \text{ ticks/yr} \]
Ec-OspA % Difference in NIP from baseline

\[ p = 4.7 \times 10^{-5} \]

(after 3 yrs application)
Ec-OspA RTV field trial Conclusions

• In the fields with higher prevalence of protective OspA ab (NY1, NY2 and NY4) we observed significant ($pX^2 < 0.01$) reductions in nymphal infection prevalence (NIP) in a cumulative, time-dependent manner;

• Reductions in NIP varied between 23% and 75% for fields treated for 3 and 5 years respectively.
Ec-OspA RTV Licensing

• **2012**: The technology was licensed to US Biologic, Inc.
Acknowledgements

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• Funding Federal Agencies:
• Thank you for your attention