Host Genetic Resistance Sustains HVT Protective Efficacy Comparable to CVI988/Rispens’ in Lines of Chickens Relatively Resistant to Marek’s Disease

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MD and Control of MD

- MD is caused by an α-herpesvirus known as Marek’s disease virus (MDV).

- MD has been controlled by wide use of MD vaccines in commercial chickens since 1970

Three Commonly Used Vaccines

- HVT has been used to prevent MD in US commercial chickens since 1970 (Witter, 1987. Avian Dis. 31:752).

- The HVT (FC126) + SB-1 bivalent vaccine has been licensed for use in US since 1983 (Witter, 1987. Avian Dis. 31:752).

- CVI988/Rispens was imported to US in 1990 (Witter et al., 1995. Avian Dis. 39:269).

- CVI988/Rispens remains as the gold standard of MD vaccines (Witter et al., 1992. In: 4th Intl Symp. on MD. pp315).
Factors Affecting Vaccine Efficacy

- Many factors affect vaccine efficacy, which include:
  - Vaccinal viruses (Serotypes 1, 2, and 3)
  - vaccine dosage
  - number of vaccinations
  - age at vaccination
  - the time interval between vaccination and infection
  - maternal antibody
  - host genetics

(Chang et al., 2010; Gavora and Spencer, 1979; Gimeno, 2008; Islam et al., 2007; Sharma and Graham, 1982; Witter, 1997; Witter and Lee, 1984; Wu et al., 2009).
**MHC and Vaccine Efficacy**

- **MHC** B haplotypes affect host immunoresponse to MD vaccines.
- Chickens with **B*2, B*13, B*15, or B*21** haplotype(s) respond to serotype 1 vaccines with a higher immunoresponse than chickens with other B haplotypes.
  

- Chickens with **B*5** respond to serotype 2 vaccine better than serotype 1 vaccine.
  
Non-MHC Genetic Background and Vaccine Efficacy

- vv+MDV challenge of HVT vaccinated chickens from two inbred progenitor lines (63 & 72) and a series of 19 recombinant congenic strains (RCS),

  - line 6₃: PI = 72%
  - line 7₂: PI = 0%
  - RCS: PI ranged 43% – 82%

(Chang et al., 2010. Poult. Sci. 89:2083-2091).

- Chicken line non-MHC genetic background by vaccine interaction may exist and affect vaccinal protective efficacy.

(Chang et al., 2012. World J. Vaccines, in press)
This Study

- To re-examine host genetics effect on vaccine protective efficacy.
  - Using commercially recommended dosages.
  - Using experimental lines of chickens (same B*2 haplotype).
  - Using commercial egg layers (While egg layers: MHC B*2, B*15, B*21; Brown egg layers: MHC unknown)
  - Vaccinated and challenged under controlled experimental conditions.
Vaccination and Infection

- **Vaccination**: Chickens from each line
  - unvaccinated (control)
  - vaccinated with a commercial dosage of HVT or CVI988/Rispens.

- **Infection**: Chickens of all trials were challenged on day 5 post hatch with 500 PFU of the vv+ 648A MDV intraabdominally.
Phenotype Observations

- **Chick mortality:** died between hatch day and 7 DPI and were removed from the data set prior to analyses.

- **MD:** Chickens died after 8 DPI or developed visceral gross tumors and/or nerve enlargement(s).

- **Non-MD:** Chickens euthanized at the end of trials without any gross tumor.
# MD% and PI under commercial PFU dosages

## Experimental chickens:

<table>
<thead>
<tr>
<th>Line</th>
<th>Vaccine</th>
<th>MD%</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line 6(_3) (B*2)</td>
<td>Rispens 1</td>
<td>33 (9^b)</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Rispens 2</td>
<td>27 (8^b)</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>HVT 1</td>
<td>17 (7^b)</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>HVT 2</td>
<td>14 (7^b)</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>Unvac.</td>
<td>97 (3^a)</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Line</th>
<th>Vaccine</th>
<th>MD%</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Line 7(_2) (B*2)</td>
<td>Rispens 1</td>
<td>73 (8^b)</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Rispens 2</td>
<td>31 (9^c)</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>HVT 1</td>
<td>100 (0^a)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>HVT 2</td>
<td>90 (6^{ab})</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Unvac</td>
<td>100 (0^a)</td>
<td>0</td>
</tr>
</tbody>
</table>

## Commercial Chickens:

<table>
<thead>
<tr>
<th>Line</th>
<th>Vaccine</th>
<th>MD%</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>White egg layers (B<em>2, B</em>15, B*21)</td>
<td>Rispens 1</td>
<td>54 (8^b)</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>Rispens 2</td>
<td>24 (7^c)</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>HVT 1</td>
<td>60 (8^b)</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>HVT 2</td>
<td>46 (8^{bc})</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Unvac</td>
<td>100 (0^a)</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Line</th>
<th>Vaccine</th>
<th>MD%</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown egg layers (MHC B*?)</td>
<td>Rispens 1</td>
<td>49 (8^b)</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Rispens 2</td>
<td>8 (4^c)</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>HVT 1</td>
<td>42 (8^b)</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>HVT 2</td>
<td>53 (8^b)</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>Unvac</td>
<td>97 (3^a)</td>
<td>0</td>
</tr>
</tbody>
</table>
Line 63:

Tests Between Groups

<table>
<thead>
<tr>
<th>Test</th>
<th>ChiSquare</th>
<th>DF</th>
<th>Prob&gt;ChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log-Rank</td>
<td>93.6392</td>
<td>4</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>Wilcoxon</td>
<td>80.6152</td>
<td>4</td>
<td>&lt;.0001*</td>
</tr>
</tbody>
</table>

Unvaccinated

Line 72:

Tests Between Groups

<table>
<thead>
<tr>
<th>Test</th>
<th>ChiSquare</th>
<th>DF</th>
<th>Prob&gt;ChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log-Rank</td>
<td>154.5119</td>
<td>4</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>Wilcoxon</td>
<td>130.5551</td>
<td>4</td>
<td>&lt;.0001*</td>
</tr>
</tbody>
</table>

Unvaccinated

HVT 1
HVT 2
CVI988/Rispens 1
CVI988/Rispens 2
CVI988/Rispens 2
CVI988/Rispens 1
HVT 1
HVT 2
CVI988/Rispens 1
CVI988/Rispens 2
White egg layers:

Brown egg layers:
Both HVT 1 and HVT 2 conveyed comparable protective efficacy as did the CVI988/Rispens 1 and 2, in chickens from the highly inbred experimental line 63, based on MD%, PI and survival days.
Similar results were observed in chickens from the two commercial egg layer flocks except:

- CVI988/Rispens 2 protected White egg layers and Brown egg layers significantly better than CVI988/Rispens 1 and the HVTs.
Summary (Continued)

Similar results were observed in chickens from the two commercial egg layer flocks except:

- CVI988/Rispens 2 protected White egg layers and Brown egg layers significantly better than CVI988/Rispens 1 and the HVTs.
Discussions

- HVT protective efficacy was strikingly different between the lines 6_3 and 7_2 chickens.

- The good protective efficacy of HVT in MD resistant lines (6_3, white egg layers, and brown egg layers) was highly likely attributable to the host genetic resistance to MD.
Discussions (Continued)

- HVT is relatively less expensive
- HVT should be used to protect chickens like line 63, but not something like line 72.
- The observed superior protection of CVI988/Rispens 2 - due to higher titers of vaccinal viruses in a single (commercial) dosage and host MHC B haplotypes?
Thank you for your attention!